2002 Annual Meeting
October 20–23, 2002

Hyatt Regency Albuquerque
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Encore Presentations: Abstracts marked with an “E” are Encore Presentations. Encore Presentations undergo the same peer review process as do Original Presentations, but may have been presented elsewhere or published in abstract form only prior to the 2002 Annual Meeting. For Encore Presentations, the abstract title, authors, and original citation (if provided) are published in Pharmacotherapy. The full abstract will be published in the meeting program book.

ORIGINAL RESEARCH

These papers describe original research in therapeutics, pharmacokinetics, pharmacodynamics, pharmacoeconomics, pharmacoepidemiology, and pharmacogenomics.

Admission

1. Development of a new taxonomy to classify clinical pharmacy recommendations. Angela B. Hoth, Pharm.D., Barry L. Carter, Pharm.D., FCCP, BCPS, Cynthia K. Schulte, Pharm.D. candidate, Joseph Niss, M.D., Ronald I. Shorr, M.D., Gary E. Rosenthal, M.D., Peter J. Kabolii, M.D.; Veterans Administration Medical Center; University of Iowa, Iowa City, IA.

PURPOSE: Development and reliability testing of a taxonomy to classify clinical pharmacy recommendations.

METHODS: The taxonomy categorized recommendations according to the problem type that prompted an intervention and the response required to implement a recommendation. Six problem categories (pharmaceutical issues, risk to patient, medication/indication issues, efficacy issues, cost, record update) were subdivided into 18 unique categories to identify a specific therapeutic problem addressed in a recommendation. Twelve response categories required to enact the recommendation were used. Each recommendation required a single problem and response category. Seven reviewers (3 Pharm.D.s, 4 M.D.s) categorized recommendations from a random sample of patients evaluated by a clinical pharmacist between 7/1/01 and 5/31/02. Inter-rater reliability was determined for each reviewer pair and the group using the K statistic. Time to categorize recommendations was also recorded.

RESULTS: Reviewers categorized 146 recommendations for 21 patients (mean 7; range 1-17). Inter-rater agreement for the 18 therapeutic problem subcategories was good (overall K = 0.42, range 0.29-0.66). Greatest agreement occurred between Pharm.D. reviewers (K = 0.60) followed by Pharm.D.-M.D. pairs (K = 0.51) and M.D. pairs (K = 0.42). Reliability improved at the level of the six therapeutic categories (overall K = 0.54, median 0.62, range 0.29-0.71). Inter-rater agreement for the 12 response categories was high (overall K = 0.72, range 0.67-0.81). Completion of categorization averaged 4.6 minutes per patient (range 1-11).

CONCLUSION: This taxonomy provides a reliable method to evaluate clinical pharmacy recommendations based on the therapeutic problem and specific action required. This tool may be used clinically and in research to document clinical pharmacy activities in a standardized format.

2. Influence of the Internet on ACCP membership. Susan Miller, Pharm.D., Julie Wright, Pharm.D., BCPS, University of Missouri at Kansas City, Kansas City, MO.

PURPOSE: The 2003 ACCP membership goal is to increase its members by 4%. ACCP must reach a diverse pharmacists population who may be naïve to its organizational mission and goals. Due to extensive Internet use by pharmacists, ACCP’s Web page accessibility was evaluated.

METHODS: Using 8 distinct terms included in ACCPs membership statement, we searched the top 10 Internet search engines, rated by audience reach, to measure the frequency of encountering the ACCP site within the first 50 results. From the first 20 results of each search, the number of Web sites that link to pharmacy organizations, and subsequently link to ACCP, was determined. Additionally ACCP link accessibility was determined among other pharmacy related Web sites including: academic institutions, credentialing and licensing boards, national organizations, and popular pharmacy journals.

RESULTS: The incidence of ACCP Web page appearance in the first 50 results was greatest with the search terms “clinical pharmacy” (100%) and “pharmacy advocacy” (90%). Twenty four percent of searches resulted in links to professional pharmacy organizations. Seventeen percent included an ACCP link. The proportion of Web sites with links to ACCP were: national organizations 100%, journals 55%, student organizations 36%, pharmacies 24%, and credentialing/licensing boards 7%. Links consistently worked, but few (8%) included a description of ACCP.

CONCLUSIONS: Enhanced Internet exposure could increase ACCP membership. Enhanced exposure should be pursued through requests to post ACCP links on all pharmacy school and state boards of pharmacy Web sites, promotion of Web site link reciprocity among professional organizations, and ACCP Web site optimization to maximize priority listings from search engines.


PURPOSE: To evaluate the specificity and sensitivity of drug-drug interaction screening programs commonly available on hand-held personal data assistants (PDAs).

METHODS: Twenty-one drug pairs were selected from patient medication profiles. Selected drugs pairs represented potentially significant (could harm patients) interactions, non-interacting drug pairs, and pairs exhibiting desirable pharmacodynamic interactions. Five PDA-based programs (Ifacts, Mosbyix, DrDrugs, PepID PDC, Epocrates) were obtained from their providers. Each program was examined for the presence or absence of an interaction for each drug pair. Both drugs in each pair were individually searched to determine search engine proficiency. Interaction results were compared to a standard drug interaction reference (Hansten and Horn). The sensitivity (proportion of true positives) and specificity (proportion of true negatives) was calculated for each program.

RESULTS: Of the 21 pairs of drugs, 15 represented potentially significant interactions and six were either non-interacting pairs or of minimal clinical importance. The mean (range) sensitivity of the PDA programs was 0.63 (0.4-0.87); the mean (range) specificity was 0.63 (0.4-0.83). For comparison, the Physicians Desk Reference (PDR 2002 edition) had a sensitivity and specificity for these same interactions of 0.33 and 0.50, respectively. Of the 21 interactions, the PDA programs agreed with the reference standard on an average of 13 (62%) of the interactions (range 9-15).

CONCLUSIONS: Using PDA-based drug interaction references for patient management should be approached with caution. While these programs are generally superior to the PDR as a source of drug interaction information, users should be aware of the limitations of these programs as surrogates for standard drug interaction references and good clinical judgment.

4. Safety of concomitant treatment with moxifloxacin and selective serotonin reuptake inhibitors. Shurjeel H. Choudhri, M.D., Daniel Haverstock, M.S., Frank Kruesnann, Ph.D.; Bayer Corporation, West Haven, CT; Bayer AG, Wuppertal, Germany.

PURPOSE: To compare the safety profile of IV and PO moxifloxacin (MXF) with that of comparator antibiotics (COMP) in patients receiving concomitant therapy with selective serotonin reuptake inhibitors (SSRIs).

METHODS: Data were pooled from 27 global, randomized, controlled MXF trials. WHO-DD codes were used to identify all patients who had received concomitant therapy with an SSRI and MXF or COMP. Comparators used most frequently in PO studies were cefuroxime, clarithromycin, cephalaxin and amoxicillin while alatrofloxacin/trovafloxacin, levofloxacin and the combination of amoxicillin/clavulanate and clarithromycin were the comparators in the IV studies. Study population was subdivided into 4 groups: MXF, MXF + SSRI, COMP, COMP + SSRI. CPM criteria were used to identify QTc outliers.

RESULTS: Of the 12,788 patients included in the analysis, 450 took at an SSRI concomitantly with antibiotic therapy (238 on MXF, 212 on COMP). Paired ECGs were available for 100 (55 MXF, 45 COMP) of these patients. The mean QTc change was +4 and +5 msec in the PO and IV MXF +SSRI groups respectively compared to a mean change of +6 and +3 in the PO and IV MXF groups. No QTc outliers were identified in either the PO or IV MXF ± SSRI patients. The incidence of cardiovascular adverse events was similar between the 4 groups.

CONCLUSIONS: The mean QTc interval change was similar for patients who were treated with IV or PO MXF alone or MXF + SSRI. The cardiovascular safety profile of moxifloxacin was not significantly affected by concomitant therapy with SSRIs.

PURPOSE: The Naranjo scale has not been evaluated in critically ill patients. Hence, reliability and validity of the Naranjo criteria for assessing ADEs in critically ill patients were studied.

METHODS: Abnormal laboratory values were reviewed to identify ADEs during a 3-month period in a 38-bed surgical ICU. ADEs were classified into possible, probable and definite categories by a pharmacist. In cases of uncertainty, a panel of three experts was convened. Four raters independently reviewed the same ADEs using the Naranjo criteria to test inter-rater (between raters) reliability; reported as a weighted k statistic. The raters used the Naranjo criteria again 3-4 weeks later and a weighted k statistic was calculated for test-retest reliability. Naranjo criteria were compared to expert opinion for criterion validity for each rater; reported as a weighted statistic and Spearman rank (r_s) coefficient.

RESULTS: k statistic between raters ranged from 0.140-0.479. Weighted k ranged from 0.5402-0.9371 for test-retest reliability; k statistic for the criterion validity ranged from 0.009 to 0.106 and was not statistically significant (p>0.05). Correlations ranged from r_s = 0.385 to 0.545 and all values were statistically significant (p<0.05).

CONCLUSION: k statistic of less than 0.5 for all inter-rater reliabilities indicates the Naranjo criteria is fair, at best, in the acute care setting. Inter-rater reliability for was good to excellent for all raters. Naranjo criteria had a moderate to substantial correlation with expert opinion. Overall, it appears the Naranjo criteria needs modification for use in the ICU to improve inter-rater reliability and criterion validity.


PURPOSE: To develop a tool that can be used to make accurate predictions of drug-drug interactions including those that have not been identified in drug labeling or standard drug interaction reference texts.

METHODS: A database containing over 11,000 drug interaction articles was searched for references containing information on specific drug metabolic pathways (e.g., cytochrome P450 and P-glycoprotein). In addition, a database containing data on metabolic pathways inhibited or induced (including P-glycoprotein) were identified. Only data derived from human in vivo data was included. Just over 5500 articles met the search criteria and data from over 250 drugs was noted. After discarding unused or uncommon drugs, about 220 drugs were included.

RESULTS: For each drug, the enzyme(s) responsible for its metabolism is noted, as is the drugs capability to inhibit or induce a P450 enzyme(s) or P-glycoprotein. To determine if two drugs are likely to interact, one simply compares the CYP enzyme responsible for one drug's metabolism with the enzyme(s) inhibited or induced by the second drug. For example, if a drug that is a substrate for CYP3A4 is administered with an inhibitor of CYP3A4, one can assume a reduction in the clearance of the CYP3A4 substrate will occur. The table contains 109 drugs that are known to be substrates of CYP3A4 and 25 drugs that inhibit CYP3A4. There are 2725 possible interactions between the CYP3A4 substrates and inhibitors. Only a minority of these interactions have been studied on.

CONCLUSIONS: Metabolic drug interactions can be easily predicted and when combined with assessment of patient risk factors, potential patient harm can be prevented.


INTRODUCTION: Clarithromycin, a macrolide antibiotic, is frequently prescribed for respiratory tract infections and Helicobacter pylori induced duodenal ulcer. The common side-effects of clarithromycin are mild and transient with <1% of abnormal liver function tests reported. In rare cases, idiosyncratic hepatotoxicity is rare but severe, and clinicians should be aware of this potential adverse effect. Timely referral to a transplant center may be warranted. In addition, the potential cross hypersensitivity between clarithromycin and tacrolium (a macrolide immunosuppressant), he was placed on cyclosporine based immunosuppression. The patient is now 24 months status post liver transplantation with normal liver function.

CONCLUSION: We believe this patient's hepatic failure was due to an idiosyncratic reaction from clarithromycin and that symptoms were delayed as a result of concomitant therapy with corticosteroids. Macrolide-induced idiosyncratic hepatotoxicity is rare but severe, and clinicians should be aware of this potential adverse effect. Timely referral to a transplant center may be warranted. In addition, the potential cross hypersensitivity between clarithromycin and tacrolium (a macrolide immunosuppressant) should be avoided.


PURPOSE: To assess provider perceptions of the pharmacists’ role, including increasing provider awareness of drug interactions, as part of the era of physician order entry (POE) with automated drug alerts (ADAs).

METHODS: A cross-sectional survey conducted from October-December 2000 of 263 eligible providers at a large, multi-facility VA healthcare system utilizing POE with embedded ADAs. Questions assessed knowledge of 21 possible drug and disease-state interactions, perceptions about the importance of pharmacists= tasks and experiences with ADAs (18 items).

RESULTS: Response rate was 64% (168/263). Providers recognized a median of 49% (range 11%-64%) of 10 drug interactions and 55% (range 24%-67%) of 7 disease-state interactions. Recognition of severe/life-threatening interactions was 53%. Internists and younger providers recognized more interactions than non-medical specialists (p<0.001) as did those with more clinic days (p<0.021). There was general agreement about the value of pharmacist tasks: processing/filling prescriptions 98%, warning about drug interactions 93%, patient counseling 90%, multidisciplinary team participation 83%, ADE surveillance 82%, optimizing/managing therapy 81%. Although providers are receptive to receiving ADAs, feel ADAs improve confidence in recognizing interactions (98%), and improve safety (55%); only 4% would change therapy based on an ADA compared to 54% who felt more inclined to change medications based on pharmacist recommendations. ADAs included non-relevant alerts (55%) and system slowdowns (44%).

CONCLUSIONS: Providers need methods to improve their ability to recognize drug interactions. While clinicians favor ADA systems as one means to this end, they agree that more relevant information about interactions is needed. ADAs do not substitute for pharmacy services, which remain valuable resources to providers and may significantly contribute to increasing provider recognition of interactions.

11. Recurring chemotherapy-associated alopecia areata: case report and review of the literature. Susannah E. Mott, Pharm.D., Christopher Fausel, Pharm.D., BCPS, BCOP; University of Tennessee Health Science Center, Memphis, TN; Indiana University Hospital, Indianapolis, IN.

OBJECTIVE: To report a case of recurring partial alopecia areata resulting from chemotherapy.

CASE SUMMARY: A 52-year-old woman with stage IIIC ovarian cancer and stage I uterine cancer presents with recurring alopecia areata of her eyebrows, eyelashes, arms, legs, and pubic hair beginning five months post-cessation of paclitaxel and carboplatin chemotherapy. Alopecia areata universalis occurred from chemotherapy.

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autoimmune reaction resulting in attack of hair follicles, as a result of chemical alteration from chemotherapy.

CONCLUSION: Oncology health-care practitioners need to evaluate unique, clinical presentations of alopecia for underlying pathology. We report an interesting case of cyclic alopecia area of a cancer survivor potentially related to autoimmune changes instigated by chemotherapy.

12. Evaluation of the interaction between warfarin and ginkgo biloba extract. Chia-Feng Lai, M.S., Chia-Chung Chang, B.S., Chia-Hung Fu, B.S., Chi-Ming Chen, Ph.D., Hsiang-Yin Chen, M.S., Pharm.D.; Taipei Medical University; Taipei Municipal Wan-Fang Hospital, Taipei, Taiwan.

PURPOSE: Six bleeding cases have been reported with the use of ginkgo biloba extract (EGB 761), and one was linked to concurrent use of warfarin. The objective of the study was to evaluate the effect of EGB 761, a standardized ginkgo biloba extract, on warfarin and coagulation function.

METHODS: To recognize the influence of EGB 761 on pharmacokinetics and pharmacodynamics of warfarin, changes in warfarin plasma concentration and prothrombin time (PT) after coadministration with EGB 761 was studied in a Sprague Dawley rat model. Clinical cases with concurrent use of two drugs were also retrospectively reviewed to evaluate the relationship between EGB 761 and international normalized ratio (INR). Changes of coagulation parameters, including platelet counts, INR, bleeding time, clotting time, was determined in twelve healthy volunteers taking EGB 761 120 mg once daily for 28 days.

RESULTS: A significant decrease in the area under plasma concentration-time curves (AUC) from 22.54 ± 2.67 to 17.27 ± 1.64 µg/mL, was detected with coadministration of EGB 761 under a multiple dosing design. Similarly, maximal PT and area under the PT versus time curve were significantly reduced with EGB 761 treatment group. (p<0.01) There was no significant change in INR after adding EGB 761 in 21 clinical cases. (p=0.551)

CONCLUSIONS: No clinically significant change in coagulation parameters was observed when finishing the regimen.

13. Incidence of infusion-related reactions with infliximab: effect of pretreatment. Anthony T. Gerlach, Pharm.D., Sondra J. Sierawski, R.Ph., Helen Hollis, R.N.; Ohio State University Medical Center, Columbus, OH.

INTRODUCTION: Infliximab is a monoclonal antibody that causes infusion related reactions in up to 17% of patients. Volunteer reporting of adverse drug reactions demonstrated that infliximab was associated with a high incidence of infusion related reactions at our institution. The purpose of this study was to prospectively monitor the use of infliximab for safety.

METHODS: Data was prospectively collected for any patient who received infliximab from August 2001 to February 2002. Data collected included demographics, indication, dosing acetaminophen (APAP) and diphenhydramine pretreatment, and adverse effects. Infusion related ADRs were defined as headache, fever, chills, respiratory symptoms (tachypnea and dyspnea), skin reactions, visual disturbances, nausea, hypertension, and hypoxemia. Statistical analysis was performed by Fisher's exact test for nominal data and independent t test for continuous data.

RESULTS: Forty-one patients who received 62 doses of infliximab were evaluated. Pretreatment with (APAP) and diphenhydramine was given in 58% (36/62) of the cases, and the overall incidence of infusion related reactions was 18% (11/62).

Pretreatment N=36 No Pretreatment N=26 P value
Average Age 52 (±14.6) 36.5 (±16.7) NS
% Female 83 65 NS
Indication Infusion-related reaction 4 16 <0.05
Crohn's Disease 4 9 NS
Rheumatoid Arthritis 32 32 NS
Average Dose 266 mg (±59) 322 mg (±134) NS
ADRs 2 9 <0.05
N=Non-significant

CONCLUSIONS: Patients with rheumatoid arthritis are more likely to be pretreated for infusion related ADRs, and pretreatment with APAP and diphenhydramine is associated with statistically significant fewer infusion related ADRs. Targets for education and improvement have been identified.


PURPOSE: Existing grapefruit juice (GFJ)-drug interaction studies have been conducted using double-strength, frozen concentrates of white grapefruits. The purpose of this study is to 1) characterize the types and pattern of GFJ consumption by the public; 2) assess the frequency of the occurrence of GFJ-drug interactions.

METHODS: A random sample of 225 people in the Chicago area was interviewed. Data collection includes demographics, medical history, current medications, types, amount and frequency of grapefruit products consumed, and subjects' knowledge in GFJ-drug interactions.

RESULTS: Of the 225 participants, 171 (76%) reported drinking GFJ, while 133 (59%) reported eating grapefruit at least once in their lifetime. GFJ consumption was most popular in the second, fifth, and sixth decade of life. Red or ruby-pink GFJ was consumed by the majority (70%) and less than 1% consumed concentrated grapefruits. Most GFJ consumers (53%) had less than 12 contraindications yearly. One hundred twenty-two respondents (54%) were taking prescription drugs and consuming GFJ concomitantly. Of these 122 respondents, 31 (25%) were taking known interacting medications. The most common chronic disease in these respondents was cardiovascular diseases (51%), followed by hypercholesterolemia (32%). Forty-eight percent of them were unaware of GFJ-drug interactions.

CONCLUSIONS: The overall incidence of GFJ-drug interaction is 25% among people taking prescription medications. However, the design of the existing GFJ-drug interaction studies does not reflect the pattern of GFJ consumption by the public. Since red grapefruit contains less inhibitory components of CYP3A4, the magnitude of this interaction might have been exaggerated by the published studies.

15E. Venlafaxine-induced ecchymosis. Maha Sadak, B.S., Pharm.D., Henry Cohen, B.S., M.S., Pharm.D., Nancy Talavera, M.D.; Kingsbrook Jewish Medical Center; Long Island University, Brooklyn, NY.


Analgesia


PURPOSE: Patients with terminal illness are often referred to hospices, where nurses treat pain and other symptoms. This project evaluates the attitudes and knowledge of pain pharmacotherapy in hospice nurses, and derives data on actual pain assessment and management.

METHODS: Questions were administered to assess attitudes and knowledge regarding pain in a group of hospice nurses (n=41). The content was derived from current standards and has been validated by recognized experts. Charts were reviewed (n=25) to evaluate pain assessment and management.

RESULTS: Nurses generally had six or more years experience in hospice (81%). Most (91%) felt comfortable/very comfortable with pain assessment, but many (73%) were uncomfortable/very uncomfortable with equianalgesic conversions. Weaknesses identified by questionnaire included therapeutics, adverse effects, dosing/dilution, and addiction. Strengths included physiology, perception, assessment, and interdisciplinary cooperation. On admission 96% of charts revealed a pain assessment, only 72% using a validated tool. Drug-related problems were common (96% of charts), and included excessive acetaminophen use, inappropriate prophylaxis and add-on, potential adverse drug effect, and therapeutic duplications. Others included incorrect dosing, inappropriate selection, and lack of prophylactic bowel regimens. Overall, 80% of charts revealed inappropriate assessment and management of pain.

CONCLUSION: These results indicate a need for hospice nurses to pursue an improved understanding of the assessment and management of pain. Issues related to pain assessment and pharmacotherapy were common, confirming the need for improved knowledge about pain. This data provides a platform for clinically trained pharmacists to explore potential roles as hospice consultants, ranging from staff development to patient management.

Cardiology

17. Questioning a class effect: does angiotensin-converting enzyme inhibitor tissue penetration influence markers of myocardial infarction risk? James P. Tiskouris, Pharm.D., Joseph A. Suarez, M.D., Martin Ziska, B.S., Gary E. Meyerrose, M.D.; Texas Tech University Health Sciences Center, Lubbock, TX.

There is a common belief in a class effect amongst ACE inhibitors (ACEI). This is unsubstantiated for acute myocardial infarction (AMI). Because vascular tissue is a primary source of the endogenous fibrinolytic, tissue plasminogen activator (t-PA) and its inhibitor plasminogen activator inhibitor-1 (PAI-1), and ACE inhibition in vascular tissue favorably influences the fibrinolytic system, we hypothesized that a high-tissue penetrating ACEI would provide more favorable reduction in PAI-1 and increase in t-PA after AMI compared to a low-tissue penetrating ACEI.

METHODS: In a randomized open-label trial, patients received a high-tissue penetrating ACEI (Enalapril) or low-tissue penetrator (Quinapril) for 14 days following AMI. PAI-1 and t-PA antigen (ng/ml) were measured at baseline, then 12 hours, and Day 1, Day 2, Day 3, Day 7, Day 14 after drug initiation.

RESULTS: There was no difference in baseline PAI-1 or t-PA antigen with...
18. Clinical experience with ultra low-dose amiodarone (100 mg/day).
Maria G. Tanzi, Pharm.D., Marieke D. Schoen, Pharm.D., BCPS, Jerry L. Bauman, Pharm.D., BCPS, FACC, University of Illinois in Chicago, Chicago, IL.

PURPOSE: In an attempt to reduce toxicity while maintaining effectiveness, many centers routinely decrease patients (pts) to 100 mg/day of amiodarone (amio) despite the lack of evidence for this dosage. Therefore, we report our experience with ultra low-dose amio (100 mg/day) compared to standard low-dose (200 mg/day) in the prevention of supraventricular and ventricular arrhythmias.

METHODS: We screened our database of 204 patients enrolled in a collaboratively managed amiodarone clinic for those being treated with amio 100 mg/day at 6 months. A control group was established by randomly selecting patients on amio 200 mg/day in a 2:1 ratio.

RESULTS: Comparisons were made between 25 pts who fulfilled the criteria for inclusion (100 mg/day) and 50 controls (200 mg/day). There were no significant differences in age, sex, and indications for therapy between the 2 groups. At 21.2 ± 17.5 months of therapy, recurrence of the pts tachycardia occurred in 7/25 (28%) on 100 mg/day compared to 10/50 (20%) on 200 mg/day for 18.4 ± 14.3 months of therapy (p=NS). Drug discontinuation was similar between the 100 mg/day 5/25 (20%) and 200 mg/day 11/50 (22%) groups (p=NS).

CONCLUSION: In patients being successfully maintained on 200 mg/day amio, the dosage can be reduced to 100 mg/day without a significant loss in effectiveness.

Brian G. Katona, Pharm.D., David L. Larimer, R.Ph., Jay C. Horwood, M.D., M.S., Gary Peters, M.D.; AstraZenea, Wilmington, DE.

PURPOSE: Critically analyze and update the effectiveness of oral anticoagulant (OA) therapy in patients with acute coronary syndromes (ACS).

METHODS: MEDLINE, EMBASE, and Current Contents were searched between 1998 and 2002. All randomized, controlled trials were identified and placed in the categories of low (INR < 2.0), moderate (INR 2-3), or high intensity anticoagulation (INR >3). With or without concomitant aspirin use. We then updated the meta-analysis of Anand and Yusuf (JAMA 1999, 282: 2056-67), using identical statistical methods, comparing the effectiveness of OA therapy on the composite endpoint of death, myocardial infarction, and stroke versus major bleeding.

RESULTS: 5 major randomized clinical trials, which enrolled a total of 13,704 patients, were added to the 12,396 patients of Anand, et al.

<table>
<thead>
<tr>
<th>Level of Intensity</th>
<th>Events OA</th>
<th>Events Control</th>
<th>P value</th>
<th>Odds Ratio</th>
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<tbody>
<tr>
<td>Moderate and High vs. 2180868 ± 12.3%</td>
<td>474/3797 (12.5%)</td>
<td>&lt;0.0001</td>
<td>0.73 (0.63-0.85)</td>
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<tr>
<td>Low + ASA vs. ASA</td>
<td>1237667 (18.3%)</td>
<td>1267667 (18.7%)</td>
<td>0.51</td>
<td>0.97 (0.88-1.1)</td>
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(P=NS)

CONCLUSIONS: With or without concomitant aspirin, moderate or high dose OA, but not low dose OA prevents death, recurrent myocardial infarction, and stroke worse than aspirin alone in patients with ACS. All OA-containing regimens confer a higher major bleeding risk than ASA alone.

20. Cost-savings associated with a decreased need for potassium supplementation in heart failure patients on spironolactone.
Amber L. Belles, Pharm.D., Jerry L. Bauman, Pharm.D., FACC, Mary Ross Southworth, Pharm.D., Robert J. DiDomenico, Pharm.D., Stephanie H. Dunlap, M.D., Lucy A. Fashighbauer, B.S., Larisa M. Humma, Pharm.D., BCPS; University of Illinois at Chicago, Chicago, IL.

PURPOSE: Spironolactone has been shown to improve heart failure outcomes. We sought to determine whether spironolactone use in heart failure was associated with a cost savings compared to a decreased need for potassium supplementation.

METHODS: We reviewed clinic records for patients with severe heart failure receiving standard therapy including an ACE inhibitor and compared patient costs of K ± spironolactone (1) between patients on and not on spironolactone (2) before and after spironolactone initiation specifically for those taking spironolactone.

RESULTS: Of 94 patients identified, 44 were on chronic spironolactone therapy (mean ± SD dose: 27 ± 10 mg/day). Eighteen (41%) spironolactone-treated patients and 31 (62%) non-treated patients required K to maintain serum K within normal limits (≤5.0) median (range) K dose was 40 (20-180) mg/d (with and 40 (16-80) mg/day without spironolactone. Median (range) monthly cost of K ± spironolactone was $10.70 (5.37-238.35) with and $50.60 (5.99-101.16) without spironolactone (p<0.01). Among 28 spironolactone-treated patients with available data, 18 (64%) required K before and 15 (54%) required K after spironolactone initiation. Median (range) monthly cost of K ± spironolactone was $50.60 (12.65-101.16) before and $33.20 (3.57-238.35) after spironolactone initiation (p<0.05). Further analysis revealed possible racial differences in K requirements with spironolactone; median (range) K dose was 20 (14.25-112) mg/d in Caucasians and 40 (20-180) mg/d in African Americans (p=0.06).

CONCLUSIONS: Heart failure patients treated with spironolactone may derive savings associated with reduced K requirements. Our data suggest that there may be racial differences in K requirements with spironolactone and thus, cost savings may also differ by race.

21. Sustained impact of a pharmacist-based lipid optimization program for chronic heart disease patients.
Robert J. Straka, Pharm.D., BCPS, Kelly Z. Hadsall, Pharm.D., Ali Toumadj, Pharm.D., Susan Cooper, R.Ph., M.D., James Smith, M.D., University of Minnesota, Minneapolis, MN; HealthPartners, Bloomington, MN.

BACKGROUND: Intensive programs to optimize the management of hypercholesterolemia have demonstrated effectiveness in achieving target LDL-C (<100mg/dL) in chronic heart disease (CHD) patients. We previously reported results of a 28-week, multi-clinic, controlled study comparing a pharmacist-based model (intervention group) to usual care (control group). The ACTION Trial (Pharmacootherapy 2000;20:1234) documented a 35.6mg/dL (27%) reduction in the average LDL-C in the intervention group (n=550) compared to a 6.7mg/dL (4.6%) drop in the control arm (n=331). (p<0.01) from mean (SD) baseline values of 135mg/dL (±28) and 135 (±26) respectively (p<0.01). The need to follow-up intervention group participants has resource related implications.

PURPOSE: To evaluate the need for follow-up of patients post completion of an intensive program aimed at optimizing management of hypercholesterolemia. METHODS: Electronic records were used to retrieve the last available fasting lipid panels up to 17.5 months (out to 7/30/2001) following the interventions of the ACTION Trial. Unpaired t test and Chi-squared analysis were used for between group comparisons for continuous and dichotomous data respectively.

RESULTS: Of 94 patients identified, 44 were on chronic spironolactone therapy (mean ± SD dose: 27 ± 10 mg/day). Eighteen (41%) spironolactone-treated patients and 31 (62%) non-treated patients required K to maintain serum K within normal limits (≤5.0) median (range) K dose was 40 (20-180) mg/d (with and 40 (16-80) mg/day without spironolactone. Median (range) monthly cost of K ± spironolactone was $10.70 (5.37-238.35) with and $50.60 (5.99-101.16) without spironolactone (p<0.01). Among 28 spironolactone-treated patients with available data, 18 (64%) required K before and 15 (54%) required K after spironolactone initiation. Median (range) monthly cost of K ± spironolactone was $50.60 (12.65-101.16) before and $33.20 (3.57-238.35) after spironolactone initiation (p<0.05). Further analysis revealed possible racial differences in K requirements with spironolactone; median (range) K dose was 20 (14.25-112) mg/d in Caucasians and 40 (20-180) mg/d in African Americans (p=0.06).

CONCLUSIONS: Heart failure patients treated with spironolactone may derive savings associated with reduced K requirements. Our data suggest that there may be racial differences in K requirements with spironolactone and thus, cost savings may also differ by race.
physical exam, serum chemistry panel and an ECG. Patients receiving any QT-prolonging drugs or had congenital long-QT-syndrome were excluded. The QTc interval was calculated using Bazett’s formula. Students’ paired t test was used to compare the T1 and T2 mean QTc intervals.

RESULTS: The mean QTc at T1 was 421.6 ± 75 msec (range 266-694), and at T2 was 439 ± 63.36 msec (range 338-862, p=0.026). Patients who received the appropriate levofloxacin dose based on manufacturers guidelines (40%) had a T1 and T2 mean QTc of 415 ± 37 msec, and 433 ± 44 msec, respectively. Patients receiving double the levofloxacin dose (60%), had a T1 and T2 mean QTc of 424 ± 67 msec, and 443 ± 74 msec, respectively. Nine patients had a T1 and T2 mean QTc moderately increase from < 450 msec (393 ± 52) to ≥ 450 msec (500 ± 22). When available, serum electrolytes were normal, calcium (n=47), potassium (n=49), and magnesium (n=19). None of our patients developed signs or symptoms of dysrhythmia.

CONCLUSION: Intravenous levofloxacin significantly prolonged the QTc interval by 18 ± 57 msec in our patients.

23. The effects of renal failure and hypoalbuminemia on the protein binding of cerivastatin in hemodialysis patients. Rita Neilan, Pharm.D., Henry Cohen, M.S., Pharm.D., Robert V. DiGregorio, Pharm.D., Sonia Borra, M.D., Joseph P. Reilly, Pharm.D., Roopali Sharma, Pharm.D.; Kingsbrook Jewish Medical Center; Long Island University, Brooklyn, NY.

PURPOSE: Cerivastatin is approximately 99-99.5% protein bound primarily to albumin, therefore, under normal conditions, the fraction unbound (fu) is <1%. The objective of this prospective, open-label study is to evaluate the effects of renal failure and hypoalbuminemia on the protein binding of single dose cerivastatin.

METHODS: Eighty eligible adult hypoalbuminemic patients receiving hemodialysis were randomized to receive a single dose of cerivastatin 0.2 mg (n=9) or 0.4 mg (n=9) two hours before hemodialysis. Cerivastatin total and unbound concentrations pre- and post-hemodialysis were determined by HPLC.

RESULTS: The mean albumin level and Clcr for both groups was 3.16 ± 0.40 g/dL, and 11.45 ± 5.30 mL/min, respectively. The mean pre-hemodialysis and post-hemodialysis BUN for both groups was 59.3 mg/dL and 16.7 mg/dL, respectively. The mean fu cerivastatin pre-hemodialysis was 2.12% (range 1.17-2.95%). The mean fu cerivastatin post-hemodialysis was 1.62% (range 1.05-2.81%), remaining above normal. The correlation obtained with fu cerivastatin utilizing Pearsons’ correlation coefficient was greatest (fair to good) with albumin, and least (little to fair) with Clcr. However, the correlations were not statistically significant (p>0.05), plausibly due to the small sample size. No adverse events occurred.

CONCLUSION: In 18 hemodialysis patients, the cerivastatin fu was found to be 2-3 times the normal range in all samples assayed. Since most statins are highly protein bound, an increased risk of adverse effects in renal failure patients with hypoalbuminemia is plausible. However, this was a single dose study; a multiple dose study is necessary to corroborate our findings.

24. Impact of an intravenous and oral amiodarone regimen in the post-open heart surgery Atrial Fibrillation Suppression Trial II. C. Michael White, Pharm.D., James S. Kalus, Pharm.D., Michael F. Caron, Pharm.D., Nicholas A. Wiegert, B.S., University of Wisconsin, Madison, WI.

PURPOSE: In the Atrial Fibrillation Suppression Trial (AFIST I), we found adding prophylactic oral amiodarone to patients receiving beta-blockers was associated with a reduced incidence of atrial fibrillation (AF) in low-risk cardiac surgery patients. The objective of this multiple dose study is to corroborate our findings in 18 hemodialysis patients on cerivastatin, to determine if this effect is dose dependent.

METHODS: Atrial fibrillation suppression trial II, a multiple dose study is necessary to corroborate our findings. Since most statins are highly protein bound, an increased risk of adverse effects in renal failure patients with hypoalbuminemia is plausible. However, this was a single dose study; a multiple dose study is necessary to corroborate our findings.

RESULTS: The mean albumin level and Clcr for both groups was 3.16 ± 0.40 g/dL, and 11.45 ± 5.30 mL/min, respectively. The mean pre-hemodialysis and post-hemodialysis BUN for both groups was 59.3 mg/dL and 16.7 mg/dL, respectively. The mean fu cerivastatin pre-hemodialysis was 2.12% (range 1.17-2.95%). The mean fu cerivastatin post-hemodialysis was 1.62% (range 1.05-2.81%), remaining above normal. The correlation obtained with fu cerivastatin utilizing Pearsons’ correlation coefficient was greatest (fair to good) with albumin, and least (little to fair) with Clcr. However, the correlations were not statistically significant (p>0.05), plausibly due to the small sample size. No adverse events occurred.

CONCLUSION: In 18 hemodialysis patients, the cerivastatin fu was found to be 2-3 times the normal range in all samples assayed. Since most statins are highly protein bound, an increased risk of adverse effects in renal failure patients with hypoalbuminemia is plausible. However, this was a single dose study; a multiple dose study is necessary to corroborate our findings.

25. What is the effect of amiodarone on P-wave variables in cardiac surgery patients? James S. Kalus, Pharm.D., Michael F. Caron, Pharm.D., Xinchun Liu, B.S., Heidi L. Rose, R.N., Jeffrey Kluger, M.D., C. Michael White, Pharm.D.; Hartford Hospital, Hartford, CT; University of Connecticut, Storrs, CT.

PURPOSE: The P-wave represents atrial depolarization on the 12-lead electrocardiogram. P-wave duration measurements in patients with paroxysmal atrial fibrillation are longer than measurements in healthy controls, suggesting delayed atrial depolarization in patients with paroxysmal atrial fibrillation. Atrial fibrillation most commonly occurs after cardiac surgery on postoperative days 2 and 3 and prophylactic amiodarone administered postoperatively may decrease the occurrence of this common surgical complication. We evaluated the effects of amiodarone on P-wave duration in order to define a mechanism for its effect on the development of postoperative atrial fibrillation.

METHODS: Patients (n=160, 65.8 ± 7.6 years, 76.6% male, 21.3% valve surgery) were randomized to amiodarone or placebo for 5 days (1 gram intravenously on the day of surgery and 1200 mg orally on postoperative days 1-4). 12-lead electrocardiograms were taken on the day of surgery through postoperative day 4 and P-waves were measured by a blinded investigator.

RESULTS: On postoperative day 2, average and minimum P-wave duration among patients receiving amiodarone were reduced by 10.3% (p=0.009) and 24.3% (p=0.0004), respectively, compared to the placebo group. On postoperative day 3, there was a 22% decrease in minimum P-wave duration (p=0.0007).

CONCLUSION: Amiodarone shortened P-wave duration on the postoperative days when atrial fibrillation is most likely to occur. These results suggest that delayed atrial depolarization in post-cardiac surgery patients is attenuated by amiodarone. This effect may explain the role of amiodarone in reducing the occurrence of postoperative atrial fibrillation.

26. Regional isoproterenol increases defibrillation energy requirements. Jason Sims, Pharm.D., Kell L. Schoff, B.S., Jennifer M. Loeb, B.S., Nicholas A. Wiegert, B.S., University of Wisconsin, Madison, WI.

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27. Evaluation of perioperative β-blocker use for the prevention of cardiovascular complications in elective, noncardiac surgery. Bradi L. Frei, Pharm.D., Chris R. Frei, Pharm.D., Robert L. Talbert, Pharm.D., BCPS; University of Texas at Austin, Austin, TX; University of Texas Health Science Center, San Antonio, TX.

PURPOSE: To evaluate perioperative β-blocker use in patients at risk for post-surgery cardiovascular complications undergoing elective, noncardiac surgery.

METHODS: We conducted a retrospective, cohort study, using medical record data, of adult patients undergoing major noncardiac surgery with general anesthesia at a university teaching hospital during a 6-month period in 1999. Patients with two or more cardiac risk factors or with documented coronary artery disease were classified as high risk and considered eligible for perioperative treatment with a β-blocker unless contraindications to its use were present. Cardiac risk factors were ≥ 65 years, hypertension, smoking, total cholesterol ≥ 240 mg/dL, and diabetes mellitus. Death from all causes was determined for all 96 patients. β-blocker use was determined for each patient 48 hours before surgery and on the day of surgery. The primary outcome measure was a comparison of the incidence of cardiovascular complications in patients receiving perioperative β-blockers (21%) compared to those not receiving β-blockers (43%) at discharge.

CONCLUSIONS: β-blockers are substantially undertreated at our institution despite guidelines recommending their use in high-risk patients. β-blockers were more likely to be used in patients with CAD, which could account for the increased mortality rate among those patients receiving β-blockers.

28. Ibutilide is less proarrhythmogenic when instilled into the pericardial fluid space. Michael R. Ujhelyi, Pharm.D., Kelly Z. Hadsell, Pharm.D.; Medtronic, Minneapolis, MN.

BACKGROUND: Pericardial delivery (PD) of antiarrhythmic drugs yields pericardial fluid concentrations that are 1000X greater than intravenous delivery (IV). This dosing advantage may be offset by increased proarrhythmia, although this may not be true for water soluble antiarrhythmics (i.e. ibutilide) because vascular uptake could limit ventricular tissue diffusion (Circ 2000;102:I16721) and increase ventricular proarrhythmia.

METHODS: We assessed ibutilide’s potential to induce sustained polymorphic ventricular tachycardia (PVT) in 9 chronic (6 weeks) AV blocked dogs that developed LVP hypotrophy (heartweight bodyweight=0.93±0.13). Dogs were randomized to 3 sequential PD doses (1.0, 3.8 and 15 ug/kg, N=4) or 2 sequential IV doses (7.5 and 7.5 ug/kg, N=6) based upon clinical dose of 15 ug/kg. IB doses were infused for 5 minutes, followed 45 minutes later by endocardial right and left refractory period (ERP) testing, and programmed electrical stimulation (PES). This protocol was repeated with each sequential dose.
RESULTS: Incidence of spontaneous PVT, PES-induced PVT with short-long-short stimuli, and death due to incessant PVT. Spontaneous PVT occurred at the lowest IV dose (7.5 µg/kg) vs. the highest PD dose (15 µg/kg). Time to spontaneous PVT was also significantly shorter with IV vs. PD ibutilide (7.1 ± 2.2 vs. 42 ± 12 minutes, p<0.05). Similarly, PES-induced PVT and death occurred at lower IV versus PD doses. All IV doses caused electrical instability (PVCs and PVT) such that ERP could not be determined. For PD, the 1.9 and 3.8 µg/kg had no effect on ERP, while the 15 µg/kg PD dose prolonged IV ERP by 30-50% at cycle lengths 750-1500 (p<0.05) ms but did not affect IV ERP indicating ERP dispersion.

CONCLUSIONS: Pericardial ibutilide is less proarrhythmic than IV delivery even at higher doses. This suggests that pericardial ibutilide delivery has a larger ventricular proarrhythmia safety margin than intravenous ibutilide delivery.


BACKGROUND: The Medtronic Jewel AF (model 7250) is an ICD with pacing and defibrillation therapies to terminate atrial tachyarrhythmias (AT) and ventricular fibrillation (VF). Jewel AF may limit the use antiarrhythmic drug (AAD) usage because the device has several means to treat and/or prevent AT. The Jewel AF multicenter 'AF only' (no VT/VF) study was examined to determine AAD (Vanhagen Williams class I and III) usage patterns after device implant and determine the role of hybrid device plus drug therapy for AT management.

METHODS: Enrollment required ≥2 symptomatic AT events 3 months pre-implant and refractory or intolerant of ≥1 Class I, II, III or IV AAD. Of the 144 patients, 132 had ≥6 months follow up. This cohort was followed for 12 ± 6 months and AAD was tabulated at implant, 3, 6, 12 and 18-months. AAD use was at investigator's discretion.

RESULTS: From the time of device implant, 103 of 132 (77%) patients used an AAD at least once during follow up, while 23 never received an AAD. At implant, 80 (60%) patients were on AAD therapy AAD at implant consisted of amiodarone (54%) or sotalol (28%) treatment, which remained constant at 6, 12 and 18-month follow-ups. During follow up, 62 patients had no changes to AAD therapy (stable), while 70 patients had unstable AAD therapy where 23 patients started, 21 stopped, and 26 switched AAD therapy. Interestingly, the majority (96%) of the 70 patients who had an AAD change did so within the first 6 months after implant. From the 6-month follow up, nearly 40% of patients remained stable off AAD therapy. Moreover, patients that were classified as stable AAD therapy had significantly fewer device treated AT/AF episodes/week than patients who were classified as unstable AAD (0.12 range 0.6-2 vs. 0.56 range 0.21-7, p<0.05). However, this difference only occurred during the 0-3 month follow up period after implant. After this time, AT/AF episodes decrease in the unstable group equalizing the stable AAD group (0.08 range 0.0-1.6 vs. 0.0-0.5, p=0.52).

CONCLUSIONS: AAD therapy is unstable during the first 0-3months after Jewel AF implant. Unstable AAD therapy correlates with greater number of device treated AT/AF episodes, suggesting a hybrid therapy approach. After 6-months, approximately 40% of Jewel AF patients are managed without AAD therapy and this correlates with a lower AT/AF frequency.


PURPOSE: We recently showed, in a randomized trial, that amiodarone plus pacing significantly decreased postoperative atrial fibrillation after open-heart surgery, compared to amiodarone, pacing and placebo. The purpose of this sub-study was to compare index hospital admission and 30 days cost between the three groups.

METHODS: A piggyback cost analysis of the clinical trial was conducted from a hospital perspective. The study timeframe was 30 days from day of surgery. Hospital charges and readmissions were obtained from hospital databases. Charges were converted to costs using cost-to-charge ratios. Costs were compared using analysis of variance. RESULTS: Index hospital costs were >$20,000 in 35%, 33%, 34% and 29% of the placebo, amiodarone, pacing and amiodarone plus pacing patients, respectively (p=0.05). Costs (mean ± SD) for the index admission were $27,026 ± 30,226 in the placebo, $22,725 ± 17,661 in the amiodarone, $33,868 ± 60,309 in the pacing and $18,697 ± 8,174 in the amiodarone plus biatrial pacing groups (p=0.27). There was a trend towards a difference in the number of hospital readmissions (placebo:0.04 ± 0.20, amiodarone: 0.08 ± 0.27, pacing: 0.00 ± 0.00, amiodarone plus pacing 0.16 ± 0.44; p=0.08) although readmission costs were similar (placebo: $452 ± 2,799; amiodarone: $662 ± 2,184; pacing: $0.00 ± 0.00; amiodarone plus pacing: $1,153 ± 3,165; p=0.49). Cumulative costs (index + readmissions) at 30 days were $27,478 ± 30,191, $23,557 ± 18,146, $33,688 ± 60,309 and $20,284 ± 11,551 among placebo, amiodarone, pacing and amiodarone plus pacing patients, respectively (p=0.38).

CONCLUSIONS: Since amiodarone plus pacing is more efficacious and has similar costs to alternative therapies, this novel strategy is a cost-effective option in post-operative atrial fibrillation prevention. Larger studies should be undertaken, powered to detect cost differences between strategies to lower atrial fibrillation after open-heart surgery.

31. Cost-effectiveness of GPIIb/IIIa inhibitors in a national database of acute myocardial infarction patients. Patrick L. McColm, Pharm.D., David A. Foster, Ph.D., Jeffrey S. Riemsnyder, M.D., Eli Lilly & Co., Indianapolis, IN; Solucient, Inc., Ann Arbor, MI.

PURPOSE: To determine cost-effectiveness (C/E) of adjunctive GPIIb/IIIa inhibitor use during percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI) patients.

METHODS: Data (1/1/2000-6/30/2001) from Solucient’s (Evaston, IL) national all-payer database were analyzed for any AMI patient undergoing PCI and receiving a GPIIb/IIIa inhibitor compared to non-GPIIb/IIIa recipients. Risk adjustment for mortality was performed by logistic regression using published methods to account for differences in patient and hospital characteristics using all pertinent variables contained in the data set (age, sex, diagnoses, procedures, clinical grouping, length of stay hospital size, census division, teaching status, urban or rural setting). Incremental costs were determined by least squares regression to fit general linear models. C/E was estimated using published methods. Mortality and cost results refer to the in-hospital period.

RESULTS: Data were from 32,529 patients in 99 hospitals. C/E was calculated for abciximab since only it demonstrated a significant difference in the effectiveness measure (survival). The C/E was <$15,000 per life year gained.


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32E. Weight loss does not alter sympathetically mediated vascular tone in normotensive obese humans. Alexee V. Agapitov, M.D., Marcelo L. Correa, M.D., John M. Dopp, Pharm.D., Christine A. Sinkey, R.N., Virend K. Somers, M.D., Bradley G. Phillips, Pharm.D., University of Iowa, Iowa City, IA; Mayo Clinic, Rochester, MN.

PURPOSE: Obesity is associated with sympathoactivation, as assessed by microneurographic muscle sympathetic nerve activity (MSNA). Weight loss has been shown to decrease MSNA. However, it is unclear whether MSNA reflects sympathetic vascular tone.

METHODS: Forearm vascular resistance (FVR) responses to intrabrachial phenylephrine (120 µg/min; sufficient to block bloodconstriction to nonpinephrine) were used to evaluate the sympathetic contribution to basal vascular tone in 19 obese normotensive subjects (4 males; 39 ± 2 years) and 14 age and gender-matched lean subjects (3 males; 39 ± 2 years). Nitroprusside (10 µg/minute) was used to evaluate vascular smooth muscle dilator responsiveness. Measurements were repeated in all obese subjects after 12 weeks of hypocaloric diet and orlistat treatment and in 8 lean subjects after 6 months of orlistat treatment. C/E was calculated for abciximab since only it demonstrated a significant survival benefit vs. the non-GPIIb/IIIa group and it possessed a favored C/E ratio.

CONCLUSION: These recent data provide additional insight into contemporary use of GPIIb/IIIa inhibitors in AMI patients undergoing PCI in actual clinical practice. Moreover, the present study demonstrated a significant survival benefit vs. the non-GPIIb/IIIa group and it possessed a favorable C/E ratio.
34. Evaluating two approaches for dyslipidemia management: pharmacist-managed lipid clinic and physician-treated patients. Janet L. Ritter, Pharm.D., BCPS; Our Lady of the Lakes Medical Center, Baton Rouge, LA; University of Illinois at Chicago, Chicago, IL; Cardinal Health Provider

PURPOSE: The purpose of this study is to assess the effectiveness of a pharmacist-managed Lipid Clinic (LC) and a primary care physician (PCP) managed patients in attaining the NCEP - ATP III guidelines.

METHODS: The study was conducted in a private outpatient clinic in a group medical practice. All LC patients (age 18 or older) managed by the clinical pharmacist and a stratified random sample of physician treated patients, were enrolled in this retrospective chart-review study. The sample frame included patients who attended one or more office visits within the LC or their PCP (internist or family practitioner) between June 1, 2001 and December 31, 2001.

RESULTS: One hundred fifty-two LC and 45 PCP patients were enrolled in this study. LDL elevation from baseline was higher in the LC group, with 72% and 26% of patients reaching the goal of 200 mg/dL or less in the LC and PCP groups respectively. In the LC group, the percentage of patients reaching LDL goals was 21% and 42% for patients with LDL > 160 mg/dL and 75% of patients with LDL > 190 mg/dL. In the PCP group, the percentage of patients reaching LDL goals was 8% and 32% for patients with LDL > 160 mg/dL and 75% of patients with LDL > 190 mg/dL.

CONCLUSIONS: LCD patients 22 ± 8* 93 ± 9 3.3 ± 0.2 -80 ± 2 -58 ± 4 22 ± 8*

Cmax (µg/L) 2.1 ± 0.6 1.7 ± 0.2 -16%

Clrenal (mL/min) 74 ± 10 81 ± 22 +10%

CONCLUSIONS: Elevated MSNA in normotensive obese subjects, and decreases in MSNA with weight loss, do not translate into alterations in sympathetically mediated vascular tone.

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36. Bleeding risk in patients on low-molecular weight heparin for anticoagulation in atrial fibrillation. Roberta Tankanow, M.S., Teri Peterson, M.S.; VAMC, Boise, ID; Tamarind, O., Virginia; Idaho State University, Pocatello, ID.

PURPOSE: To determine the relationship of renal function and low-molecular weight heparin (LMWH) dosing to bleeding and thrombosis in a group of patients anticoagulated for atrial fibrillation (AF).

METHODS: A total of 230 patients receiving LMWH for AF during a 6 month period were retrospectively reviewed and evaluated based on estimated creatinine clearance (CrCl) and dosing (units/kg/day). Renal dysfunction was additionally defined as a calculated estimate of creatinine clearance ≤ 30 ml/min, or a serum creatinine (SCr) ≥ 2 mg/dL. Thrombosis and bleeding were characterized according to standard definitions.

RESULTS: Any bleeding occurred in 25.3% of patients with renal dysfunction (n=49) and 12.3% of patients with adequate renal function, and dosing was 133.8 ± 53.3 and 137.4 ± 59 units/kg/d, respectively. However, mean CrCl was 41 ± 23.5 and 44.5 ± 24.2 ml/min (p=NS) in patients with bleeding (n=48) and those without, and dosing was 136.4 ± 53.7 and 136.3 ± 58 units/kg/day (p=NS), respectively. CrCl and dosing were also similar in patients with and without major bleeding (n=46), but when analysis was restricted to patients with renal dysfunction, the mean dose was actually less in patients with major bleeding (96.5 ± 13.1 vs. 137.3 ± 54.4 units/kg/d; p<0.001). In all patients, dosing, but not CrCl predicted thrombosis (p=0.17). The mean dose in patients with thrombosis was 109.5 ± 40.8 vs. 136.4 ± 57.9 in the other patients (p=0.13).

CONCLUSIONS: Renal dysfunction is a risk factor for bleeding independent of LMWH dose, and lower doses may not protect against thrombosis.


Hawthorn is currently being evaluated for the treatment of heart failure. Beneficial effects may be due to the flavonoid components of hawthorn. However, these components may also affect p-glycoprotein function and cause interactions with drugs that are p-glycoprotein substrates such as digoxin.

PURPOSE: To determine the effect of hawthorn on digoxin pharmacokinetic parameters.

METHODS: Randomized, crossover trial in 8 healthy volunteers evaluating digoxin 0.25 mg alone (D) and digoxin 0.25 mg twice with hawthorn 450 mg twice daily (D + H) for three weeks. Seventy-two hour pharmacokinetic studies were performed for both treatment groups.

RESULTS: Summary of the pharmacokinetic parameters are shown below (mean ± standard deviation).

<table>
<thead>
<tr>
<th>Variable</th>
<th>D</th>
<th>D/H</th>
<th>%Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUCC_H (µg/hr/L)</td>
<td>23 ±4</td>
<td>22 ±4</td>
<td>-6%</td>
</tr>
<tr>
<td>AUCC (µg/L)</td>
<td>83 ±28</td>
<td>73 ±20</td>
<td>-11%</td>
</tr>
<tr>
<td>Cmax (µg/L)</td>
<td>21.6 ±1</td>
<td>18 ±0.2</td>
<td>-16%</td>
</tr>
<tr>
<td>Cmax (µg/L)</td>
<td>0.84 ±0.2</td>
<td>0.65 ±0.2</td>
<td>-22%</td>
</tr>
<tr>
<td>Tmax (hours)</td>
<td>1.4 ±0.7</td>
<td>1.1 ±0.1</td>
<td>-17%</td>
</tr>
<tr>
<td>T1/2a (hours)</td>
<td>1.4 ±0.5</td>
<td>1.5 ±0.5</td>
<td>+9%</td>
</tr>
<tr>
<td>CL_H (ml/min)</td>
<td>59 ±10</td>
<td>50 ±10</td>
<td>-14%</td>
</tr>
<tr>
<td>CL_H (ml/min)</td>
<td>82 ±6</td>
<td>82 ±2</td>
<td>-10%</td>
</tr>
</tbody>
</table>

Liver serum digoxin concentrations were slightly lower in the D/H group. However, no statistical differences were observed between the two treatment groups (p>0.05).
CONCLUSIONS: Hawthorn did not significantly alter the pharmacokinetic parameters for digoxin following three weeks of concomitant therapy. These results also suggest that hawthorn does not significantly alter p-glycoprotein function.


PURPOSE: Previous research has shown grape juice (PGJ) to have a demonstrable effect on inhibiting platelet aggregation, leading some to question whether PGJ may be given in lieu of aspirin, the gold standard antiplatelet agent. However, a direct comparison of PGJ to aspirin has not yet been performed. This study assessed the hypothesis that the antiplatelet effects of PGJ and aspirin are similar.

METHODS: We studied 13 healthy volunteers (mean ± SD age = 25.5 ± 5.9 years) in a randomized, prospective, crossover study. Each subject received 4 treatments (separately) for 4 weeks: PGJ 10 mL/kg/day, PGJ 5 mL/kg/day, white grape juice (WGJ) 10 mL/kg/day, and aspirin 325 mg/day. There was a 4-week washout period in-between treatments. Platelet aggregation was measured at the beginning and end of each treatment period using whole blood impedance aggregometry with collagen (1.0 μg/mL) and arachidonic acid (0.5 μM) as pro-aggregates.

RESULTS: Platelet aggregation in response to collagen was inhibited an average of ± SD of 71 ± 22% with aspirin, -5 ± 24% with PGJ 10 mL/kg/day, -16 ± 16% with PGJ 5 mL/kg/day, and -4 ± 18% with WGJ (p<0.0001 for all versus aspirin). Arachidonic acid-induced platelet aggregation was inhibited 100 ± 0% with aspirin, 0 ± 33% with PGJ 10 mL/kg/day, 0 ± 13% with PGJ 5 mL/kg/day, and 15 ± 31% with WGJ (p<0.0001 for all versus aspirin).

CONCLUSIONS: The antiplatelet effects of PGJ are inferior to those of aspirin. This study contradicts previous research demonstrating PGJ's antiplatelet effect with PGJ. Patients and clinicians should therefore not think of aspirin and PGJ as interchangeable inhibitors of platelet aggregation.

41. Congestive heart failure therapies within managed care. James Jackson, Pharm.D., Eileen Farrelly, M.P.H., David Ziska, Pharm.D., Feride Frech, R.Ph., M.H., Samantha Hilde; Applied Health Outcomes; Novartis Pharmaceuticals Corporation, Tampa, FL.

Presented at the 6th Annual Scientific Meeting of the Heart Failure Society of America, Boston, MA, September 23, 2002.

42. Polyamine as the mediator of TNF-α induced vascular endothelial cell injury. Shewan M. Aziz, R.P.H., Ph.D.; BCPOR Michael Tolson, M.D.; Bennett Yu, M.D., Jay Schwab, R.P.H., BCNP; James A. Roczek, M.D.; Eastern Maine Medical Center, Bangor, ME; University of Kentucky, Lexington, KY; Henry Ford Hospital, Detroit, MI; Tulane Medical Center, New Orleans, LA.

PURPOSE: Endothelial cell injury/dysfunction is believed to be one of the first events in the development of atherosclerosis. Although ample evidence demonstrates the role of tumor necrosis factor-α (TNF-α) in this process, the specific intracellular signaling mechanism, which mediates cellular injury, has yet to be explored. This study was conducted to determine whether polyamines play an essential role in cell growth, inflammation, and gene expression, and also comprise an obligatory link between the initiating stimuli, TNF-α, and changes in endothelial cells responses and metabolism.

METHODS: Cellular polyamine levels as well as polyamine biosynthesis and uptake were measured in cultured porcine pulmonary artery endothelial cells exposed to increasing levels of TNF-α (250, 500 or 1000 U/mL) for 24 hours. In addition, oxidative stress is involved in a number of TNF-α-mediated effects, cellular oxidation, measured as 2,7-dichlorofluorescein (DCF) fluorescence, and polyamine metabolism were measured in cells treated with TNF-α and/or dimethylthiourea (DMTU), a scavenger of reactive oxygen species.

RESULTS: TNF-α treated produced a significant increase in the cellular levels of putrescine and spermidine but not spermine. An increase in intracellular levels of putrescine and spermidine was correlated with their enhanced uptake into cultured endothelial cells exposed to TNF-α. Treatment with TNF-α also increased endothelial cell activity and mRNA steady state levels of ornithine decarboxylase (ODC), a regulatory enzyme in polyamine biosynthesis. Although DMTU increased ODC activity and mRNA level, it attenuated both TNF-α-mediated oxidative stress and TNF-α-induced disturbances in polyamine metabolism.

CONCLUSIONS: The data indicates that polyamines may mediate TNF-α-induced cellular responses and that both upregulation of polyamine biosynthesis and transport are involved in this process. In addition, it appears that TNF-α-mediated oxidative stress may be responsible for disturbances in cellular polyamine metabolism.


PURPOSE: The chronopharmacokinetics of a graded release, once-daily diltiazem HCl formulation (GRD) were evaluated to identify variations in morning (7AM or B럼) vs. evening (10PM) dosing.

METHODS: Single-dose and multiple-dose (once-daily for 7 days), open-label, randomized, two-way crossover studies of GRD 360 mg were completed in 48 healthy, fasting volunteers. Meals and beverages were standardized, and subjects remained seated upright. 2 to 4 hours post dose. Serial sample collections were sampled via direct venipuncture up to 48 hours post dose and analyzed for diltiazem and its two major metabolites by HPLC. The primary parameters used to assess the data were AUCint, AUCinf, AUC 6 AM-12 Noon, C max, and T max. Statistical comparisons using ANOVA were evaluated after logarithmic transformation of dose-dependent parameters.

RESULTS: In the single-dose study, GRD administered in the evening exhibited 17% greater bioavailability compared to morning administration (AUCint – 2401.98 [1141.03, 4205.82] ng•ml•hr vs. AUCint – 2063.36 [1114.08, 3712.64] ng•ml•hr; p<0.05). Diltiazem steady-state concentrations were 15% higher following the seven-day administration of GRD 360 mg in the evening compared to administration in the morning (Cave=17.13 [50.79 ng/mL] vs. Cave=45.77 [60.39 ng/mL]; p=0.0561). The evening schedule also provided more than two-fold higher plasma diltiazem levels in the critical morning hours, when both blood pressure and the incidence of cardiovascular events is the highest (AUC 6 AM-12 Noon=1369.67 [430.65 PM vs. 607.30 [260.69ng•hour/mL AM dosing p=0.0001]).

CONCLUSIONS: Administration of GRD in the evening results in greater bioavailability and substantially higher plasma levels of diltiazem between 6 AM and 12 Noon, when blood pressure is highest in most individuals.

44. Pharmacokinetics of eplerenone coadministered with other medications. Dwan S. Tolbert, Ph.D., Susan E. Reid, M.Ed., Barbara Roniker, M.D.; Takeda Pharmaceuticals, Lincolnshire, IL; Pharmacia Corporation, Skokie, IL.

PURPOSE: Hypertensive patients often have additional medical conditions requiring pharmacological intervention. These studies evaluated the pharmacokinetics and safety of the coadministration of eplerenone, the selective aldosterone blocker, with various drug classes.

METHODS: Randomized, placebo-controlled studies in 275 healthy adults and 16 diabetic patients given multiple doses of eplerenone (100 mg QD) coadministered with standard doses of a concomitant medication. Coadministered drugs: cytochrome P450 3A4 (CYP 3A4) substrates (cyclosporine, simvastatin, warfarin, midazolam, Ortho-Novum 1/35®), CYP 3A4 inhibitors (saquinavir, indinavir, 500 mg), CYP 3A4 inducers (ketokonazole, fluvoxamine, verapamil, erythromycin); highly protein-bound drugs (glyburide, warfarin); or high renally cleared drugs (digoxin).

RESULTS: Coadministered CYP 3A4 inhibitors increased eplerenone exposure (AUCint and C max p<0.05), clinically significantly (ketokonazole), or statistically significantly (fluvoxamine, saquinavir, verapamil, erythromycin). Clinically insignificant decreases in eplerenone plasma concentrations were observed with coadministration of CYP 3A4 substrates and inducers. No clinically significant changes were observed when eplerenone was coadministered with highly protein-bound drugs or high renally cleared drugs. Coadministration of all compounds with eplerenone was well tolerated.

CONCLUSIONS: When eplerenone is coadministered with CYP 3A4 inhibitors, eplerenone should be given at the lowest recommended dose (50 mg), except when coadministered with ketokonazole, when the eplerenone dose should not exceed 25 mg. Eplerenone coadministration with CYP 3A4 substrates, inducers, highly protein-bound drugs, or highly renally cleared drugs does not clinically significantly alter the pharmacokinetics of eplerenone or the concomitant medication and does not require dosage adjustment.

45. Safety, tolerability, and pharmacokinetics of eplerenone, a selective aldosterone blocker. Dwan S. Tolbert, Ph.D., Susan E. Reid, M.Ed., Barbara Roniker, M.D.; Takeda Pharmaceuticals, Lincolnshire, IL; Pharmacia Corporation, Skokie, IL.

PURPOSE: The selective aldosterone blocker (SAB) eplerenone reduces blood pressure in patients with mild to moderate hypertension. These studies evaluated the pharmacokinetics, safety, and tolerability of eplerenone in healthy subjects.

METHODS: Data from 7 separate trials (N=81) were used to evaluate eplerenone's pharmacokinetics following single and multiple doses in non-Japanese (n=97) and Japanese subjects (n=60); absorption, distribution, metabolism, and elimination of eplerenone were determined following a single 100 mg oral dose, (C1) eplerenone (n=6). The effects of high fat, food, and grapefruit juice on the pharmacokinetics of eplerenone were evaluated following single 100 mg oral doses (n=16).

RESULTS: Mean eplerenone AUC and C max values increased with increasing eplerenone doses, but were less than dose-proportional. No statistically significant differences in AUC (90% CI 0.79-1.32), C max (90% CI 0.78-1.05), CL/F, Tmax, or T1/2 were found between Japanese and non-Japanese subjects following single and multiple doses of eplerenone. There was rapid oral absorption of radioactivity following eplerenone. Eplerenone was extensively metabolized with <10% of
the drug eliminated as unchanged eplerenone. Co-administration of a high fat meal, antacid or grapefruit juice did not have a significant effect on eplerenone’s rate or extent of absorption.

CONCLUSIONS: This analysis establishes the pharmacokinetic properties of eplerenone and demonstrates that there are no pharmacokinetic differences between Japanese and non-Japanese subjects following single and multiple oral doses of eplerenone. Eplerenone’s pharmacokinetics were not influenced by the presence of a high fat meal, antacid, or grapefruit juice. Eplerenone was well tolerated across all groups.

46. Pharmacokinetics of eplerenone in special populations. Dwin S. Tolbert, Ph.D., Susan E. Reid, M.Ed., Barbara Roniker, M.D.; Takeda Pharmaceuticals, Lincolnshire, IL; Pharmacia Corporation, Skokie, IL.

PURPOSE: The selective aldosterone blocker (SAB) eplerenone reduces blood pressure in patients with mild to moderate hypertension. The effects of age, gender, race, and renal or hepatic impairment on eplerenone’s pharmacokinetic parameters were evaluated.

METHODS: These studies involved 218 pediatric and adult subjects. Eplerenone dose ranges: 12.5 mg QD (2-5 years), 50 mg QD (6-11 years), 100 mg QD (12-16 years); 100 mg QD in adults (18-65 years) and adults with renal impairment. Eplerenone 400 mg QD was administered to adults with hepatic impairment. Single and multiple dose pharmacokinetics were assessed.

RESULTS: There were no statistically or clinically significant differences in AUC0-24, Cmax, or Tmax between adult and pediatric patients. No significant differences were observed in eplerenone pharmacokinetics for either race or gender. Statistically, but clinically insignificant differences in AUC0-24 were found between adult patients with hepatic impairment and healthy adults (95% CI 1.121, 1.789), or between healthy young and elderly subjects (95% CI 1.214, 1.741), or between dialysis patients and healthy adult subjects (95% CI 0.593, 0.921). No significant differences in the incidence of adverse events or clinical laboratory parameters were found between treatment groups.

CONCLUSIONS: Patients with moderate hepatic impairment and subjects older than 65 years had increased eplerenone exposure as reflected in AUC. These increases were clinically insignificant and do not warrant eplerenone dosage adjustments. Renal impairment had no significant effect on eplerenone pharmacokinetics. No statistically or clinically significant differences were observed between pediatric and adult patients. Race and gender had no effect on eplerenone pharmacokinetics.


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48. Evaluation of cholesterol goal attainments in patients enrolled in a pharmacist-managed dyslipidemia clinic within a Veterans Affairs medical center. Melissa M. Middelwright, D.Ph., B.C.S.; James H. Quillen Veterans Affairs Medical Center, Johnson City, TN; Pfizer, Inc., Concord, NC.

PURPOSE: To compare the percentage of patients achieving low-density lipoprotein cholesterol (LDL-C) goals in a pharmacist managed dyslipidemia clinic within a veterans administration medical center to the results of LDL-C goal attainment reported in the Lipid Treatment Assessment Project (L-TAP). L-TAP is a multi-center study across the United States investigating LDL-C goal attainment.

METHODS: Lipid panel results were reviewed and analyzed for 867 patients receiving dyslipidemia therapy counseling by a pharmacist during a three-month period between January, 2002 and March, 2002. Analysis included utilization of Microsoft Access® for descriptive statistics.

RESULTS: The months of January, February, and March 2002 were independently assessed, in addition to, a composite of all three months. The high-risk category with an LDL-C goal of <100 mg/dl constituted the largest percentage of patients seen with 70.8% of the visits, followed by 26.1% with a goal of <130 mg/dl and 2.9% with a goal of <160 mg/dl. Patients with LDL-C goals <100 mg/dl, <130 mg/dl, and <160 mg/dl achieved their goal 60.1%, 58.9% and 80.0% of the time, respectively. L-TAP reported LDL-C goal achievements of 18%, 37%, and 68% for LDL-C target goals of <100 mg/dl, <130 mg/dl, <160 mg/dl, respectively.

CONCLUSION: Pharmacist managed dyslipidemia clinics could achieve greater LDL-C goal attainment when compared to national prevalence data. Patients in the highest risk category seems to receive the greatest benefit. The results of this research may serve as a basis for the establishment of more dyslipidemia clinics within the Veterans administration medical center networks.

49E. Effect of spironolactone in ambulatory heart failure patients receiving conventional therapy. Alisha D. Vassar, Pharm.D., Sharon Starling, R.Ph., Amy Creighton, M.S.; Mercy Medical Center, Springfield, OH; Riverside Methodist Hospital, Columbus, OH; Grant Medical Center, Columbus, OH.

Presented at the Great Lakes Pharmacy Resident Conference, Indianapolis, IN, April 2002.

50E. Aspirin use for primary cardiovascular risk reduction in postmenopausal women. K.K. Dang, Pharm.D., Georgy Csako, M.D., Amy Heck, Pharm.D., Robert Wesley, Ph.D., MacDonald Horne, M.D., Richard O. Cannon, M.D., Robert Lederman, M.D., Frank Pucino, Pharm.D.; Warren F. Magnuson Clinical Center, Bethesda, MD; National Institutes of Health, Bethesda, MD; National Institutes of Health, Bethesda, MD; Purdue University, West Lafayette, IN.


51E. Modulation of potassium currents in a canine model of atrial fibrillation: impact of antioxidant therapy. Cynthia A. Carnes, Pharm.D., Ph.D., Spencer J. Dech, M.A., Tomohiro Nakayama, Ph.D., D.V.M., Jennifer Wierschin, John A. Bauer, Ph.D., Robert L. Hamlin, Ph.D., D.V.M., David R. Van Wagoner, Ph.D.; Ohio State University, Columbus, OH; Cleveland Clinic Foundation, Cleveland, OH.

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52. Patient assessment and modification of risk factors for ventricular arrhythmias prior to the administration of ibutilide. Anne P. Spencer, Pharm.D., Kenneth W. Kenyon, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate the assessment and modification of patient-specific characteristics which portend the development of ventricular arrhythmias with ibutilide administration.

METHODS: A retrospective review of medical records was performed on all patients (n=464) receiving ibutilide at our institution from 1996 to present. Data were collected regarding baseline serum levels of potassium (K+), magnesium (Mg2+), pre-conversion QTc interval, and ibutilide dose administered. Assessment criteria included: serum K+ < 4.0 mEq/L without potassium supplementation, serum Mg2+ < 2.0 mEq/L without magnesium supplementation, QTc interval > 440 msec, and inappropriate ibutilide dose. Patients were categorized based on the number of risk factors present prior to ibutilide administration. In addition, the prevalence of each risk factor was calculated.

RESULTS: Twenty-seven (42.2%) patients had one risk factor for the development of ventricular arrhythmias present, and 4 (6.2%) had two risk factors present prior to ibutilide infusion. Eighteen (28.1%) patients had a serum K+ < 4.0 mEq/L, however, 5 (7.8%) did not receive supplementation prior to ibutilide administration as indicated. Similarly, 24 (37.5%) had a serum Mg2+ < 2.0 mEq/L, of whom 5 (7.8%) did not receive supplementation. Twenty-six (40.6%) patients had a QTc interval > 440 msec on baseline electrocardiogram. An inappropriate ibutilide dose was utilized in 2 (3.1%) of patients.

CONCLUSIONS: Appropriate patient assessment and risk factor modification occurred in 33 (51.6%) of patients undergoing chemical cardioversion with ibutilide. Information derived from this evaluation will be used to support the development of a process to ensure patient risk-factor modification prior to ibutilide dispensing.


PURPOSE: This study reviewed the safety and efficacy of ibutilide at a non-teaching, community hospital.

METHODS: Medical records of 52 patients, detailing 56 courses of ibutilide therapy between March of 1999 and May of 2002 were reviewed retrospectively. Patients past medical history, hospital course, baseline EKG and echocardiographic data, medication use prior to and after ibutilide therapy, conversion rate, and adverse effects were recorded.

RESULTS: Ibutilide led to conversion to sinus rhythm in 46% of patients with atrial fibrillation and 87% of patients with atrial flutter. The average time to conversion was 35 minutes. Nineteen patients experienced an electrophysiographic event within 4 hours of receiving ibutilide, including 2 cases of sustained ventricular tachycardia and 1 case of torsades de pointes. Thirteen of these patients had an identifiable risk factor such as electrolyte imbalance, prolonged baseline QTc, or pretreatment with a Class Ia or III antiarrhythmic. Fifteen patients received ibutilide without adequate washout of a previous antiarrhythmic, with ensuing non-life-threatening arrhythmias within 4 hours of receiving ibutilide. None of the 25 patients who received a Class I or III antiarrhythmic within 4 hours of receiving ibutilide experienced a significant electrophysiographic event and 2 reverted back to atrial fibrillation on admission.

CONCLUSION: Conversion rates and occurrence of adverse events with ibutilide at our community hospital are similar to those reported in the literature. Policy changes to insure electrolyte balance prior to administration of ibutilide and proper weight-based dosing would likely reduce the...
54. Blood pressure measurement: selection of appropriate cuff size for office and home monitoring. Deborah S. King, Pharm.D., Marion R. Wolff, M.D., M.P.H., T. Kristopher Harrell, Pharm.D., Sara L. Noble, Pharm.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: To identify demographics associated with selection of appropriate cuff size and determine the size most commonly needed for accurate blood pressure (BP) measurement.

METHODS: Consecutive adult patients seen in a hypertension clinic were evaluated over a 2-week period. BP was measured using a mercury sphygmomanometer. Cuff size was determined by measuring midway between the suprasternal notch and the olecranon process. The size of cuff was selected based on the circumference and AHA recommendations: small-adult (<8.5 in), regular-adult (9.5-12.5 in), large-adult (13-16.5 in), thigh (>16.5 in). Data on age, race, sex, and BMI were systematically recorded.

RESULTS: Of the 167 patients assessed, 22% required a regular cuff: all those normal weight (9%, BMI <25) and less than half of those overweight. The majority were overweight (27%, BMI ≥25-29.9) or obese (65%, BMI ≥30). A large cuff was required in 48% and 79% of those, respectively, and a thigh cuff in 5% and 11%. No significant differences were found between white males and females in either mean arm circumference (12.5 in) or BMI (28.4). Black females and males had significantly larger arm circumferences (13.5 in; 13 in) and BMI (31.8, 30.7).

CONCLUSIONS: Increased attention should be given to proper cuff size used for office assessment and when recommending equipment for home use. As the incidence of overweight and obesity reach epidemic levels, a regular cuff is not appropriate for the majority of adults. Though equipment is routinely supplied with only a regular cuff, the large cuff is most often needed and should be the standard cuff provided.

55. Differences in the correlations of non-HDL-c and LDL-c with apolipoprotein B in patients receiving pravastatin monotherapy or pravastatin plus cholestyramine. Eric K. Gupta, Pharm.D., Matthew K. Ito, Pharm.D., FCCP, BCPS; University of the Pacific, Stockton, CA; Veterans Affairs San Diego Healthcare System, San Diego, CA.

PURPOSE: Non-HDL-c is a secondary target (NCEP III) in patients with a constellation of triglycerides and cholesterol levels for all the apolipoprotein B-containing lipoprotein particles such as VLDL-remnants, IDL, and LDL. Thus, LDL-c may underestimate apo B concentrations, especially in subjects receiving therapies that may increase triglycerides (i.e. cholestyramine). Therefore, the purpose of this investigation is to compare the difference in correlation between non-HDL-c and LDL-c to apo B in patients receiving pravastatin or pravastatin plus cholestyramine.

METHODS: Fasting lipoprotein profiles from a prior study (Am J Cardiol 1997;80:799-802), involving 59 patients with CHD randomized to white pravastatin monotherapy (20 or 40 mg) or combination pravastatin (10 or 20 mg) plus cholestyramine (8 g) for 12 weeks, was used to determine correlations between apo B with non-HDL-c and LDL-c.

RESULTS: Both non-HDL-c and LDL-c were highly correlated with apo B (p<0.0001 for all comparisons) in the monotherapy group at baseline (r=0.71, 0.64, respectively) and at 12 weeks (r=0.87, 0.80, respectively), and in the combination therapy group at baseline (r=0.85, 0.84, respectively) and at 12 weeks (r=0.82, 0.69, respectively). Also, non-HDL-c and LDL-c were highly correlated to apo B in patients with triglycerides below the median value of 178 mg/dL (r=0.85, 0.82, respectively), and in patients with triglycerides above the median value (r=0.77, 0.71, respectively).

CONCLUSIONS: Although there were no significant differences between the correlations of non-HDL-c and LDL-c to apo B, non-HDL-c had numerically higher correlations, than LDL-c, with apo B in both treatment groups and across different triglyceride strata.


PURPOSE: Despite demonstrated efficacy in stroke prevention, warfarin is underutilized in patients with atrial fibrillation (AF). We sought to determine the extent and determinants of warfarin use in Ohio Medicaid patients with new-onset AF.

METHODS: We performed a retrospective cohort analysis using Ohio Medicaid administrative billing data that included claims from all institutions, providers, and pharmacies providing services to Ohio Medicaid enrollees. The cohort included all 11,699 continuously enrolled fee-for-service recipients of Ohio Medicaid with a new diagnosis of nonvalvular AF between 1998 and 2000. We determined incident warfarin use and presence of risk factors for stroke and hemorrhage by searching claims records for corresponding ICD-9-CM and National Drug Codes. Univariate and multivariable analyses were performed to examine the association of risk factors with warfarin use.

RESULTS: Only 9.7% of all patients and 11.9% of those without apparent contraindications filled prescriptions for warfarin in the period from 7 days preceding to 30 days after the development of AF. Hypertension and congestive heart failure independently predicted increased warfarin use. Younger age (<55), older age (>85), prior intracranial hemorrhage, prior gastrointestinal hemorrhage, predisposition to falls, alcohol/drug abuse, renal impairment, and conditions perceived as barriers to compliance predicted decreased warfarin use.

57. Use of dobutamine and milrinone in decompensated heart failure patients at a university teaching hospital. Julie B. Cooper, Pharm.D., Debbie Montague M.S., Jo E. Rodgers Pharm.D., J. Herbert Patterson, Pharm.D.; University of North Carolina, Chapel Hill, NC.

PURPOSE: Although, intravenous inotropes are the standard of care for treating decompensated heart failure (HF) patients with low output symptoms, little published information guides inotrope selection. The purpose of this medication use evaluation (MUE) was to determine the potential impact of an inotrope selection algorithm on HF symptoms, duration of therapy, and length of hospitalization at a university teaching hospital.

METHODS: Over a six month period, a prospective MUE was conducted of consecutive patients admitted to a cardiology service who received dobutamine or milrinone for decompensated HF. Data pertaining to agent selection, duration of therapy, and the HF symptom score were collected. An algorithm was constructed based on rational for inotrope selection including risk for hypotension, presence or absence of ischemia, and concomitant medications (β-blockers, hydralazine). Clinical data were compared to the algorithm and analyzed by the Mantel-Haenszel test.

RESULTS: Of the 56 patients assessed (mean age: 61 years, 50% male, mean left ventricular ejection fraction- 26%), 50% of inotrope selection was consistent with the algorithm. While no change in duration of therapy or length of hospitalization occurred, most patients experienced an improvement in HF symptom score after treatment consistent with the algorithm.

CONCLUSIONS: An algorithm based approach for inotrope selection in the treatment of decompensated HF may improve patients’ symptomatic outcomes.

Critical Care

58. Safety of dexmedetomidine in the clinical setting. Joseph F. Dasta, M.S., Sandra L. Kane, Pharm.D., M.S., Amy J. Durschi, M.S., Dex Registry Study Group; Ohio State University, Columbus, OH, University of Pittsburgh Medical Center, Pittsburgh, PA; Abbott Laboratories, Abbott Park, IL.

PURPOSE: Since the safety profile of new drugs used in the clinical setting often differs from controlled studies, we compared dosing and adverse drug reactions (ADRs) of dexmedetomidine (Dex) in the naturalistic setting to data from clinical trials.

METHODS: Investigators from eight institutions collected data on 88 patients prescribed Dex as part of sedation therapy.

RESULTS: Only 33% of patients received a loading dose. The initial dosage averaged 0.31 µg/kg/hour (0.1 to 0.7) while the maximum dosage averaged 0.54 µg/kg/hour (0.8 µg/kg/hour in six patients). Duration of therapy averaged 22.1 hours, while 25% received Dex beyond 24 hours. 17% (15 patients) developed hypotension, which is lower than 30% from the package insert. Causality estimates of these patients were: 2 doubtful, 4 possible, 5 probable, and 4 highly probable. Regarding severity, four patients experienced no changes providing survival, five required increased monitoring, four required additional laboratory tests, change in vital signs or discontinuing the drug, and three patients required treatment, or experienced an increased length of stay. Bradycardia developed in five (6%) patients, which is similar to 8% from the package insert. Causality estimates of these patients were: 2 probable and 3 highly probable, and all bradycardic patients only required increased monitoring. No patient developed hypertension, while 16% of patients experienced hypertension in clinical trials.

CONCLUSION: Dex was well tolerated and generally administered within
59. Implementation and evaluation of an intestinal insulin therapy protocol in the surgical intensive care unit. Kelly S. Lewis, Pharm.D., David Baldwin, M.D., James A. Colombo, M.D., Lisa Pint, R.N., David M. Rothenberg, M.D.; Rush Presbyterian St. Lukes Medical Center, Chicago, IL.

PURPOSE: The hormonal changes associated with surgical stress induce a number of metabolic changes in both diabetic and non-diabetic patients. Tight glucose control improves outcome in post-surgical patients. There is no standard of care for the management of hyperglycemia. A multidisciplinary team developed and implemented an intensive insulin therapy (IIT) protocol in the ICU. This study documented intraoperative and postoperative compliance with the protocol.

METHODS: A multi-disciplinary ICU team developed a nursing-driven IIT protocol designed to maintain glucose levels between 80 and 120 mg/dL. Protocol compliance was then evaluated prospectively in all cardiac and vascular surgery patients. Appropriateness of IIT initiation and insulin titration were evaluated and episodes of hyperglycemia and hypoglycemia were documented. Reasonable conversions from IV infusion to SQ insulin also were applied.

RESULTS: 29 patients (9 diabetic) were evaluated over a one month period. Initiation of the protocol in the operating room occurred in 3 of 29 patients, even though intraoperative glucose measurements were > 120 mg/dL in all patients. Appropriate initiation of insulin infusion in the ICU and titration to maintain glucose in the target range occurred in 100% and 83% of patients, respectively. The overall rates of hyperglycemia and hypoglycemic episodes were 2.4 and 19.8 per 100 blood glucose measurements, respectively. IV to SQ insulin conversion was done appropriately in 93% of patients.

CONCLUSION: This study illustrates the effectiveness of a multidisciplinary team approach devised to standardize insulin management in a surgical intensive care unit.

60. Interferon-γ increases dipeptide transport via increased expression of the oligopeptide transporter h-PEPT1 in cultured human intestinal monolayers. David R. Foster, Pharm.D., Christopher P. Landowski, M.S., Lynda S. Welage, Pharm.D., FCCP; University of Michigan, Ann Arbor, MI.

METHODS: Caco-2 monolayers were grown on permeable supports at 37°C. The effects of critical illness on the permeation of peptides and peptidomimetic drugs (actively absorbed via the oligopeptide transporter, h-PEPT1) are relatively unknown. We evaluated the impact of interferon (IFN-γ) on h-PEPT1 expression, and peptide permeability in cultured human intestinal monolayers (Caco-2 cells) using the dipeptide glycylsarcosine (Gly-Sar).

RESULTS: IFN-γ (50 ng/ml) for 48 hours. Total RNA was isolated and RT-PCR was used to determine the expression of the IFN-γ. To assess peptide permeation, treated cells were incubated with IFN-γ (50-100 ng/ml) for 48 hours. The [3H]gly-Sar (10 µMOL) was added to the apical chambers of the cell supports, basolateral concentrations were serially sampled and h-PEPT1 expression by 14.2% and 11.5%, respectively (p=0.019). IFN-γ (p=0.003) and 28.4% in controls (p=0.006).

CONCLUSIONS: This study illustrates the effectiveness of a multidisciplinary team approach devised to standardize insulin management in a surgical intensive care unit.

Drug Delivery

63. Anticholinergic side effects with long-term transdermal oxybutynin for overactive bladder symptoms. G. Willy Davila, M.D., Roger R. Dmochowski, M.D., Steven W. Sanders, Pharm.D.; Cleveland Clinic Florida, Weston, FL; North Texas Center for Urinary Control, Fort Worth, TX; Watson Laboratories, Inc., Salt Lake City, UT.

PURPOSE: To determine if esomeprazole pellets from opened capsules are stable when suspended in common beverages.

METHODS: Esomeprazole pellets were stable after suspension in various common beverages. Administration of pellets from an opened capsule in tap water, yogurt, orange juice or apple juice is a practical alternative for patients unable to swallow intact capsules.


65. Physico-chemical stability of L-asparaginase in polyvinylchloride-free bags. Laurence Guicherd, Daniel Antier, Pharm.D., Ph.D., Stephanie Dallay, Jacqueline Graslin, Pharm.D.; Trousseau University Hospital, Tours, France.

PURPOSE: Because of the French public purchasing law, drug suppliers often change in hospital. However, the pharmacist has to guaranty the physico-chemical stability of all delivered preparation, especially cytotoxics prepared in centralised unit. Our hospital recently purchased L-asparaginase (L-asp, a cytotoxic agent used to treat leukaemia — and salines bags polyvinylchloride-free (PVC)-free used to dilute the drug. Given stability data were lacking, the pharmacy aimed to evaluate the stability of ASP in PVC-free bags.

METHODS: For this study, we used ASP (Labs Aventis, France) and PVC-free salines bags 250 mL (FREEFLEX™, Labs Fresenius, France). Stability parameters were: i) visual control; ii) pH; iii) ASP assay by spectrophotometry (λ = 287 nm). All data were compared to bottles of glass (saline, 250 mL). Three concentrations of ASP were tested (13000 UI; 15000 UI; 17000 UI) and preparations were stored at 4°C during the study period and maintained at 25°C for 6 hours before control.

RESULTS: Nor visual aspect perturbation neither significant variation of the concentration (p<0.01) between PVC-free bags and bottle have been observed during the 7-day period of study. We just remarked a pH variation at 24-hour control, followed by a coming back to basal level.

DISCUSSION: Data related to pH measurements suggest an interaction between ASP and PVC-free bag and bottle of glass, then compensated by the buffer effect of the solution. Nevertheless, ASP appeared to be stable in PVC-free bags over a 7-day period when kept at 4°C and infused at room temperature.


INTRODUCTION: As a tool to delivering high quality and consistent information to the public, the medical communications departments of pharmaceutical companies develop standard response letters (SRLs) that are sent to health care providers who request information. Requests for information must be unsolicited and the SRLs must be complete and provide balanced information.

PURPOSE: The purpose of the study was to evaluate the format and content of SRLs provided in response to pharmacists’ questions. METHODS: A sample of 19 SRLs had been obtained from a variety of pharmaceutical companies, including our own, in a single-blinded method. Questions were posed for information, that could not be not answered by the package insert (PI), by callers who identified themselves as pharmacists in either hospital or community practice. The SRLs were then reviewed by a committee of medical communications staff including those who use SRLs to respond to questions from callers, assessing the question, presence or absence of summary bullets, the format of the body of the SRL, presence or absence of conclusions, presence or absence of disclaimer about the approved indication and references.

RESULTS: Twenty-one (21%) of the SRLs did not directly respond to the question asked. A further 10% used a combination of two or three SRLs to provide a response. It was incompletely addressed in either SRL. Some bullet points were found in only 10% of SRLs. The median length of the SRLs was 3 pages with a range of 1 to 7. Few of the SRLs did more than summarize the information to the public, the medical communications departments of pharmaceutical companies, including our own, in a single-blinded method.

CONCLUSIONS: There is a wide variety in the quality of standard response letters. At best, 97% of preceptors had an advanced degree, 89% had a strong PE experience, and 79% had an established record in the field. Preceptors indicated programs were at least two years in length (84%), with available resources such as a medical library (97%), a computer center (87%), and a clinical research center (66%). Programs provided fellows with research skills.

67. Evaluation of drug safety-related knowledge, attitude, and behaviors among college students in Taiwan. Fei-Yuan Hsiao, M.S. candidate, Yi-Chun Chang, B.S., Wuan-Jin Lee, B.S., Ying-Chi Lin, B.S., Hsiang-Yin Chen, M.S., Pharm.D.; Taipei Medical University; Taipei Municipal Wan-Fang Hospital, Taipei, Taiwan.

PURPOSE: This study was designed to evaluate the knowledge, attitude, and behaviors towards to drug safety and pharmacists’ role in first year college students in Taiwan.

METHODS: A total number of 148 departments in 25 universities were sampled by stratified randomization. Three sections of questionnaire were designed and validated. The first section included 10 dichotomous questions to test the knowledge of drug safety. The attitude and trusting toward pharmacists were also evaluated by 3 questions and 1 question in 5-point scale. The final section contained 10 questions in a 5-point scale to access the behaviors related to safe use of drug.

RESULTS: Out of 6820 forms, 6270 was completed with a completed rate of 91.9%. Mean score of knowledge was 6.55 ± 2.25 for all responders, and 6.47 ± 2.26 and 7.00 ± 2.01 for non-health science and health science related students, respectively (p<0.05). The students showed positive attitude and trustiness toward pharmacists’ profession with a mean score of 12.64 ± 2.19 and 3.59 ± 0.70. Average behavior score was 34.06 ± 2.09 with a perfect score of 50, indicating warranty of efforts to improve the safe use of medications. However, students major in different health professionals showed distinct level of trustiness to pharmacists, with mean score of 3.91 ± 0.66 and 3.69 ± 0.62 for medical, pharmacy, and nursing students, (p<0.001).

CONCLUSION: College students, as a sample representing well-educated public, are still in a lack of appropriate knowledge, attitude and behavior related to safe use of drug. Pharmacists should take a more active role to provide education for medication safety.

68. Medication use evaluation of fenoldopam use at a major teaching institution. Ann L. Adams, Pharm.D., Michelle A. Leady, Pharm.D.; University of Michigan Health-System, Ann Arbor, MI.

BACKGROUND: Fenoldopam mesylate is a dopamine D1-like receptor agonist that vasodilates the peripheral and renal vasculature resulting in its ability to be successfully used in patients with severe or malignant hypertension. Its renal vasodilatory effects offer an advantage over other agents commonly used for malignant hypertension and have expanded its potential use to include prevention of nephropathy in patients at risk of contrast media-induced renal dysfunction. In February of 1999, fenoldopam mesylate was approved by the pharmacy and therapeutics committee at our institution with restriction to specific criteria due its higher cost compared to alternative agents.

PURPOSE: A medication use evaluation was performed to determine whether adherence to approved restrictions had occurred.

METHODS: All patients that received fenoldopam were included in this retrospective review. Review of information contained in an electronic database was performed.

RESULTS: One hundred forty-four patients received fenoldopam between January 1, 1999 and January 31, 2002. Appropriate use occurred in 130/141 (92.2%) patients. Approval from one of the approving services was not obtained in 11/141 (7.8%) cases. Adverse events reported for fenoldopam included headache, somnolence, nausea, vomiting, abdominal pain and hypertension. The total drug cost for fenoldopam during this time was $364,926.54, which included $15,568.45 for unapproved uses.

CONCLUSION: With few exceptions, adherence to restrictive criteria occurred with fenoldopam, limiting the financial impact to our institution.

Education


PURPOSE: 1) To describe the extent to which pharmacoeconomic (PE) fellowships adhere to American College of Clinical Pharmacy (ACCP) guidelines developed in 1999. 2) To determine whether programs established before and after 1999 differ in compliance with guidelines.

METHODS: A 28-item survey was sent to preceptors via the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Web site. Preceptors were identified via ACCP and ISPOR fellowship directories as well as ISPOR’s Web site and membership roster. Preceptors currently involved in programs were included in the analysis. χ² and Fisher’s exact tests were performed.

RESULTS: Forty-nine preceptors completed the survey and 38 met inclusion criteria. Of these, 82% were involved in a program established prior to 1999. Over 90% of preceptors had an advanced degree, 89% had a strong PE experience, and 79% had an established record in the field. Preceptors indicated programs were at least two years in length (84%), with available resources such as a medical library (97%), a computer center (87%), and a clinical research center (66%). Programs provided fellows with research skills.
including the conceptualization (82%), administration (71%), and data management (85%) of research projects. However, only 32% of programs devoted 80% or more of the fellow’s time toward applied PE research activities.

RESULTS: In the latter six months, patients who attended the warfarin education class had statistically significantly smaller time lapses between INR laboratory blood draws (p<0.02). Also in the study’s second six months, the percentage of INR values within the target range was significantly higher in the group of patients who had attended the class than in the group that did not (p<0.02). The patients who attended the class also had fewer adverse events and fewer deviations from the target INR range.

CONCLUSION: The results indicate that a group anticoagulant education class led by a pharmacist increased patient adherence to monthly monitoring, increased the frequency that INRs were within the therapeutic range, and decreased large variations from the desired INR ranges.

73. Evaluation of the utilization of game-based teaching strategies in a pharmacotherapeutics course. Dennis Parker, Jr., Pharm.D., Denise Rhoney, Pharm.D.; Wayne State University, Detroit, MI.

PURPOSE: Discussion sessions are traditionally based upon passive learning, although active learning may be more effective as it promotes critical thinking and integration of knowledge. We implemented a game-based learning tool called “Central Nervous System (CNS) Survivor” in the second professional year pharmacotherapeutics course. A student satisfaction survey was given to assess student attitudes toward the game.

METHODS: Students were divided into 4 groups which were named based upon the lobes of the brain. Groups competed against each other in a 4-game series of “challenges,” similar to the popular television game, during designated discussion sessions of the CNS module. The challenges emphasized teamwork and an extensive review of the material via a multi-media approach. A student satisfaction survey consisting of 38 items was employed upon completion of the game. Likert Scales (1-4) were used to evaluate the perception and effectiveness of this teaching tool. Descriptive statistics were used to evaluate the responses.

RESULTS: All students in the class (n=133) completed the survey. The majority of students attended all games (83%). Although 86% of students listed extra credit as a reason for attending, most (77%) said they would have attended if extra credit were not awarded. Most students (56%) indicated that reviews in previous classes had not been helpful and almost all (92%) preferred active learning. Over 75% of students thought that the game was useful in improving teamwork, critical thinking skills, and scores on examinations. Overall, 99% were satisfied with the game and 97% felt that “CNS Survivor” was an innovative teaching tool.

CONCLUSIONS: The use of game-based discussion sessions can promote active learning and better retention than traditional lecture based reviews. Innovative teaching strategies such as gaming can be used to create an environment of enjoyment which improves students perception of learning. Validating active learning via subjective measures deserves further investigation.


PURPOSE: The purpose of this study was to develop and evaluate the optimal patient education guideline for cancer patients receiving chemotherapy in the hospital.

METHODS: Patient medication teachings including verbal instruction and written materials were provided by a pharmacist for cancer patients receiving chemotherapy on the first or second day of hospitalization. After providing medication teaching a written survey was performed in order to measure the patient’s satisfaction with the medication teachings and to evaluate the effectiveness of the patient medication teaching.

RESULTS: Verbal patient medication teachings and written materials covering the topics of the cancer, chemotherapy agents and adverse effects were provided for hospitalized cancer patients receiving chemotherapy. This individual patient medication teaching was provided at bedside of hospitalized cancer patients. Written surveys were also performed in all patients after the medication teaching was completed. The results of 37 written surveys revealed that almost all patients (96.3%) felt that medication teaching was a must in order to understand and accept the chemotherapy for cancer patients. In addition, almost all patients (92.6%) stated that they were extremely satisfied with the medication teaching provided by the pharmacist.

The levels of understandings on the chemotherapeutic agents (p<0.05), side effects of chemotherapeutic agents (p<0.05), and symptoms of cancer (p<0.05) were significantly higher after the patient medication teaching was provided.

CONCLUSIONS: The results of this study show that a well-developed patient medication teaching by a pharmacist increased patient’s level of medication knowledge, which would ultimately increase patient’s medication compliance rate.

75. Meta-analysis of medication adherence interventions in the pharmacy setting. Liza Takiya, Pharm.D., Andrew M. Peterson, Pharm.D., Rebecca Finley, Pharm.D.; University of the Sciences in Philadelphia; Philadelphia College of Pharmacy, Philadelphia, PA.
PURPOSE: To examine the effect of pharmacy-based interventions targeting medication adherence and identify successful interventions.

METHODS: Literature search was performed between 1970-December, 2000 using Medline, IPA, PsychLit, ERIC, and Embase. Randomized, controlled trials written in the English language with at least 10 subjects per group were screened. Further, the intervention must have been directed toward a patient or caregiver and the article must have reported adequate adherence and sample size data. Each article was reviewed by two reviewers and entered into a database. All adherence measures were converted to common effect size (ES) using Cohen’s d or d'. A random effects model was employed and the ANOVA and Q-test were used for statistical testing. Any p<0.05 was considered significant.

RESULTS: Seven articles, totaling 1201 patients were identified. Four of the seven studies reported more than one intervention, yielding 14 separate intervention groups. Six interventions were behavioral (EI), two were educational (EI), and six were a combination (CI) of EI and CI. Hypertension was the most common disease state (n=5). Mean intervention duration was two months (<1 month-6 months). The Q-test supported homogeneity for all groups. The overall ES was 0.8. The ES for each intervention type was 0.05 (95% CI, -0.03-0.12), 0.03 (95% CI, -0.13-0.2), 0.14 (95% CI, 0.04-0.24) for the EI, EI, and CI, respectively.

CONCLUSIONS: The combination of educational and behavioral interventions was most successful in enhancing medication adherence. More well-designed articles need to be performed regarding medication adherence interventions in the pharmacy setting.

76E. The impact of supplemental instruction sessions in a problem-based learning curriculum. Brandon J. Sucher, Pharm.D., Brian Crabtree, Pharm.D., BCPS, Palm Beach Atlantic College, West Palm Beach, FL; University of Mississippi, Jackson, MS.


77. Influence of a pharmacist-managed diabetes self-management education service on patient behavioral outcomes. L. Brian Cross, Pharm.D., CDE, Diane Pojanowski, Pharm.D., Jennifer Campbell, Pharm.D., CDE, Gail Hamann, Pharm.D., BCPS, CDE, University of Tennessee Health Science Center; Regional Medical Center, Memphis, TN.

PURPOSE: The purpose of this research was to evaluate the influence of a pharmacist-managed diabetes self-management education (DSME) Service on behavioral outcomes in patients with diabetes.

METHODS: A retrospective study was done to evaluate 163 patients who attended a pharmacist-managed DSME during the year 2001. Patients were contacted by telephone within 6 months of completing DSME for follow-up assessment of changes in lifestyle behavioral goals set during DSME. Behavioral goals were assessed by frequency of occurrence: all of the time, most of the time, some of the time, never.

RESULTS: Patient goals for changes in lifestyle behavior were represented by seven behavior categories:  glucose monitoring, skipping meals, exercise, carry fast acting glucose for hypoglycemia treatment, dietary changes, examine feet regularly, record glucose and bring log to physician appointments. At least 63% of patients reported meeting behavioral goals set during DSME all of the time or most of the time for all goals except the topic of changes in exercise patterns (bring log to physician appointments). At least 91% change in diet 77%, do not skip meals 72%, carry fast acting glucose source 66%, monitors glucose 63%. Fifty-four percent of patients stated they had made changes in exercise patterns only some of the time or never.

CONCLUSIONS: A pharmacist-managed DSME Service may influence behavioral changes in patients with diabetes through increasing patients’ awareness of important self-care issues.

Endocrinology

78E. Clinical outcomes of a pharmacist-managed diabetes self-management education service. Diane Pojanowski, Pharm.D., L. Brian Cross, Pharm.D., CDE, Jennifer Campbell, Pharm.D., CDE, Gail Hamann, Pharm.D., BCPS, CDE, University of Tennessee Health Science Center; Regional Medical Center, Memphis, TN.

Presented at the 33rd Annual Southeastern Residency Conference, Athens, GA, April 2002.

79. Relationship of gender and obesity to youth-onset type 2 diabetes. William D. Linn, Pharm.D., Thomas C. Shank, Pharm.D.; University of Texas; Pfizer Pharmaceuticals, San Antonio, TX.

PURPOSE: Studies have shown an increasing prevalence of type 2 diabetes in pediatric patients with diabetes. Most of these patients’ body mass index (BMI) exceeded the 85th percentile and there was a higher prevalence in females. This study evaluates this relationship in a predominantly Hispanic population.

METHODS: In December 2001 a diabetes screening project was performed in San Antonio, TX. Data were collected on demographics, vital signs, a full lipid profile, and a random or fasting glucose. A Body Mass Index (BMI) was calculated using the formula: BMI = wt in Kg/Ht in meters2. Glucose intolerance was defined as having a random glucose >140 mg/dL or a fasting glucose >110 mg/dL. The data were imported into a relational database (Access) for analysis.

RESULTS: A complete data set was available for 530 patients < 18 years of age. There were 292 males and 248 females. For those with a BMI ≤ 27, 15% of the males and 18% of the females exhibited glucose intolerance. For the cohort with a BMI ≥ 27, 14% of the males and 24% of the females had glucose intolerance.

CONCLUSIONS: These data are concordant with other data that there is a gender bias in youth-onset type 2 diabetes. This may relate to differences in lifestyle activities and the diet’s role in insulin sensitivities and insulin resistance. Pharmacists need to be aware of the increasing prevalence of type 2 diabetes in this population and the implications for using oral hypoglycemic medications in adolescents.

80. Evaluation of metformin utilization and subsequent formulary removal in a community hospital setting. Jacqueline L. Fein, Pharm.D., BCPS, Mac i. Sandberg, M.D., Tom Ollis, R.Ph., M.S., CHE; Rutgers University, Piscataway, NJ; Hunterdon Medical Center, Flemington, NJ.

PURPOSE: Despite specific contraindications provided by the manufacturer, studies of prescribing patterns suggest that 25-50% of patients at risk for lactic acidosis are prescribed metformin. We evaluated metformin utilization in our institution because of patient safety concerns. Based on our results, the Pharmacy and Therapeutics Committee removed metformin from the formulary. We present utilization patterns of metformin both before and after its removal from formulary in a community hospital setting.

METHODS: Medical records of patients prescribed metformin over two separate 2-month time periods (before and after formulary removal) were reviewed. Information including patient age, gender, physician, schedule, and adverse drug event occurrence was collected. Each record was reviewed for metformin contraindications and conditions causing hypoxemia, which may increase the risk of lactic acidosis.

RESULTS: The preliminary review contained data for 33 inpatients. Potential risk for lactic acidosis was detected in 27.2% (9/33) of patients. Some identified risk factors included sepsis or pneumonia (9%, 3/33), acute cardiac conditions (6%, 2/33), contrast studies (6%, 2/33), corticosteroid use (3%, 1/33). After metformin formulary removal, potential risk for lactic acidosis was detected in 14.2% of patients (2/14) prescribed metformin. No adverse drug events were noted during the study period.

CONCLUSION: Our initial study demonstrated inappropriate metformin prescribing in 27% of reviewed patients. This trend was reduced after formulary removal of metformin and physician education. We will continue to monitor our patients for inappropriate utilization of metformin and provide education regarding specific contraindications.

81. Evaluation of men’s knowledge and perceptions of osteoporosis risk and lifestyle modifications. Sherry Coleman, Pharm.D., BCPS, Robert L. Page, Pharm.D., BCPS; University of Colorado Health Sciences Center, Denver, CO.

PURPOSE: The purpose of this study was to evaluate men’s knowledge of risk factors for osteoporosis, behavioral exercises, and calcium/vitamin D intake; their perceived level of risk, and actual risk for osteoporosis.

METHODS: One hundred community dwelling men ≥ 18 years of age were surveyed by a pharmacy healthcare provider for demographic data; personal risk factors; and osteoporosis knowledge regarding risk factors, exercises, and appropriate calcium and vitamin D intake.

RESULTS: Eighty-one percent (age 52 ± 17 years, range 18-86) had knowledge of osteoporosis. Twenty-seven percent perceived they were at risk, but most felt it was low. Thirty-four percent had ≥ 3 osteoporosis risk factors. The majority of subjects correctly identified the following risk factors: low calcium (85%), inactivity (77%), family history (71%), personal fracture history (60%), and smoking (56%). Many did not identify low testosterone (65%), Caucasion race (62%), high caffeine (60%), and excessive alcohol consumption (54%) as risk factors. Sixty-seven percent incorrectly chose obesity as a risk. Most incorrectly identified swimming (80%) and cycling (69%) as bone-building exercises. Seventy percent did not know the recommended consumption of calcium and vitamin D. Fifty-four percent, 16%, and 9% reported taking a daily multivitamin, calcium supplements, and vitamin D supplements, respectively. Patients taking calcium supplements appeared more knowledgeable about osteoporosis risk.

CONCLUSION: Most men understand a working definition of osteoporosis, but knowledge and perceptions of risk factors and lifestyle modifications are lacking. Pharmacists can play an important role in educating men about osteoporosis risks and interventions.

82. Screening and identifying impaired fasting glucose in high-risk patients in the community pharmacy setting. Brian K. Irons, Pharm.D., BCPS, Arthur Nelson, Ph.D., Kathleen A. Snella, Pharm.D., BCPS, Rebecca B. Sleeper, Pharm.D., BCPS, Mauvi Villarreal, M.S.; Texas Tech University Health Sciences Center, Amarillo, TX.
PURPOSE: The ADA recommends screening for impaired fasting glucose (IFG) in patients at an increased risk for the development of type 2 diabetes. The goal of this study was to document the ability of pharmacists in the community setting to identify patients with IFG. The primary objective was to determine the frequency of IFG among high-risk patients identified and screened. A secondary objective was to assess patient characteristics that correlate with a positive IFG screen.

METHODS: Patients at risk for type 2 diabetes, assessed via a predetermined rating scale using known diabetes risk factors, were identified in participating community health centers in Texas. Patients at least 18 years of age were included if they scored > 10 on the rating scale, were fasting at least 8 hours, and if fasting plasma levels were < 126 mg/dL. Patients were categorized with having IFG (110-125 mg/dL) or normal glucose (< 110 mg/dL). Univariate analysis was used to determine patient characteristics that correlated with a positive screen for IFG.

RESULTS: A total of 575 patients were screened. Forty-six of 252 (18.2%) patients who met the inclusion criteria were identified as having IFG. No demographic, diabetes risk factor, or lipid parameter specifically correlated with a positive IFG screen.

CONCLUSIONS: Screening high-risk patients in the community pharmacy setting may be an effective way to identify patients with IFG as nearly one in five patients identified and screened demonstrated characteristics important secondary to their significant risk of developing diabetes.

83. A retrospective evaluation of performance measurements in adult patients with diabetes mellitus.
Frances C. Farnsworth, Pharm.D., Brigitte L. Sicat, Pharm.D., BC-ADM, Patricia M. Selig, M.S., FNP, CDE; Virginia Commonwealth University, Medical College of Virginia, Richmond, VA.

PURPOSE: In April 2001, the American Medical Association, the Joint Commission on Accreditation of Healthcare Organizations, and the National Committee for Quality Assurance developed a consensus statement on coordinated performance measurements for the management of adult patients with diabetes. This study evaluated selected performance measurements to assess and improve the quality of care received by patients at an interdisciplinary Internal Medicine Clinic.

METHODS: A retrospective chart analysis was performed on 288 randomly selected patients who had diabetes. This study evaluated selected performance measurements to assess and improve the quality of care received by patients at an interdisciplinary Internal Medicine Clinic.

RESULTS: The percentage of patients with SBP > 130 mm Hg or DBP > 85 mm Hg were 57% and 59%, respectively. Of patients with documented hypertension, 7% had 7% and 59% had an LDL > 100 mg/dL. Of patients without contraindications to therapy, 51% of patients had no documentation of aspirin, 29% had no documentation of ACE-I use, and 39% of patients with LDL > 100 mg/dL were not receiving lipid lowering therapy. Candidates for aspirin, ACE-I, or lipid lowering therapy not receiving treatment were evaluated for the documentation of a contraindication to drug use.

RESULTS: The percentage of patients with SBP > 130 mm Hg or DBP > 85 mm Hg were 57% and 38%, respectively. Of patients with documented laboratory values, 68% had a HbA1c > 7% and 59% had an LDL > 100 mg/dL. Of patients without contraindications to therapy, 51% of patients had no documentation of aspirin, 29% had no documentation of ACE-I use, and 39% of patients with LDL > 100 mg/dL were not receiving lipid lowering therapy.

CONCLUSIONS: The results of this study revealed that SBP, glycosylated hemoglobin (HbA1c), and LDL cholesterol were not optimally controlled in over 50% of patients. These results indicate that more attention should be given to control these major risk factors. The evaluation of patients who were not on an optimal amount of therapy may reveal several areas for intervention.

84. Comparison of efficacy between acipimox and fenofibrate in patients with hyperlipidemia. Jung M. Oh, Pharm.D., Seungmi Kim, M.S.; Sookmyung Women's University, Seoul, Korea.

PURPOSE: The objective of this study was to compare the efficacy of acipimox and fenofibrate for the treatment of hyperlipidemia.

METHODS: This study performed a retrospective comparison of acipimox (250 mg PO TID) and fenofibrate (200 mg PO qday) by comparing the means of changes in total cholesterol, triglyceride, HDL-C, LDL-C, and TC/HDL-C ratio at 3, 6, and 9 months of the treatments.

RESULTS: A total of 103 patients (41 in acipimox group and 62 in fenofibrate group) were evaluated. In general, acipimox- and fenofibrate-treated groups were comparable with respect to demographic characteristics. After treatments both acipimox and fenofibrate produced a significant reduction in total cholesterol from baseline (9.7% with acipimox; 11.3% with fenofibrate) and triglyceride levels (52.6% with acipimox, p<0.001; 54.3% with fenofibrate, p<0.001). HDL-C levels after treatments increased by 8.4% and 9.3% with acipimox and fenofibrate, respectively. The mean changes of total cholesterol, triglyceride, and HDL-C were not significantly different between the two treatments (p>0.05). The mean changes of LDL-C levels were 4.4% with acipimox and 2.0% with fenofibrate after treatments. There was a significant reduction in TC/HDL-C ratio from baseline for both drugs (15.2% with acipimox; 18.0% with fenofibrate), and the reduction of TC/HDL-C ratio was not significantly different between the two drugs (p>0.05).

CONCLUSIONS: Both acipimox- and fenofibrate-treated groups experienced significant changes in total cholesterol, triglyceride, HDL-C, and TC/HDL-C ratio from the baseline after treatments. However, LDL-C levels did not change significantly in both groups. The changes in total cholesterol, triglyceride, HDL-C, LDL-C and TC/HDL-C ratio between acipimox and fenofibrate treated groups were similar.

85. Rapid weight gain with thiazolidinediones: results from a meta-analysis.
Elaine Chiquette, Pharm.D., Michael Dolker, Ph.D., Charles Lucas, M.D.; Aventis Pharmaceuticals, Bridgewater, NJ; Roche Laboratories, Nutley, NJ.

PURPOSE:TZDs activate PPAR-γ causing pre-adipocytes to differentiate into mature fat cells. We conducted a meta-analysis to quantify the weight gain observed within 6 months of initiating TZDs as monotherapy or combination therapy for type 2 diabetes.

METHODS: English citations were identified through December 2001 from 3 electronic databases, references of pertinent articles, ADA abstracts and manufacturers. We limited our review to randomized controlled trials (RCTs) that lasted at least 12 weeks and compared TZDs monotherapy or in combination to placebo. We adopted the DerSimonian and Laird empirical Bayes random-effects estimator to calculate the pooled measures of TZDs effect on weight.

RESULTS: Only 11 RCTs reported the impact of TZDs on weight (6 rosiglitazone and 5 pioglitazone). The heterogeneity testing identified 4 trials as significant outliers. Most of these trials (3/4) were conducted in Japan (baseline weight 61 kg and >6 months duration). Compared to control, TZD increased weight by 0.84 kg (95% CI 0.59, 1.09) in these normal weight Japanese subjects. After excluding the outliers the impact of TZDs was reduced from 184.95 (df=10) to 15.04 (df=6), p=0.02. The pooled analysis found TZDs to induce a weight gain of 3.6 kg or 7.9 lbs (95% CI 3.3, 4.0 kg) over 6 months. There were insufficient data to examine the association between weight gain and time of treatment and efficacy (HbA1c reduction) or the effect of different combinations and weight gain.

CONCLUSION: This meta-analysis shows that compared with placebo, TZDs alone or combined to sulfonylureas or metformin results in statistically and clinically significant increases in weight within 6 months of therapy.

86. Evaluation of metformin monitoring in veteran patients undergoing procedures involving non-ionic intravenous contrast dye.
David Parra, Pharm.D., BCPS, Anna Lindlief, Pharm.D., Nick P. Beckey, Pharm.D., BCPS, Sonia Reyes, R.N., M.S.; West Palm Beach VA Medical Center, West Palm Beach, FL; University of Minnesota, Minneapolis, MN.

PURPOSE: Intravascular radiocontrast studies can lead to acute renal dysfunction and lactic acidosis in patients receiving metformin. It is recommended metformin be withheld 48 hours post-procedure and reinstituted after renal function has been re-evaluated. The objective of this research was to evaluate the efficacy of a computer generated consult in promoting timely evaluation of renal function post-procedure, and measure the incidence and magnitude of serum creatinine elevations.

METHODS: In October 1999 an electronic consult was created for use by the Imaging Service when patients on metformin received intravenous contrast dye. Ordering of the consult generates an electronic notification to a team of pharmacists responsible for providing a 48 hour follow-up (excluding one patient) was 2.68 ± 1.69 days. Average time from procedure to laboratory follow-up (excluding one patient) was 2.68 ± 1.69 days. Average serum creatinine pre- and post-procedure was 1.10 ± 0.19 mg/dL and 1.12 ± 0.23 mg/dL, respectively (p>0.05). Four patients developed contrast-induced nephropathy (increase in serum creatinine of 25%). Serum creatinine was ≥ 1.5 mg/dL in three of these patients, necessitating the temporary discontinuation of metformin. Eight additional patients, with borderline serum creatinine levels at baseline (1.4-1.6 mg/dL), had increases in serum creatinine to 1.5-1.6 mg/dL post procedure, requiring further evaluation of metformin therapy.

CONCLUSIONS: These results indicate that timely follow-up occurs using the combined process of an electronic consult and pharmacists. This study also suggests that nearly 4% of diabetic patients with normal renal function develop contrast-induced nephropathy with non-ionic contrast dye. In addition, about 10% of veteran diabetic patients receiving metformin who undergo a procedure with non-ionic intravenous contrast dye will need to discontinue metformin therapy held beyond 48 hours.

Gastroenterology

87F. Pantoprazole bismuth suspension can provide oral bioavailability similar to tablet. Jeffrey Paul, Ph.D., Geraldine M. Ferron, Pharm.D., Ph.D., Sherry Ku, Ph.D., Madelyn Abeli, R.N., BSN, Mary Unruh, R.N., MSN, John Getley, D.M.D., D.O., Philip R. Mayer, Ph.D.; Wyeth-Ayerst Research, St. Davids, PA.

delivered through nasogastric and gastrostomy tubes. C. Michael White, Pharm.D., James Kalus, Pharm.D., Robert Quercia, M.S., Christopher Forttier, B.S., Alexandra Piotrowski, B.S., Albert Roach, Pharm.D., Mark B. Sostek, M.D.; University of Connecticut, Storrs, CT; Hartford Hospital, Hartford, CT; AstraZeneca LP, Wayne, PA.

PURPOSE: To determine the efficiency of delivery of the contents of an opened capsule of esomeprazole through nasogastric tubes (NGT) and gastrostomy tubes using an in vitro protocol.

METHODS: The percentage of enteric-coated pellets from an opened capsule of esomeprazole 40 mg that passed through either an 8-French NGT, a 14-French NGT, or a 20-French gastrostomy tube was measured using 2 methods. In the first, pellets were suspended in 50 mL of tap water in a syringe, injected through the tube, and counted. In the second, pellets were suspended in 25 mL of tap water in a syringe, injected, an additional 25 mL of tap water was washed through the syringe and tube, and pellets were counted. Differences were analyzed using t-tests.

RESULTS: More than 98% of pellets were delivered using the 50 mL method.

### Baseline Pellet Count (mean ± SD)

<table>
<thead>
<tr>
<th>Method</th>
<th>Pellet Count (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-French NGT</td>
<td>1242.8 ± 25.6</td>
</tr>
<tr>
<td>8-French NGT</td>
<td>1244.8 ± 32.9</td>
</tr>
<tr>
<td>14-French NGT</td>
<td>1240.8 ± 19.9</td>
</tr>
<tr>
<td>20-French gastrostomy tube</td>
<td>1231.8 ± 19.8</td>
</tr>
</tbody>
</table>

**P**<0.05 versus 14-French NG tube 50 mL method (Student t-test); **P**<0.05 versus 8-French NG tube (Bonferroni corrected t-test)

CONCLUSION: The pellets of an opened capsule of esomeprazole 40 mg suspended in water can be efficiently delivered through an NGT or gastrostomy tube. Administration of an opened esomeprazole capsule through an NGT or gastrostomy tube is likely to be as effective as oral administration in suppressing gastric acid production.

98E. Intestinal P-glycoprotein is important for mucosal defense against Listeria monocytogenes infections. Brian L. Neudeck, Pharm.D., Jennifer M. Loeb, B.S., Nancy G. Faith, B.M., Charles J. Czyprowski, Ph.D.; University of Wisconsin, Madison, WI.

Published in Gastroenterology 2002;122:97.

90. Esomeprazole: nasogastric tube administration of the contents of an opened capsule suspended in water compared with oral administration in healthy volunteers. Mark B. Sostek, M.D., Yusong Chen, Ph.D., Wendy Skammer, BSN, Helen Winter, Ph.D., June Zhao, M.D., Tommy Andersson, Ph.D., AstraZeneca LP, Wayne, PA.

PURPOSE: Nasogastric tube administration of medication may be necessary for patients unable to swallow. Bioavailability of esomeprazole was measured following oral and nasogastric administration.

METHODS: This was an open-label, 2-period crossover study with two 5-day dosing periods separated by a 7- to 14-day washout. Subjects received esomeprazole 40 mg once daily 30 minutes prior to a standardized breakfast in a randomized sequence either orally as an intact capsule (IC) or via syringe through a 16-French nasogastric tube as a suspension of enteric-coated pellets from an opened capsule (OC) in 50 mL water. Following multiple plasma concentration measurements, the AUC and Cmax for esomeprazole were determined using a one-compartment, open model. Logarithmic values for AUC and Cmax were analyzed using ANOVA to obtain the least square means of the differences between the OC and IC and the 90% confidence intervals (CI). The antilogarithms of the least square means and the CI were calculated to estimate the ratio of OC/IC and the 90% CI for the ratio.

RESULTS: Geometric means of OC/IC with 90% CI for AUC and Cmax at days 1 and 5 are presented (table). Similar bioavailability between the 2 modes of administration were found.

### Day 1

<table>
<thead>
<tr>
<th>Method</th>
<th>AUC (ng/mL•hour)</th>
<th>Cmax (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>1.03 (0.93-1.15)</td>
<td>60.87</td>
</tr>
<tr>
<td>Nasogastric Tube</td>
<td>1.14 (1.03-1.26)</td>
<td>60.16</td>
</tr>
</tbody>
</table>

CONCLUSION: An opened capsule of esomeprazole suspended in water administered via nasogastric tube is a practical alternative for patients unable to swallow the intact capsule.

91E. Lansoprazole fast-disintegrating tablets (15 mg, 30 mg), a new proton pump inhibitor formulation, is bioequivalent to lansoprazole capsules (15 mg, 30 mg). James W. Freston, M.D., Ph.D., Mitchell A. Rosenberg, M.D., Marc A. Saltzman, M.D., Yi-Lin Chiu, Ph.D., David L. Bloom, BGS, Barbara A. Bopp, Ph.D., E. David Ballard, II, M.D.; University of Connecticut Health Center, Farmington, CT; Parkway Research Center, North Miami Beach, FL; Abbott Laboratories, Abbott Park, IL; TAP Pharmaceutical Products Inc., Lake Forest, IL.

Published in Gastroenterology 2002;122(4 Suppl):A195-6.


PURPOSE: A therapeutic interchange was implemented in which patients with a diagnosis of GERD and an active prescription for a proton pump inhibitor (PPI) were converted to ranitidine 300 mg twice daily. This review was designed to compare patients who remained on ranitidine after the therapeutic conversion (non-failure patients) with those patients who were switched back to a PPI in the three months following the intervention (failure patients).

METHODS: Pharmacy records were used to identify failure patients (n=1404) and non-failure patients (n=4639) three months after implementation of the step-down initiative. A random sample of 125 patients was selected from the failure and non-failure groups. A retrospective review of computerized medical and pharmacy records was performed. A binary logistic regression model was used to identify significant predictors of failure.

RESULTS: The mean duration of ranitidine therapy prior to failure was 48.9 ± 24.7 days. Recurrence of symptoms was the most common reason for failure in the first three months after the conversion. Other risk factors for GERD (smoking, hiatal hernia, LESP-lowering medications) did not significantly predict failure.

CONCLUSION: In the three months following implementation of the initiative, obesity and duration of PPI therapy greater than two years were significant predictors of failing the step-down conversion from a PPI to ranitidine.

93E. A prospective, controlled, randomized trial of 3-, 7-, and 10-day rabeprazole-based triple therapy for H. pylori eradication in the U.S. Nimish Vakil, M.D., Howard J. Schwartz, M.D., Frank L. Lanza, M.D., Jay Barth, M.D., Anita Murthy, Pharm.D.; University of Wisconsin, Milwaukee, WI; Miami Research Associates, Miami, FL; Houston Institute for Clinical Research, Houston, TX; Elsi, Inc., Teaneck, NJ.


Geriatrics

94. An evaluation of secondary stroke prevention in elderly long-term care patients. Bradley E. Hein, Pharm.D., Tamara B. Patterson, Pharm.D.; University of Cincinnati; Skilled Care Pharmacy, Cincinnati, OH.

PURPOSE: This study evaluated secondary stroke prevention measures in elderly long-term care patients. As the elderly population increases and there are more stroke survivors, secondary prevention is crucial for both quality of life and economic reasons.

METHODS: Medical records of 418 patients with history of ischemic stroke in 25 Ohio-based nursing facilities were evaluated. Data was collected between June 2001 and December 2001. Data evaluated were the use of antiplatelet/anticoagulant therapy as well as management of stroke risk factors (blood pressure, cholesterol and diabetes, if applicable) in accordance with current practice guidelines. Reasons for not using antiplatelet/anticoagulant therapy was prescribed 87% of the time. For all patients on warfarin therapy, 52% had an INR 2-3. Blood pressure, cholesterol and diabetes were controlled in 61%, 48%, and 50% of patients, respectively. History of gastrointestinal bleed was the most common reason for not prescribing antiplatelet/anticoagulant therapy.

CONCLUSION: The great majority of stroke patients in our study received secondary prophylaxis, which compares favorably with previously published studies. Risk factor management was suboptimal in certain areas, however, ongoing clinical trials will help definitively evaluate the role and outcome of risk factor management in elderly stroke survivors.

95. The impact of an educational intervention on caregiver knowledge of diabetes mellitus in a population-adjusted clinical epidemiology program. Karen McGee, Pharm.D., Tim A. Mullinen, Pharm.D., M.S., Diana Joachim, Pharm.D., Heather Astor, Pharm.D., Janet Thames, Pharm.D.; University of South Carolina; Palmetto Health Alliance, Columbia, SC.

PURPOSE: The purpose of this study was to evaluate the impact of an educational intervention on caregivers of elderly diabetics knowledge about
general principles of Diabetic care practices in a Geriatric Day Health Center.

METHODS. Elderly diabetic patients who take insulin or oral antidiabetic medications for the treatment of DM were identified and informed consent was obtained from their caregivers. The caregivers baseline DM knowledge was then evaluated by administering “The Diabetes Knowledge Test” from the Michigan Diabetes Research and Training Center. An educational program was presented and the caregivers were re-tested.

RESULTS. 80 elderly diabetic patients were identified at Palmetto Senior Care. For the baseline DM knowledge test 47 survey questionnaires were returned by the respective caregivers representing 59% response. After the educational intervention, caregivers were again surveyed with a repeat DM knowledge test and 23 tests were returned representing a 49% response rate of those who received the intervention. The average age for the respondents was 78 years and ranged from 28 to 93. 80% of respondents were females and 19% were males. The baseline knowledge score average was 11.1 (48.2%) and ranged from 6 (26%) to 19 (83%). The reevaluation knowledge score average was 17.8 (77.5%) and ranged from 9 (39%) to 23 (100%). The difference between the percent correct post test and baseline evaluation was significantly different using a 2-sample t-test with p<0.001 (CI of 20.2, 38.5).

CONCLUSIONS: Baseline DM knowledge scores for caregivers of elderly diabetic patients were generally low. An educational intervention provided by a clinical pharmacist significantly improved DM knowledge scores in these caregivers.

96. A randomized clinical trial of functional assessment and medication management in community-dwelling elders. Mark E. Williams, M.D., Charles C. Pulliam, M.S., Pharm.D., Rebecca Hunter, Theodore M. Johnson, M.D., Justine E. Owens, Ph.D., Jean Kincaid, Ph.D., Carol Porter, M.S., Gary K. Goo, Ph.D., University of Virginia, Charlottesville, VA; Virginia Commonwealth University, Richmond, VA; University of North Carolina, Chapel Hill, NC; Emory University, Atlanta, GA.

PURPOSE: The study objective was to measure the effect of regimen changes instituted by a specialized geriatric assessment team on medication cost and physical, cognitive and affective functioning of elders taking multiple medications.

METHODS. 133 community-dwelling elders (63 intervention subjects; 77 controls) taking five or more medications participated. Drug regimen of intervention elders were modified following a comprehensive review; both groups were assessed at baseline and 6 weeks. Measures of function included [Physical] Timed Up and Go Test, Physical Performance Test (PPT), and Functional Reach Assessment (FRA); [Cognitive] sub-tests from the Wechsler Adult Intelligence Scale (WAISR) and a modified Randt Memory Test; [Affective] the Center for Epidemiological Studies Depression Scale (CES-D) and the Self-Rating Anxiety Scale (SAS); and [Health Status] the Rand 36-item Health Survey 1.0. Comorbidity was determined by ICD-9-CM and Medication Usage by “brown bag” review.

RESULTS: Intervention subjects decreased their medications by an average of 2.3 medications from baseline to post-intervention (p<0.0001). Subjects in the intervention group had a significantly lower proportion of subjects taking 10 or more medications compared to controls (8% vs. 34.7%, p<0.01). Significant reductions in medication use were observed across all therapeutic classes. Analyses to assess the effect of factors related to accessibility for health care and, b) sociodemographic factors, on the rates of AOP drug use in this population are currently ongoing.

CONCLUSIONS: The present data suggest that an important proportion of older people with OP are not receiving drugs that are FDA approved for the treatment of OP, but rather are only receiving preventative therapy. Further research is necessary to clarify reasons for these findings.


Neuropsychiatric disturbances in patients with bipolar disorder can impact caregivers and affect overall patient management.

This a priori-defined analysis investigates changes in caregiver distress, as measured by Occupational Disruptions scores associated with each individual dimension of the Neuropsychiatric Inventory—Nursing Home version (NPI/NH) rating scale. Elderly nursing-home patients with Alzheimer's dementia were randomized to either placebo or fixed-dose olanzapine (OZl: 5, 10, or 15 mg/day) for 6 weeks of double-blind therapy. Successful completers continued an 18-month-label extension, during which they received flexible-dose OZl (5-15 mg/day). After the acute phase, reductions were seen in distress ratings reported by caregivers of patients receiving low-dose (5 mg) OZl. Significant reductions occurred relative to placebo in the NPI/NH Occupational Disruptions (OPI) scores, Psychosis Total (sum of Hallucinations and Delusions scores) and Core Total (sum of Hallucinations, Delusions, and Agitation scores) scores, and in the Delusions and Irritability dimensions. Results with higher doses (10, 15 mg) were largely nonsignificant compared to placebo. However, patients entering the extension improved significantly further on the Occupational Disruptions total, Psychosis Total, and Core Total, and in the Agitation, Delusions, Disinhibition, and Irritability dimensions. These results indicate that olanzapine may significantly reduce occupational disruptions for caregivers of dementia patients with neuropsychiatric disturbances.

98. Patterns of anti-osteoporotic drug use among older community dwelling west texans and associated factors. Carlos H. Rojas-Fernandez, Pharm.D., Keilee A. Howard, M.A., M.S., Niti Goel, M.D.; Texas Tech University Health Sciences Center, Amarillo, TX; Procter & Gamble Pharma, Galveston, TX.

PURPOSE: Emerging evidence suggests that osteoporosis (OP) is under-treated in older (≥65 years) people. There are no data however, that describe anti-osteoporotic (AOP) drug use in older people living in rural areas. The purpose of the present study is to; 1) describe the community dwelling older people living in West Texas and, 2) to assess whether factors related with accessibility to health care or sociodemographic factors affect rates of AOP drug use in this population.

METHODS: This was a cross-sectional telephone survey using the Texas Tech 5000 (TT5000) survey data set as the sampling frame. The TT5000 was a survey designed to collect health status and service information from 5000 older people living in the 108 counties that comprise West Texas. Random digit dialing was used to select the study sample. To date, two waves have been conducted: the first two waves were completed in fall of 1999 and spring of 2001. These were designed to collect baseline information regarding health care status, health care utilization, functional status, disease state information, information regarding medication use, as well as demographic information. Subjects who responded as having been diagnosed with OP or osteopenia (OPE) in the second wave were selected for the present study. A questionnaire (which was pre-tested) was developed to collect information regarding the subjects self-reported diagnoses of OPE or OP, as well how the diagnosis was established and current AOP drug use which was administered over the telephone by trained interviewers. Data from the present survey [data collection completed in March 2002] was linked with data from the previous TT5000 survey waves. The SPSS statistical software package was used for analyses.

RESULTS: In the TT5000, 744 subjects indicated that they had OP or OPE, 555 of which participated in the present study and are thus compose the study sample (the remaining 25% refused or were lost to follow up). A diagnosis of OP was reported by 72%, while a diagnosis of OPE was reported by 11%. Overall, 63% were aged 65-75 years, 37% were ≥76 years, and 93% were female. The ages and frequencies of medications which were reported by the subjects were as follows: bisphosphonates (27%), raloxifene (7%), calcitonin (3%), estrogens (28%) and calcium or calcium & vitamin D products (100%). The proportion of subjects with OP who reported taking drugs that are FDA-approved for the treatment of OP was 43%. Analyses to assess the effects of; a) factors related to accessibility for health care and, b) sociodemographic factors, on the rates of AOP drug use in this population are currently ongoing.

CONCLUSIONS: The present data suggest that an important proportion of older people with OP are not receiving drugs that are FDA approved for the treatment of OP, but rather are only receiving preventative therapy. Further research is necessary to clarify reasons for these findings.

99. Does a clinical pharmacist visit improve patient drug knowledge in the elderly? Cynthia K. Schulte, Pharm.D. candidate, Angela B. Hoth, Pharm.D., Peter J. Kaboli, M.D.; Iowa City VAMC; University of Iowa, Iowa City, IA.

PURPOSE: To determine if a clinical pharmacist evaluation is associated with increased patient knowledge of drug indication.

METHODS: The study population included 159 cognitively intact patients ≥65 years of age and prescribed ≥5 scheduled medications in a VA primary care clinic from 7/01-2/02. Randomized subjects received usual care (control) or usual care plus a clinical pharmacist evaluation (intervention). Subjects started from memory the indications for each of their medications at baseline, and 3-month follow-up interviews. Medical records were used to verify response correctness. The change in knowledge from baseline to 3-months was compared between the intervention and control groups.

RESULTS: 76 intervention and control patients with a mean age of 74 years of age, were 98% male, 98% white, and 58% completed high school. No differences existed between the groups with regard to age, sex, race, or level of education (p>0.1). At baseline, intervention patients reported taking a mean of 12.5 ± 4.1 medications and controls 11.2 ± 4.0 (p<0.05). The mean percentage of drugs indicated was known for each of their medications at baseline (p<0.05). At 3-month follow-up, intervention patients reported taking 12.0 ± 4.2 medications and controls 11.5 ± 4.1 (p=0.45). Drug indication knowledge remained steady in the intervention group at 75%, but decreased to 64% in the control group (p=0.03).

CONCLUSIONS: A clinical pharmacist visit was associated with maintenance of patient knowledge of drug indication. Control patients who did not meet with a pharmacist had a significant decrease in knowledge compared to the intervention group.
100. Assessment of factors impacting medication adherence among community-dwelling older adults. Martin R. Giannamore, Pharm.D., BCPS, Laura L. Manzey, Pharm.D., BCPP, Margaret A. Olmon, R.Ph., M.B.A., Kevin A. Townsend, Pharm.D., BCPS, Pfizer Inc., Cleveland, OH.

PURPOSE: Medication adherence scores were evaluated in community-dwelling older adults to determine if a relationship existed between medication adherence and educational level, income, number of medical conditions, number of prescription medications, and receipt of pharmacist counseling.

METHODS: Surveys were analyzed from 113 older adults who voluntarily attended medication management class at the senior citizen center between August 9 and October 24, 2001. A four-question, self-reported medication adherence measurement (designed by Morisky, et al) was included in the survey. Adherence scores were categorized as "high," "medium," or "low" based on the total score for each respondent. The Chi-Square Test of independence was utilized for statistical analysis.

RESULTS: The population was comprised of mostly Caucasian (79%) females (76%) aged 76 years (mean) with either a high school (67%) or college (20%) education. Adherence scores for 95 of the respondents were categorized as follows: 4 on the study and SAA was measured by radioreceptor assay. Anticholinergic medication exposure was quantified with the CR-ACh-mod score.

101. The relationship of an anticholinergic rating scale with serum anticholinergic activity in elderly nursing home residents. Ryan M. Carnahan, Pharm.D., Brian C. Lund, Pharm.D., M.S., BCPP, Paul J. Perry, Ph.D., BCPP, Kenneth R. Culp, Ph.D., R.N., University of Iowa, Iowa City, IA.

PURPOSE: To use serum anticholinergic activity (SAA) to assess the validity of a modified version of the clinician-rated anticholinergic scale (CR-ACh-mod) in assessing anticholinergic medication exposure.

METHODS: Subjects were part of a study of delirium in elderly residents of rural long-term care facilities. Medication regimens for assessment were from taken from a baseline time-point and included prn medications if they were administered the day before blood was drawn to measure SAA. Blood was drawn on day 14 of the study and SAA was measured by radioreceptor assay. Anticholinergic medication exposure was quantified with the CR-ACh-mod.

RESULTS: The population of 96 subjects had a mean ± SD age of 87 ± 7 years (range 68-106) and 82.3% were female. The mean ± SD SAA was 0.92 ± 0.51 pmol atropine equivalents (range 0.09-2.61). The mean ± SD CR-ACh-mod score was 2.8 ± 1.0 (range 0-9). CR-ACh-mod scores were significantly associated with SAA using linear regression (r=0.68, df =0.0087). However, the scores only explained 7.1% of the variance in SAA, suggesting that Improvements in the CR-ACh-mod may increase its robustness as a measure of anticholinergic exposure.

CONCLUSIONS: These findings help support the validity of the CR-ACh-mod. However, unexplained variance in SAA suggests that the CR-ACh-mod could benefit from improvements. Future research will evaluate the effect of including factors such as dose. An alternative explanation supported by recent research is that non-drug factors contribute to SAA.

102. Evolution of antidepressant use in elderly. Carlyle Trivin, Laurent Amico, M.D., Benoit Allenet, Pharm.D., Jean Calop, Pharm.D., Alain Franco, M.D.; Center Hospital at the University of Grenoble, Grenoble, France.

PURPOSE: Although depression states in the elderly are frequent, their diagnosis is often difficult and that is why antidepressant drugs are insufficiently used. Because drug therapy of depression evolved very much these years (e.g., new medicines, widest therapeutic indications), we thought it was interesting to take stock of antidepressant prescription in elderly people.

METHODS: A study in a geriatric care unit: One month prospectve study.

RESULTS: Antidepressant were prescribed in 36% of the patients and 57% of them received also hypnotic and sedative drugs. Most of antidepressants were selective serotonin reuptake inhibitor (46.5%): paroxetine (39.3%), fluoxetine (36.2%), citalopram (36.2%). The other molecules prescribed were lamotrigine (21.4%), mianserin (14.3%), venlafaxine (14.3%), viloxazine (3.5%). Analysis of the posology showed that guidelines for antidepressant prescription in elderly people were abided, in particular the precaution of use induced by pharmacokinetics modifications due to ageing.

CONCLUSIONS: The use of Monoamine oxidase inhibitor has significantly declined; contraindications and risks are important and their prescriptions have to be well advised and restricted. At present, tricyclic antidepressants indications are mainly the treatment of neuropenic pains. Our study showed that selective serotonin reuptake inhibitors are the most used (SSRI) and we can explain it by their effectiveness and their facilities of use (low toxicity and large therapeutic safety margin). However we must be aware that use of SSRI is not without risks, adverse effects such as hyponatremia or serotoninergic syndrome can occur, and of course there are possibilities of drug interactions. Drug therapy is necessary and important in the management of depression; nevertheless we have to remember the psychoterapeutic aspect of the treatment.

103E. Effect of proton pump inhibition on 45-calcium carbonate absorption. Mary Beth O’Connel, Pharm.D., BCPS, Denyse Madden, Pharm.D., Anne Murray, M.D., Robert F. Heaneq, M.D., Lawrence J. Kerzner, M.D.; Wayne State University, Detroit, MI; University of Minnesota, Minneapolis, MN; Walgreens Pharmacy, Woodbury, MN; Hennepin County Medical Center, Minneapolis, MN; Creighton University, Omaha, NE. Presented at the Annual Meeting of the American Geriatrics Society, Washington, D.C., May 10, 2002.

104. The impact of telepharmacy on medication appropriateness and untreated conditions in elderly veterans. Sallie D. Mayer, Pharm.D., M.B.A., Christine M. Ruby, Pharm.D., BCPS, Benita E. Busch, Pharm.D., Jack I. Tewersky, M.D.; Veterans Affairs Medical Center, Durham, NC; University Medical Center, Durham, NC; University of North Carolina, Chapel Hill, NC.

PURPOSE: This study described outcomes utilizing telepharmacy, an innovative approach to providing pharmaceutical care to patients at a distance, in order to: 1) determine if a clinical pharmacist using a telemonitor and interacting with the members of the telehomecare team could improve suboptimal prescribing, and 2) document the acceptance rate of clinical pharmacist recommendations.

METHODS: Ten elderly frail ambulatory veterans who had made six or more visits to the emergency department the preceding year and live >35 miles from the facility were enrolled from November 2001 to February 2002. Telemotors were placed in patient homes and a medication history documented. Suboptimal prescribing was assessed at baseline and closeout four weeks later using the Medication Appropriateness Index (MAI) and the Assessment of Underutilization (AOU) tools. Patients were contacted via the telemonitor every one to two weeks. All clinical pharmacy interventions were documented.

RESULTS: There was a slight increase in the number of medications from baseline to closeout although the appropriateness of these medications (as indicated by the MAI score) improved significantly (p=0.03). The number of untreated conditions trended toward improvement but was not statistically significant (p=0.25). The acceptance rate for clinical pharmacist recommendations was 71% overall (65% for therapeutic and 91% for labmonitoring recommendations) at closeout.

CONCLUSION: Medication appropriateness improved significantly and untreated conditions trended toward improvement during the study period. Our results indicate that telepharmacy interventions are effective in improving medication appropriateness and pharmacy services. A clinical pharmacist working on a geriatric interdisciplinary telehomecare team can improve suboptimal prescribing.

105. The effect of telepharmacy on elderly veteran medication compliance and patient satisfaction. Benita E. Busch, Pharm.D., Christine M. Ruby, Pharm.D., BCPS, Sallie D. Mayer, Pharm.D., M.B.A., Jack I. Tewersky, M.D.; Veterans Affairs Medical Center, Durham, NC; Duke University Medical Center, Durham, NC; University of North Carolina, Chapel Hill, NC.

PURPOSE: This study described outcomes utilizing telepharmacy, an innovative approach to providing pharmaceutical care to patients at a distance, in order to: 1) determine if a clinical pharmacist using a telemonitor and interacting with the members of the telehomecare team could improve patient compliance and knowledge, and 2) describe patient satisfaction with telemedicine.

METHODS: Ten elderly veteran patients determined to be high emergency room users (> 6 in past year) and meeting criteria for frailty were enrolled in the telemedicine study. During the initial home visit to set up the telemonitor, the pharmacist obtained a complete medication history and assessed the patient/caregiver baseline knowledge and compliance. Baseline satisfaction with the use of telepharmacy was assessed during the first telemedicine visit. Closeout satisfaction was compared with baseline data. A clinical pharmacist satisfaction with the use of technology was also reported.

RESULTS: Medication Compliance (Admission 62.6% ± 16.7, Closeout 80.8% ± 6.6) improved significantly (p=0.008). Knowledge showed improvement, but was not statistically significant (p=0.05). The acceptance rate for clinical pharmacist recommendations was 71% overall (65% for therapeutic and 91% for labmonitoring recommendations). Patient satisfaction with the telemonitors was also high (mean summated score 26.5 ± 4.3) at baseline (mean summated score 22.4, range 19-25) and remained high at closeout (mean summated score 24.3, range 23-25). Pharmacist satisfaction with the telemonitors was also high (mean summated score 26.5 out of possible 35).

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CONCLUSION: Telepharmacy improves medication compliance in an elderly veteran population and satisfaction with the technology remained high throughout the study. This is a new health care model for delivery of pharmaceutical care to elderly patients at a distance.

106E. Multi-center, open label, naturalistic study of mirtazapine orally disintegrating tablets in depressed nursing home patients. Stephen P. Rose, M.D., J. Craig Nelson, M.D., Carl Saltzman, M.D., Steven B. Holland, M.D., James V. Betzel, Columbia University, New York, NY; Yale University, New Haven, CT; Massachusetts Mental Health Center, Boston, MA; Organon Pharmaceuticals Inc., West Orange, NJ.

Presented at the 32nd Annual Meeting of the American Society of Consultant Pharmacists, Chicago, IL, November 7-10, 2001.

107E. Risperidone in treating agitation and psychosis associated with dementia. Alistair Burns, M.D., Grant Ko, M.D., Fred Grossman, D.O.; Wythenshawe Hospital, Manchester, United Kingdom; Johnson & Johnson Pharmaceutical Research & Development, LLC, Titusville, NJ.


108. Evaluation of effectiveness of alendronate and calcitonin in reducing fractures in a nursing home. Shyam D. Karki, Pharm.D., BCPS, FCCP; University of Iowa, Iowa City, IA.

Residents on A & C therapies were identified through Pharmacy records and their charts were retrospectively reviewed for number of falls and fractures during the study period. The number of falls and fractures were corroborated with incident reports. There were 25 residents on A and 24 residents on C. Residents on A had 34 falls during the year before and 36 falls during the year after its initiation. They had 13 fractures before and 0 after the initiation. Residents on C had 52 falls before and 45 falls after its initiation. There were 13 fractures before and 3 fractures after its initiation. Results were analyzed by Chi Square test and no statistically significant differences were found in falls before and after the initiation of A or C. There was a statistically significant difference in number of fractures before and after initiation of both A & C.

Our results indicate the effectiveness of alendronate and calcitonin in reducing fractures in nursing home population with osteoporosis.

109. The evaluation of pain and depression in the elderly. Carla A. Zielmann, Pharm.D., BCPS; St. Louis College of Pharmacy, St. Louis MO.

PURPOSE: This evaluation was conducted to examine how often patients' self-reporting of pain or depression were addressed by physicians in an academic VAMC geriatric clinic.

METHODS: While waiting to see the physician, each patient completes a brief 4-item self-rated pain, depression, and quality of life inventory. Patients present the completed inventory to the physician at the beginning of each clinic visit. Data for this cross-sectional evaluation were collected from 100 consecutive outpatient visits in March 2002.

RESULTS: Forty-two of the 100 patients answered the question about being in pain positively and 12 answered the question about feeling sad, blue or depressed positively. The median level of pain for patients expressing pain was 3 (range 1-10 on a 10-point scale). Of the 42 patients reporting pain, 19 physicians' progress notes included pain as a problem discussed during the visit; and action in the form of non-pharmacologic therapy, a new prescription or consultation to a specialist, was taken on 11 patients. The median level of pain for a patient the physician included in the note or acted on was 4 (range 1-10). Of the 12 patients stating they felt depressed, 7 physicians' notes included depression as a problem, and 4 noted action in the form of a new prescription or consult to psychiatry.

CONCLUSIONS: Approximately one-quarter of patients reporting pain and one-third of patients reporting symptoms of depression received new therapy for these problems. More effort should be extended to address and treat these disorders in this geriatric population.

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110. A measurement tool for physician/pharmacist collaboration. Alan J. Zillich, Pharm.D., William R. Doucette, Ph.D., Barry L. Carter, Pharm.D., BCPS, FCCP; University of Iowa, Iowa City, IA.

PURPOSE: Recently, a conceptual behavioral framework has been conceived which categorizes a hierarchy of collaboration between the physician and pharmacist. However, there is no easy method for measuring collaboration. Consequently, we developed a survey tool to elicit the degree of collaboration that occurs between physicians and pharmacists. Using the behavioral framework, a 27-item questionnaire was developed and pilot-tested for reliability and validity.

METHODS: The instrument contains 8 domains (Collaborative Care, Commitment, Scope of Relations, Dependence Symmetry, Bi-Directional Communication, Trust, Interacting Behavior, and Conflict Resolution) measured with a 7-point Likert scale. Twenty-one Family Medicine physicians at a large University outpatient clinic were asked to complete this questionnaire along with a previously validated measure of collaboration, at two time points separated by a 2-4 week interval. The instrument's construct validity was measured with a 7-point Likert scale. Cronbach's alpha ranged from 0.619 to 0.925 among the domains. All inter-item correlations were statistically significant (p<0.05). Collaboration domain correlations between the two instruments were significant (r=0.756, p<0.01). The other domain scales showed similar significant correlations between surveys. Test/Re-test correlation coefficients were in the expected direction for all domains and statistically significant in 4 of the 7 domains (p<0.01).

CONCLUSIONS: Results from this initial pilot-study indicate strong reliability and inter-item correlation for this instrument. Further research is needed to evaluate this measurement tool.

111. Treatment adequacy with venlafaxine extended-release or fluoxetine. Kristina Yu-Iserenberg, Ph.D., M.P.H., R.Ph., Christina Fontes, George J. Wan, Ph.D., M.P.H., Erika C. Geissler, R.N., M.B.A.; Prescription Solutions, Costa Mesa, CA; Wyeth Research, St. Davids, PA.

PURPOSE: This study examined treatment adequacy with venlafaxine extended-release (VENXR) or fluoxetine in a managed care setting. METHODs: A retrospective pharmacy claims analysis was performed using data from Prescription Solutions. Treatment adequacy was defined using the HEDIS Antidepressant Medication Management measures for continuous therapy for 84 or 180 days at the target dose (75-150 mg/kg for VENXR; 20 mg/kg for fluoxetine). Pharmacy claims were obtained for 90 days before and 270 days after the index prescription for either VENXR or fluoxetine during the index period (01/01/00-02/28/01). The cohort included patients newly starting with either VENXR or fluoxetine and remaining on the same medication for 84 or 180 continuous days. Logistic regression was used to evaluate the impact of VENXR or fluoxetine on treatment adequacy controlling for age, gender, prescribing physician, and pharmacy benefit type.

RESULTS: VENXR (n=3991) had an adequacy rate of 79% compared to 57% for fluoxetine (n=3389) for 180 continuous days (p=0.0001). VENXR (n=1054) had an adequacy rate of 77% compared to 52% for fluoxetine (n=2251) for 180 continuous days (p=0.0001). The adjusted odds ratios (OR) of achieving treatment adequacy with VENXR versus fluoxetine were 3.05 (95% CI=2.65-3.52) for 84 continuous days and 3.57 (95% CI=3.04-4.24) for 180 continuous days.

CONCLUSIONS: Patients prescribed VENXR achieved higher treatment adequacy rates compared to fluoxetine. Patients taking VENXR were three times more likely to achieve treatment adequacy than fluoxetine. Treatment adequacy as a proxy for optimal treatment may be an important factor to consider when selecting antidepressant medication.


PURPOSE: A trial of decentralized pharmacy technicians on one of our inpatient floors was conducted to examine the impact of this novel program on the efficiency of drug distribution, quality of patient care, clinical pharmacy practice, nursing relations, medication utilization and cost, Pyxis overrides, medication charging process, nursing time, and job satisfaction.

METHODS: Nationally certified pharmacy technicians with several years of pharmacy practice, nursing relations, medication utilization and cost, Pyxis distribution duties along with secondary duties as determined by the needs of the pharmacy. Technicians were assigned primary responsibilities and nursing relations through courses provided by the Department of Education. One medical floor was selected for the decentralized technicians with incident reports.

A pilot study was conducted to examine the impact of this novel program on the efficiency of drug distribution, quality of patient care, clinical pharmacy practice, nursing relations, medication utilization and cost, Pyxis overrides, medication charging process, nursing time, and job satisfaction. The technicians' progress notes included in the note or acted on was 4 (range 1-10). Of the 12 patients stating they felt depressed, 7 physicians' notes included depression as a problem, and 4 noted action in the form of a new prescription or consult to psychiatry.

CONCLUSIONS: Approximately one-quarter of patients reporting pain and one-third of patients reporting symptoms of depression received new therapy for these problems. More effort should be extended to address and treat these disorders in this geriatric population.

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picking IV and oral medications for the decentralized technicians to further enhance the medication turn around time (TAT). To organize the decentralized technicians daily functions the following daily reports were generated, a list of patients without height (HT), weight (WT), or allergy information active PCA/patient orders, and patients on IV medications listed in the IV to PO automation dissipation program. In addition, the technicians monitored medications ordered but not verified by pharmacists and created an on time daily transfer list to assure that medications are transferred with the patients.

RESULTS: Data to measure the effectiveness of the program was collected. There was a significant decrease in the number of phone calls to the pharmacy regarding missing medication from the unit. There was a decrease in TAT of medications (emergency, stat, and drug ordered but not loaded in Pyxis) in TAT significantly increased the number of medication overrides performed in Pyxis by nurses on that floor. There was improvement in maintenance of Pyxis machines. There was better management of outdated and expired drugs. There was considerable savings in medication cost because of the decentralized technicians tracking medication use, crediting outdated, expired, and returned medications, reusing of expensive medications (Epogen, Lovenox, ointments, inhalers, eye drops), reducing IV wastes, and providing the pharmacists with a list of patients on IV medications eligible for oral conversion. The efficient removal of outdated and expired IV medications from the floor also reduces the potential for medication errors.

Our nursing and technician survey data showed a tremendous increase in satisfaction from both sides and an actual decrease in nursing time and overtime used to track missing medications or to correct Pyxis machine problems. In addition to the results mentioned above, the focus of our staff pharmacists has shifted from dealing with drug distribution issues to providing clinical pharmacy services. The availability of HT, WT, and allergy information provided by the technicians increased the performance of the Cerner® software available in the Pharmacy computer system. This software was programmed to detect and alert pharmacists performing order entry to potential adverse drug events due to inappropriate drug dosage or organ dysfunction.

CONCLUSION: The implementation of this program was a great success in regard to improved patient care, nursing relations, clinical activities, job satisfaction, and reduced medication errors and cost. Accordingly, this program was expanded to include all of our inpatient care areas. We will continue to evaluate current activities and consider new activities, such as


PURPOSE: Recent NHANES data has reported that the prevalence of the metabolic syndrome is high in US adults. This study assessed the prevalence of this syndrome in a large urban area in the Southwest. METHODS: A citywide cardiovascular screening was held in San Antonio, Texas in December 2001. A complete data set was available for 9287 adults 20 years or older. The metabolic syndrome was defined as at least 3 of the following: triglycerides (TG) ≥ 150 mg/dL; a high-density lipoprotein cholesterol (HDL-C) level < 40 mg/dL in men or < 50 mg/dL in women; a blood pressure (BP) of at least 130/85 mm Hg; or a serum glucose level of at least 110 mg/dL.

RESULTS: The prevalence of the metabolic syndrome for the Non-Hispanic cohort was 25.6%. The most common combination was TG, HDL-C, and BP. The Hispanic population had an increased rate at 30.4%. Among the Hispanic population, men were more likely to have a metabolic syndrome than women with rates of 34% and 28% respectively.

CONCLUSION: These data are concordant with the NHANES data except for the Hispanic population where the rates are higher than the NHANES rates. The geographic area has higher rates of the metabolic syndrome compared to the US. Healthcare costs related to the metabolic syndrome are tremendous. All healthcare professionals need to aggressively screen patients on dietary modifications, increased physical activity, and weight loss.

114. Community screening for diabetes: should demographics be a factor? William D. Linn, Pharm.D., Thomas C. Shank, Pharm.D.; University of Texas, Pfizer Pharmaceuticals, San Antonio, TX.

PURPOSE: The U.S. Preventive Services Task Force does not recommend routine diabetes screening in type 2 diabetes and ADA guidelines recommend screening only under certain circumstances such as having a positive family history or being of certain ethnic backgrounds. This study looks at a large community-screening project in a predominantly Hispanic population.

METHODS: A citywide screening was held in San Antonio, Texas during December 2001. Data collected included demographics, medical history, vital signs, a full lipid profile, and a fasting or random glucose.

RESULTS: A complete data set was available for 4231 males and 5339 females. Sixty two percent were Hispanic. Fifty one percent of males had a Body Mass Index (BMI) > 27 compared to 48% of females. Two percent of males and 1% of females had a random glucose (RG) > 140 mg/dL. BMI 27% respectively, had reported fasting glucose values > 110 mg/dL. For Non-Hispanics, 8% of males and 11% of females were significantly obese (BMI > 35) compared to 12% and 17% for Hispanics. Of these, 4.5% of non-Hispanic males and 25% of Hispanic females had glucose intolerance compared to 40% and 35% for Hispanics respectively.

CONCLUSIONS: Despite recommendations against community screening for diabetes, certain cities or populations might still benefit. Pharmacists are frequently involved in these activities and should understand the significance of who would benefit the most from screening programs. Being obese, especially for Hispanic females, warrants screening. This project identified several hundred people needing aggressive lifestyle modification and/or drug therapy.


PURPOSE: Preliminary research suggests that clinical pharmacists may have a favorable impact upon depression care. The objective of this investigation was to evaluate the clinical and economic impact of pharmacists under the rigor of a randomized controlled trial. METHODS: Patients were randomized to the investigation immediately after initiation of antidepressant therapy or continued intervention group managed by the referring physician (i.e., usual care). Medication adherence and resource utilization were determined from an electronic medical information system. Clinical outcomes and patient satisfaction were compared from surveys mailed six months after randomization.

RESULTS: An intent-to-treat analysis revealed that 68% of the intervention group (n=75) and 52% of the control group (n=70) completed six months of antidepressant therapy (p=0.072; OR =1.96, 95% CI 0.88–4.39) and switch rates were higher at each level (19% vs. 4%; p=0.016). Clinical and functional outcomes were similar. Patient satisfaction was greater among the patients receiving collaborative care, specifically in regard to the MMO, overall treatment, personal nature and access to care (p<0.05 all measures). Provider satisfaction scores were also favorable. Total resource utilization was similar between groups but there was a significant decline in primary care visits with the intervention group (39% decrease vs. 1% increase; p=0.015).

CONCLUSIONS: These data suggest that direct involvement of clinical pharmacists in the management of depressed patients can improve outcomes and satisfaction. Studies of this treatment model in different health care settings appear warranted.
is often not utilized. The prescribed doses of vitamin K₁ for the reversal of
warfarin, (82%), did not follow the recommended guidelines. The clinical significance
of enoxaparin. Total hip replacement and total hip fracture was the most
ineffective usage of enoxaparin; 40% could have used less expensive
savings.
D Committee was used to evaluate the cost-effectiveness of drug selection and
PT & D Committee.
PURPOSE: This study evaluated the usage of low molecular weight heparin
for prevention of venous thromboembolism prophylaxis in acute medical
illness. Jason M. Enders, Pharm.D., Paul F. Dobesh, Pharm.D., BCPS, Joy R.
Ahuja, BCPhA; Washburn Medical Center, Topeka, KS; Kansas University Medical
Center, Kansas City, KS.
M.S., FASHP, Aimee G. Adams, Pharm.D., George A. Davis, Pharm.D.;
University of Kentucky, Lexington, KY.
PURPOSE: Hospitalized, medically ill patients are at risk for development of
venous thromboembolism (VTE). The American College of Chest Physicians currently
recommends unfractionated heparin (UFH) or low-molecular weight heparin (LMWH) for prevention of VTE in medically ill patients. Despite these recommendations, we hypothesized that the risk of VTE in this patient population is often underestimated and prophylaxis is underutilized. Our objective was to evaluate the utilization and appropriateness of prophylaxis in this medically ill population.
METHODS: A retrospective review of medically ill patients was conducted at our community hospital for patients with discharge dates between 1/2001 to 3/2002. Medically ill was defined as a non-ICU ≥ 6 day stay, and a primary diagnosis of CHF, pneumonia, or acute respiratory failure. Patient demographics, VTE risk factors, VTE prophylaxis utilization, development of symptomatic VTE, and hospital mortality were collected.
RESULTS: Data on 437 patients (63.8% male, mean age 77 ± 12 years, mean length of stay 6.9 ± 5.1 days) were evaluated. Primary diagnoses of CHF (53.1%), CHF (39.1%) and acute respiratory failure (7.8%). The average number of risk factors was 2.53 ± 0.96. No prophylaxis was given to 49.4% of patients. According to published literature, appropriate prophylaxis was given in only 10.5% of patients. Symptomatic VTE occurred in 1.8% of patients. Overall, a 3% mortality rate was observed.
CONCLUSION: The rate of thromboprophylaxis utilization was lower than the rate identified by previous investigations and appropriate prophylaxis was infrequently utilized. Pharmacists should assume an increased role in improving adherence to VTE prevention guidelines.
Evaluation of enoxaparin usage for prevention of venous thromboembolism at a community-based teaching hospital. Eunice P. Chung, Pharm.D., Judy S. Ling, Pharm.D., Jean M. Paillasses, Pharm.D.; Western University of Health Sciences, Pomona, CA; Huntington Memorial Hospital, Pasadena, CA.
PURPOSE: This study evaluated the usage of low molecular weight heparin
enoxaparin for prevention of venous thromboembolism (VTE) to) determine the cost-effectiveness of drug selection and dosage, and 2) evaluate the potential cost savings for the institution by implementing the VTE prophylaxis guideline approved by the Pharmacy, Therapeutics, and Dietary PT & D Committee.
METHODS: All orders of enoxaparin 30 mg or 40 mg during the month of February 2002 (N=150) were evaluated prospectively by reviewing the medical charts. VTE prophylaxis guideline pre-approved by the hospital PT & D Committee was used to evaluate the cost-effectiveness of drug selection and dosage. The hospital acquisition cost was used to determine the potential cost savings.
RESULTS: Of the evaluable orders (112/150), 72% were determined cost-
ineffective using enoxaparin; 40% could have used less expensive unfractionated heparin and the remaining 60% could have used a lower dose of enoxaparin. Total hip replacement and total hip fracture was the most common indication (42%) for overall usage and was also the number one reason for cost-ineffective usage of enoxaparin (96%). Implementing the VTE prophylaxis guideline could have saved $4991.58 during the 4 weeks of study period, extrapolating to annual savings of $64,890.54 on drug acquisition cost.
CONCLUSION: Enoxaparin is an effective agent for VTE prophylaxis but only in patients for specific indications. First, effective dosage and frequency varies by indication. Significant cost savings can be achieved without compromising patient care, and implementing guidelines and standard orders may be effective methods.
10. PFA for central catheter clearance: does 1 mg = 2 mg? Jodie M. Fink, Pharm.D., Kenneth M. Shermock, Pharm.D., Michael A. Militello, Pharm.D., BCPS, Donna Capozzi, Pharm.D., Thomas Hutson, D.O., Pharm.D., Matt Kalan, M.D., Brian Clem, M.D., Lehigh Valley Hospital, Allentown, PA; Hiller Hospital, Goteborg, Sweden; Hilleroed Hospital, Copenhagen, Denmark; Hamilton General Hospital, Hamilton, Canada.
PURPOSE: The purpose of this study was to determine if PFA 1 mg/ml is as effective as 2 mg/ml for clearing central venous catheter occlusions.
METHODS: Adult patients with occluded Hickman catheters or implanted ports were randomized to receive PFA 1 mg or 2 mg. After PFA was instilled into the clogged lumen for 60 minutes, catheter function was assessed. A second dose was administered, if necessary. The primary endpoint was clearance rate after one dose. Clearance rates after two doses and adverse effects were also assessed. This equivalency trial required a total of 226 lumens to show that the 1 mg dose was not more than 10% worse than the 2 mg dose.
RESULTS: A total of 61 lumens (67% Hickmans, 33% ports) were enrolled. Enrollment was stopped early due to lower than expected subject accrual. PFA 1 mg was administered to 33 lumens (36% of the lumens). The first dose clearance rates were 81.1% for PFA 1 mg and 83.3% for PFA 2 mg (% difference = -2.2% [95% CI: -8.7 to 14.1] NS). Clearance rates after one or two doses were 86.5% for PFA 1 mg and 87.5% for PFA 2 mg (% difference = 1.0% NS). No bleeding events were observed.
CONCLUSION: Although the clearance rates PFA 1 mg and PFA 2 mg were similar, statistical significance was not achieved due to the small sample size. Therefore, the relative effectiveness of PFA 1 mg versus PFA 2 mg for central catheter clearance remains undetermined.
PURPOSE: An increased incidence of venous thromboembolism (VTE) was suspected among trauma and orthopedic patients receiving a low-molecular weight heparin (LMWH) at our institution during a two-month period. The objectives of this study were to determine the frequency of VTE and identify risk factors associated with VTE development in this patient population.
METHODS: A retrospective chart review of university hospital patients during a six-month period was conducted. Patients were included if they were admitted to the trauma or orthopedic surgery service and received either dalteparin or enoxaparin for prevention of VTE. The case group was defined as patients developing clinically overt VTE following LMWH administration. The control group, defined as patients meeting inclusion criteria that did not develop VTE, was selected in ratio to the cases.
RESULTS: A total of 161 patients received dalteparin and 49 received enoxaparin. Eleven (6.8%) dalteparin patients developed VTE, compared to 6 (12%) enoxaparin patients. Forty-one percent of the cases failed to receive LMWH within 48 hours of admission, compared to 14% of controls. A greater percentage of patients at high risk of developing VTE, from either single or cumulative risk factors, was found in cases (76% vs. 38-57% of controls).
CONCLUSION: We demonstrated a low incidence of VTE in trauma and orthopedic patients receiving LMWH for VTE prophylaxis. Data suggests that the increased incidence of VTE may be attributed to LMWH timing and a large percentage of patients at high risk of developing a VTE.
12. Consistency of fondaparinux superiority for venous thromboembolism prevention in orthopedic surgery according to different composite efficacy end points. David W. Hawkins, Pharm.D., Kenneth A. Bauer, M.D., Bengt I. Eriksson, M.D., Michael R. Lassen, M.D., Alexander G.G. Turpie, M.D.; Mercer University, Atlanta, GA; Beth Israel Deaconess Medical Center, Boston, MA; Sahlgrenska University Hospital, Goteborg, Sweden; Hillerod Hospital, Copenhagen, Denmark; Hamilton General Hospital, Hamilton, Canada.
PURPOSE: In a fondaparinux phase III program in major orthopedic surgery, fondaparinux demonstrated superior efficacy over enoxaparin (overall risk reduction 55.2%, p<0.001) without increasing clinically relevant bleeding. The objective of this study was to compare the efficacy of fondaparinux versus enoxaparin for venous thromboembolism (VTE) prevention, according to different composite end points, in this setting.
METHODS: In 4 multinational, randomized, double-blind, phase III trials involving hip-fracture, 2 in hip replacement, and 1 in knee replacement, predefined composite primary efficacy end point was VTE incidence up to day 11 defined as mandatory bilateral venography detection, or documented symptomatic deep-vein thrombosis (DVT) or pulmonary embolism (PE). To match the composite efficacy end points recently suggested for superiority
studies by the American College of Chest Physicians (ACCP) Consensus (any proximal DVT + fatal PE = symptomatic proven DVT or PE) and the Committee for Proprietary Medicinal Products (CPMP, any proximal DVT + symptomatic proven PE + death from any causes including fatal PE, post-hoc analyses were performed.

RESULTS: According to criteria predefined in the protocol, the efficacy endpoint incidences up to day 11 were 6.8% (182/2682) and 13.7% (317/2376) for fondaparinux versus enoxaparin, respectively (-55.2% OR [-63.1%, -45.8% CI], p<0.0001). The efficacy endpoint incidences according to ACCP criteria were 1.7% (47/2764) and 3.3% (92/2780) for fondaparinux versus enoxaparin, respectively (-49.6% OR (-65.5%, -27.3%), p<0.0001); and 2.1% (57/2775) and 3.9% (108/2797), respectively (-48.0% OR [-63.2, -27.9%], p<0.0001) according to CPMP criteria.

CONCLUSION: The superior efficacy of fondaparinux over enoxaparin for bleeding or having an elevated INR.


PURPOSE: This study compared the accuracy of international normalized ratio (INR) results from point of care (POC) testing devices to that of a standard laboratory instrument and with each other to establish and confirm reliable INR results for anticoagulation evaluation.

METHODS: Routine INRs of 42 chronically anticoagulated patients were measured with the Coaguchek ® (Roche Diagnostics) POC device using fingerstick capillary whole blood and compared to a standard laboratory instrument (Sysmex CA-500: Dade Behring, Deerfield, IL) and the older Coaguchek ® POC device using venous blood samples acquired via venipuncture. Regression methods were used to analyze the extent, significance, and variation of the relationship between the instruments. Paired sampling (t-tests) were used to measure and compare INR differences between instruments.

RESULTS: The Coaguchek S correlated positively with the laboratory instrument (r=0.97) by orthogonal regression analysis. Similarly, the Coaguchek demonstrated a favorable correlation (r=0.94) with the laboratory instrument. Additionally, the POC devices correlated positively with each other (r=0.98), with INR values of 2.0. Paired sampling revealed mean INR differences of 0.079 ± SD 0.666, p=0.44 (Coaguchek S vs. Lab Instrument) and 0.196 ± SD 0.712, p=0.09 (Coaguchek vs. Lab Instrument).

CONCLUSIONS: POC testing devices (Coaguchek S and Coaguchek) compare favorably in accuracy with a standard laboratory instrument and with each other with INR values <4 suggesting no clinical difference in therapeutic planning of anticoagulation regimens. Repeating or cross-checking INR values above 4 with POC device with the lab instrument may be warranted.


PURPOSE: To determine the optimal range of international normalized ratio (INR) in warfarinized patients with mitral valve replacement (MVR) at the teaching hospital in Southern Thailand.

METHODS: Patients with MVR who received oral anticoagulant and had INRs measured were included in this study. These associations decreased with INR values > 4. Paired sampling revealed mean INR differences of 0.079 ± SD 0.666, p=0.44 (Coaguchek S vs. Lab Instrument) and 0.196 ± SD 0.712, p=0.09 (Coaguchek vs. Lab Instrument).

CONCLUSIONS: POC testing devices (Coaguchek S and Coaguchek) compare favorably in accuracy with a standard laboratory instrument and with each other with INR values <4 suggesting no clinical difference in therapeutic planning of anticoagulation regimens. Repeating or cross-checking INR values above 4 with POC device with the lab instrument may be warranted.

125. The use of complementary and alternative medicines by patients taking digoxin, Stephen Shalansky, Pharm.D., Erin Neall, B.Sc.Pharm.; St. Paul's Hospital, University of British Columbia, Vancouver, BC, Canada.

PURPOSE: While there are many potential interactions between digoxin and complementary and alternative medicines (CAMs), the usage patterns amongst digoxin patients are unknown. The purpose of this study was to determine the prevalence of CAM use, and types of CAMs used, amongst a cohort of patients taking digoxin. Exposures to other medications reported to interact with digoxin were also recorded.

METHODS: Patients taking digoxin were identified through review of cardiovascular rehabilitation clinic, anticoagulation clinic, and fibrillation clinic records. Those consenting to participate were given a structured survey including questions regarding use during the prior month of specific CAMs and over-the-counter (OTC) medications reported to interact with digoxin. Patients were also asked about recent symptoms associated with heart failure or atrial fibrillation, and symptoms of digoxin toxicity. Prescription medication use was identified through review of the provincial prescription claims database.

RESULTS: Vitamins and herbal supplements had been used by 34 of 57 (60%) surveyed patients in the 30 days prior to the survey. While herbal products had been used by 10 patients (18%). The most common vitamins consumed were B vitamins (42%), vitamin E (32%), multivitamins (23%), and vitamin C (21%). The most common supplement was coenzyme Q10 (7.0%), while saw palmetto (4.0%) was the only herbal product was used by more than one patient. Only 2 patients (4%) used CAMs reported to interact with digoxin (one patient used cascara and C. angustifolia, one patient used ginseng). In contrast, 28% used a potentially interacting OTC medication (excluding potassium) and 83% used a potentially interacting prescription medication. There was no statistically significant association between reported signs of disease state exacerbation (CHF or atrial fibrillation) or digoxin toxicity, and the exposures queried.

CONCLUSIONS: While overall use of CAM was common amongst this cohort of digoxin patients, exposure to potentially interacting CAMs was relatively rare.


PURPOSE: To identify the prevalence of complementary and alternative medicine (CAM) use, and the associated adverse outcomes, amongst a cohort of patients taking warfarin.

METHODS: Patients taking warfarin were identified through review of pharmacy, cardiac rehabilitation clinic, anticoagulation clinic, and fibrillation clinic records. Those consenting to participate were given a structured survey including questions regarding the use over the past month of prescription CAMs and over-the-counter (OTC) medications reported to interact with warfarin. Patients were also asked about bleeding events. Prescription medication use was identified through review of the provincial prescription claims database, and INR values were obtained from laboratory records.

RESULTS: The survey was completed by 156 patients. 72 (46%) of whom reported use CAM use over the past month including 57 (37%) who had reported use CAM reported to potentially interact with warfarin. The most common potentially interacting CAMs were vitamin E (28%), garlic (10%), and chamomile (6%). Sixty-eight patients (44%) reported bleeding events over the past month. Of the 139 patients for whom INR results were available, 11 (10%) had INRs < 4 during the past month. Comparing patients who did and did not report the use of CAMs that could potentially increase the risk of bleeding or elevated INR, there was neither a significant difference in the incidence of bleeding (37% vs. 47% respectively, p=0.21) nor the incidence of INR results > 4 (4% vs. 14% respectively, p=0.10).

CONCLUSION: While use of potentially interacting CAM was common amongst this cohort of warfarin patients, it did not appear to increase the risk of bleeding or having an elevated INR.

127. Predicting the intention to use herbal medicines using the Theory of Planned Behavior in older Veterans Affairs outpatients. Adriya A. Marfalia, S.B., Gisele V. Gupchup, Ph.D., Dennis W. Raish, Ph.D., Marica M. Wines, Ph.D., Mary Bartley, Pharm.D., Brenda Bennett, Pharm.D.: University of New Mexico; Veterans Affairs Cooperative Studies Program; Clinical Research Pharmacy Coordinating Center, Albuquerque, NM.

PURPOSE: The purpose of this study was to identify the predictors of the intention to use herbal medicines within the next six months among older Veterans Affairs (VA) outpatients, using the Theory of Planned Behavior (TPB).

METHODS: A questionnaire was administered to a convenience sample of 206 outpatients at the VA hospital in Albuquerque, NM. Patients were included in the sample if they were 65 years of age or older, of non-Latino race, speaking English, did not have a known diagnosis of dementia, and were either Hispanic or non-Hispanic white. Hierarchical regression analysis was performed to identify significant predictors of intention to use herbal medicines within the next six months.

RESULTS: A useable response rate of 73.3 percent (n=151) was obtained. Hierarchical regression analysis indicated that the only significant predictor of the intention to use herbal medicines within the next six months was the respondents' attitude towards taking herbal medicines (β = 0.69, p<0.001).

Herbal Medicine


PURPOSE: While there are many potential interactions between digoxin and complementary and alternative medicines (CAMs), the usage patterns amongst digoxin patients are unknown. The purpose of this study was to determine the prevalence of CAM use, and types of CAMs used, amongst a cohort of patients taking digoxin. Exposures to other medications reported to interact with digoxin were also recorded.

METHODS: Patients taking digoxin were identified through review of cardiovascular rehabilitation clinic, anticoagulation clinic, and fibrillation clinic records. Those consenting to participate were given a structured survey including questions regarding use during the prior month of specific CAMs and over-the-counter (OTC) medications reported to interact with digoxin. Patients were also asked about recent symptoms associated with heart failure or atrial fibrillation, and symptoms of digoxin toxicity. Prescription medication use was identified through review of the provincial prescription claims database.

RESULTS: Vitamins and herbal supplements had been used by 34 of 57 (60%) surveyed patients in the 30 days prior to the survey. While herbal products had been used by 10 patients (18%). The most common vitamins consumed were B vitamins (42%), vitamin E (32%), multivitamins (23%), and vitamin C (21%). The most common supplement was coenzyme Q10 (7.0%), while saw palmetto (4.0%) was the only herbal product was used by more than one patient. Only 2 patients (4%) used CAMs reported to interact with digoxin (one patient used cascara and C. angustifolia, one patient used ginseng). In contrast, 28% used a potentially interacting OTC medication (excluding potassium) and 83% used a potentially interacting prescription medication. There was no statistically significant association between reported signs of disease state exacerbation (CHF or atrial fibrillation) or digoxin toxicity, and the exposures queried.

CONCLUSIONS: While overall use of CAM was common amongst this cohort of digoxin patients, exposure to potentially interacting CAMs was relatively rare.
The other variables in the TPB, subjective norms, or what others think about taking herbal medicines, and perceived behavioral control, were not significant predictors of intention to use herbal medicines within the next six months. The Adjusted R² for the hierarchical regression model was 0.58, p<0.001.

CONCLUSION: Attitude towards taking herbal medicines is a strong predictor of the intention to use herbal medicines within the next six months among older VA outpatients. These findings have important implications for pharmacy practitioners as they develop counseling strategies about herbal medicines for older VA outpatients.

128. Comparison of recommendations made by pharmacists and health food store employees in a depressed patient. James K. Glisson, M.D., Pharm.D., Holly E. Rogers, Pharm.D., Sara L. Noble, Pharm.D.; University of Mississippi Medical Center; Pfizer, Inc.; Jackson, MS.

PURPOSE: Literature regarding health food store employees’ and pharmacists’ recommendations for alternative therapies is scarce. This study was conducted to evaluate the advice pharmacists and health food store employees provide to consumers concerning the use of dietary supplements in a given case scenario dealing with anxiety and depression.

METHODS: The survey was performed as a simulated consumer case encounter in 32 health food stores and 38 retail pharmacies. Prior to conducting the survey, the case scenario was reviewed and approved by a board certified primary care physician. All customer questions were asked in a specific order to maintain consistency, and each investigator made notes during the interaction, providing additional information only if elicited, such as the use of St. John’s Wort.

RESULTS: Past medical history, concurrent medications, and allergies were not consistently determined prior to the given advice. Eighty-eight percent of health food stores employees and 60% of pharmacists suggested the use of at least one product; however, less than 20% in each group asked about concurrent medications. Twelve pharmacists, 32%, recommended seeing a physician for evaluation; however, no person asked about existing medical conditions. Only 1 health food store employee asked if any allergies existed, and eight stated that it was appropriate to use the recommended product during pregnancy. No pharmacists made this recommendation. Finally, approximately 75% of those surveyed stated the recommended products were devoid of side effects.

CONCLUSION: The quality of information provided to consumers as they consider the use and purchase of dietary supplements is of major concern. This study identifies several areas that need addressing.

129. Use of dietary supplements in a rural Mississippi clinic population. J. Emmy Steevens, Pharm.D., James K. Glisson, M.D., Pharm.D., Holly E. Rogers, Pharm.D., Emily C. Dix, Ph.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: Demographics of dietary supplement users in metropolitan areas are well documented. Limited data exists on usage patterns in rural areas. The purpose of this investigation was to determine patients’ patterns, reasons for use, opinions regarding safety, regulation and efficacy, and patients’ perceptions of health care provider knowledge of dietary supplements.

METHODS: This study was conducted in a rural, Mississippi family medicine clinic. Patients provided information such as frequency, number and approximate monthly expenditure of supplements, and how likely they would be to take recommendations by a physician, pharmacist, health food store employee, or friend. Patients were asked to rate their perception of the dietary supplement knowledge of pharmacists, physicians, and health food store employees.

RESULTS: One hundred fifty-one patients completed the survey. The majority of dietary supplement users were white (88.2%) and female (71.6%). The most common reasons for use were general health (68.6%), energy (28.4%) and weight loss (19.6%). The most common sources for information on dietary supplements were physicians (35.3%), friends (25.5%), relatives (23.5%), and magazines (22.5%). When asked to identify the best source of information, patients differed (31%) were cited most frequently, followed by pharmacists (9%), and herbalists (8%). Both users and nonusers agreed dietary supplements undergo the same federal government approval process as pharmaceutical drugs, requiring them to be proven safe before sold in stores.

CONCLUSION: This study demonstrates patient misperception of quality and regulatory issues concerning supplements. It describes patient willingness to discuss and implement recommendations for supplement use with non-healthcare providers despite believing physicians and pharmacists are knowledgeable.

130. The clinic at the health food store: employee recommendations for depression and product analysis by HPLC. Holly E. Rogers, Pharm.D., James K. Glisson, M.D., Pharm.D., Ethab A. Abourashed, Ph.D., Richard L. Ogletree, Pharm.D., Charles D. Hufford, Ph.D., Ikhlas Khan, Ph.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: Increasing numbers of patients are self-medicating with dietary supplements. Significant concern exists among healthcare providers regarding the composition, safety, and efficacy of these supplements. Furthermore, patients may receive medical advice within health food stores. The purpose of this study was to determine specific products health food store employees recommend for depression and to compare the actual content of these products to the stated label content. METHODS: Twelve health food stores were selected for inclusion. A single investigator conducted all inquiries by approaching one employee within each store and asking, “What do you recommend for depression?” Five additional questions were then posed to elicit further information. Products containing St. John’s Wort were purchased and analyzed for hypericin and pseudohypericin content via HPLC and then used to calculate total hypericins content.

RESULTS: Numerous comments made by health food store employees regarding St. John’s Wort and the treatment of depression were inaccurate and potentially unsafe. No products contained ± 10% of the stated label claim for hypericin, and two products contained 0% hypericin. However, two products total hypericins content was within ± 10% of the label claim for hypericin alone.

CONCLUSIONS: Health food store employees offer healthcare advice regarding the treatment of depression with dietary supplements. Furthermore, the discrepancies noted between actual product content and manufacturers’ label claims continue to raise concern for those patients who choose to employ these agents as medical treatment. These inconsistencies will continue to be a significant barrier to acceptance by the conventional medical community until reliable, good quality products are available.

131. Complementary and alternative medicine: Tennessee pharmacists’ use, counseling and referral practices. Peter A. Chyka, Pharm.D., Glen E. Farr, Pharm.D.; University of Tennessee Health Science Center, Memphis, TN.

PURPOSE: To determine the extent and variety of Tennessee pharmacists’ use of complementary and alternative medicine (CAM) therapies and providing advice or referral thereon. METHODS: During Autumn 2001 a 60-item survey was administered to pharmacists who participated in one of five continuing education programs conducted throughout Tennessee. Inclusion criteria included completion of all survey elements and a Pharmacy practice in Tennessee.

RESULTS: A total of 650 surveys were submitted and 349 met the inclusion criteria. Of these, 317 pharmacists (90.8%) personally used (n=299, 85.6%), advised patients (n=425, 73.9%) or referred individuals (n=427, 76.5%) for CAM, termed “CAM-practice.” The top two approaches for which pharmacists were unsure of the definition were body work (48.4%) and biofeedback (32.4%), that they personally used were dietary supplements (61.0%) and spiritual healing (54.7%), for which they referred patients were dietary supplements (55.0%) and chiropractic (38.7%), and on which they counseled patients were dietary supplements (66.5%) and spiritual healing (33.8%). The use of CAM was more likely (OR=2.8, CI 1.5, 5.2) by a pharmacist in a community pharmacy practice (90.5%) compared those in other practices (77.3%). The number of years in practice and geographic region did not affect the use of CAM-practice. An adverse event from CAM in the past year was suspected more often by pharmacists who did not CAM-practice (75.0%) than those who did so (29.3%, p<0.001). Further education on CAM was desired by 79.4% of respondents.

CONCLUSIONS: Pharmacists use CAM therapies and provide advice or referral thereon; they desire additional education on CAM.

132. Prospective randomized evaluation of herbal product use in surgical patients. José D. Rivera, Pharm.D., Mona Liza R. Valentín, Pharm.D., Emmett L. McGuire, M.D., Kaloll Chaudhuri, M.D.; University of Texas; Texas Tech University Health Science Center, El Paso, TX.

PURPOSE: To evaluate the use of herbal supplements among surgical patients in a predominantly Hispanic population. METHODS: Prospective randomized evaluation of patients aged 18 years or older scheduled for surgery. Prior to surgery, a 15 to 30 minute semi-structured interview was conducted focusing on the use of herbal products that have associated with adverse events. Two days after surgery, the interviewer conducted a chart review recording any complications that the patient experienced during or after surgery.

RESULTS: Seventy percent of our sample (N=115) admitted to using herbal products. About 58% of patients rated the products as “excellent” in treating their conditions and 92% of them did not inform their physician of their use. Among the herbal products that were used, 18% of the products are known to cause adverse reactions, 12% are associated with causing drug interactions, and 10% are known to negatively interact with specific disease states. Nine patients who reported using herbs had complications during and two days post surgery.

CONCLUSION: With the growing use of herbal products and because most user do not inform their physician, there is increasing concern related possible herbal related adverse events during surgery. The current study documented at least 141 instances that may lead to herbal related adverse events. Eleven percent of herbal users had documented complications during surgery. A thorough examination of a patient’s medication history including use of herbal products should consistently be performed in order to minimize complications during and after surgery.
133. Use of herbal products in asthmatic living on the U.S./Mexican border. José O. Rivera, Pharm.D., Harold W. Hughes, M.D., Sean M. Connery, M.S.; University of Texas; Texas Tech University, El Paso, TX.

PURPOSE: To evaluate the prevalence of herbal products (HP) usage in adult, asthmatic requiring hospitalization.

METHODS: A retrospective chart review of admissions for asthma was conducted to determine HP use. Subsequently, a prospective, semi-structured interview analysis was conducted in patients who were admitted for asthma exacerbations for a one-year period. A bilingual interviewer was used to evaluate types and frequency of HP use specifically for the treatment of asthma.

RESULTS: A total of 67 cases were reviewed retrospectively while 60 were interviewed. We found no documentation of HP use by chart review while prospective interviews showed 41.7% using HP. Of the 25 who used HP the most common were: oregano 28%, chamomile 20%, garlic 16%, eucalyptus 12%, and lemon 12%. A total of 8 patients reported taking an HP that could possibly result in a drug interaction with an anti-asthma medication or could actually exacerbate the asthma. In addition, another 16 patients reported using an HP that could interact with other drugs or cause other types of adverse reactions. Of greatest concern is the use of these herbs as essential oils either taken internally or applied directly to nasal passages.

CONCLUSION: There is an obvious lack of documentation regarding herbal product use in medical records most likely due to the fact that many healthcare providers are not be aware of the potential effects of herbal products. Some herbal products used in our population could actually interact with anti-asthma agents and/or result in compromised asthma control, therefore this information should be included in routine history examinations.

HIV/AIDS


PURPOSE: HIV-1 PIs are associated with glucose intolerance. Gestational diabetes (GD) is associated with maternal-fetal complications. We investigated the placental (PL) and fetal outcomes following in utero exposure to NFV treatment.

METHODS: A total of 21 female Sprague-Dawley rats were randomly assigned to a control (C), low dose (LD) NFV (100 mg/kg/d) or high dose (HD) NFV-treated (400 mg/kg/d) group. Rats were mated overnight. Sperm-positive vaginal smears denoted day 0 of pregnancy. Necropsy was performed at day 20 of gestation. The placenta and fetuses were isolated, weighed and measured. Fetal livers (FL) were removed and weighed. Maternal plasma glucose (MPG) was determined. Two pathologists performed histology reviews in a blinded-manner. Data were analyzed by ANOVA, Tukey post hoc testing, and with significance at p<0.05.

RESULTS: Necropsy was performed on 7 C (total of 100 concepti), 8 LD (118 concepti) and 6 HD NFV-treated (77 concepti) dams. The mean ± SEM PL weight ratio was 33.0 ± 0.005 gms and 32 ± 0.008 gms in C, LD and HD NFV-treated groups, respectively (p<0.001). The PL surface area (SA) was significantly larger in the HD and NFV-treated groups as compared to C (p<0.05). A significantly lower FL weight ratio was observed in the HD and NFV-treated groups as compared to C (p<0.001). NFV-treated dams had higher glucose levels, but the difference was not statistically significant. Diffuse congestion, multifocal telangiectasia, and myeloid and erythroid hyperplasia were observed for all FL in both LD and HD NFV-treated dams.

CONCLUSIONS: Our data suggest the alterations in PL weight and SA and FL weight ratios are consistent with experimental model of GD, despite a lack of statistical difference in MPG.

135. Effect of ritonavir-containing regimens on lipids compared to other protease inhibitors. Susan Haselcorn, Pharm.D., Mariel Segara-Newnam, Pharm.D., BCP5; Veterans Affairs Medical Center, West Palm Beach, FL.

BACKGROUND: Protease inhibitor (PI) therapy may cause increases in lipids. Ritonavir appears to cause the largest increase in a dose-dependent fashion. However, there are limited data on how different protease inhibitors compare with each other within the same patient.

PURPOSE: To evaluate the effect of ritonavir-containing regimens on triglycerides (TG) and total cholesterol (TC) compared to other PIs in patients followed at an ambulatory clinic.

METHODS: Patients on ritonavir-containing PI regimens after treatment failure with other PIs were evaluated. All patients who had lipid values available while on other PI and after ritonavir were included. The following data were collected: age, body mass index, anti-retroviral regimen, TC and TG during non-ritonavir PI therapy and after ritonavir therapy. The addition or change in lipid-lowering therapy was also recorded. Eleven patients were needed for 90% power to detect a 50-point change in TC or TG. The institutional review board approved the study.

RESULTS: Eighteen patients were eligible for inclusion. Fifty-six percent of patients were receiving ritonavir 100 mg BID and 38% were receiving ritonavir 400 mg BID. A significant increase in both TC and TG was seen in patients receiving ritonavir-containing regimens compared to other PIs (TC 229 vs. 204 and TG 313 vs. 213, p<0.05, paired t-test). Three patients were receiving lipid-lowering therapy prior to ritonavir with one needing a dose adjustment after the addition of ritonavir. Two patients were started on lipid-lowering therapy and one on low fat diet after ritonavir was initiated. The clinical pharmacist is following these patients.

CONCLUSIONS: Patients who are to start ritonavir therapy need to be closely monitored for changes in TC and TG. Changes or addition of lipid-lowering therapy may be needed even if other PI did not cause a change in lipid values. A clinical pharmacist can provide the follow up necessary and adjust medications as indicated.

136. Characteristics of metabolic abnormalities and lipodystrophy associated with drug therapy in human immunodeficiency virus-infected children. Sandra Benavides, Pharm.D., Katalin Koranyi, M.D., Milap C. Nahata, Pharm.D.; Ohio State University, The Children's Hospital, Columbus, OH.

OBJECTIVES: The objective of the study was to assess the characteristics of metabolic abnormalities and lipodystrophy in HIV infected children and determine their association with antiretroviral medications.

METHODS: Medical records of all pediatric patients seen at the Immunodeficiency Clinic at Children's Hospital, Columbus, Ohio from July 1, 1999 to July 31, 2001 were reviewed. The data on patient demographics, date of diagnosis, antiretroviral medication history, laboratory results, and evidence of lipodystrophy were collected. Endpoints included evidence of lipodystrophy, elevated serum glucose, cholesterol and/or triglyceride concentrations. Descriptive statistics were compiled and patients were stratified into two groups (evidence of abnormality or not) for each endpoint. Cross tabulations were used to determine if antiretroviral history differed between groups.

RESULTS: Twenty-two pediatric patients (M =13, F =9), ages 1.6-16.4 years, were included in the study. Of these patients, two (9.1%) developed lipodystrophy, 13 (51%) hypercholesterolemia, 13 (51%) hypertriglyceridemia, and one hyperglycemia. Mean serum cholesterol concentrations was 206 mg/dL (SD ± 37) and mean serum triglyceride concentration was 232 mg/dL (SD ± 154). These values were statistically higher than normal values for pediatric patients. The lack of significant utilization was approaching significance (p=0.06) for those patients developing lipodystrophy. Increased serum glucose, cholesterol and triglyceride concentrations did not correlate with any specific agent or length of treatment with any specific drug. The correlation among the disorders was not significant.

CONCLUSIONS: Pediatric patients infected with HIV developed elevations in cholesterol and triglycerides. As also seen in the adult HIV literature, the specific agents or cause of these abnormalities is not clearly defined.

137E. Abacavir systemic clearance in children is highly influenced by glucuronidation phenotype. John H. Rodman, Pharm.D., Shane J. Cross, Pharm.D., Lawrence E., Smith, M.D., M.P.H., C. Rose, Brian L. Robbins, Ph.D., Gregory K. Yuen, Pharm.D., St. Jude Children's Research Hospital, Memphis, TN; Children's National Medical Center, Washington D.C.; GlaxoSmithKline, Research Triangle Park, NC.

Presented at the 14th Annual International AIDS Conference, Barcelona, Italy, July 7-12, 2002.

Infectious Diseases

138. Impact of clinical pharmacists on vaccination rates in medicine, surgery, and infectious disease services: a randomized, controlled trial. Peter Duma, Pharm.D., John Dougherty, Pharm.D., Monica Shieh, Pharm.D.; Wayne State University; Harper University Hospital, Detroit, MI.

PURPOSE: We evaluated the impact of clinical pharmacist (CP) on inpatient pneumococcal (PV) and influenza vaccination rates (IV) in 3 patient care services: medicine, surgery and infectious diseases (ID).

METHODS: Patients admitted to Harper University Hospital from 11/01 to 3/02 and who were being followed by a CP on the medicine, surgery or ID service were enrolled. Patients were randomized (by admission date) to active CP involvement for vaccination or usual care. Screening and recommendations were incorporated into the CP's daily schedule.

RESULTS: IV and PV rates increased in all groups (p<0.05) except for IV in the surgery group.

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Medicine</th>
<th>Surgery</th>
<th>PV Rates</th>
<th>IV Rates</th>
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<td>Influenza</td>
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<td>Pneumococcal</td>
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<td>N</td>
<td>Age</td>
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<td>25</td>
</tr>
</tbody>
</table>
139. Impact of new and proposed MIC breakpoint changes on the in vitro activity of penicillin and ceftriaxone against non-meningeal isolates of Streptococcus pneumoniae. Michael B. Kays, Pharm.D., Gerald A. Denys, Ph.D., Daryl J. Hoban, Ph.D.; Purdue University, Indianapolis, IN; Clianian Health Partners, Inc., Methodist Hospital, Indianapolis, IN; International Health Management Associates, Inc., Schaumberg, IL.

The clinical significance of β-lactam resistance in non-meningeal (NM) isolates of Streptococcus pneumoniae (SP) is debatable. Penicillin (PEN) and ceftriaxone (CTRX) MIC breakpoints (BP) were originally based on achievable CSF concentrations. In 2000, the Drug-Resistant Spor Therapeutic Working Group (DRSPWG) recommended separate PEN BP for patients with pneumococcal pneumonia. In 2002, the NCCLS increased CTRX BP for NM isolates of SP.

PURPOSE: To evaluate the impact of MIC BP changes on the in vitro activity of PEN and CTRX against NM isolates of SP.

METHODS: Clinical, non-duplicate SP isolates (n=7,375) cultured from NM (respiratory, blood) sources from 1999 to 2002 were studied. PEN and CTRX MICs were determined by E-test according to manufacturer’s guidelines. PEN MICs were interpreted using the NCCLS BP (susceptible [S], ≤0.06 µg/ml; intermediate [I], 0.12-1 µg/ml; resistant [R], ≥2 µg/ml) and the proposed DRSPWG BP. CTRX MICs were determined by the previous NCCLS BP (≤0.5 µg/ml; I, 1 µg/ml; R, ≥2 µg/ml; M100-S11, 2001) and the new NCCLS BP (S, ≤1 µg/ml; I, 2 µg/ml; R, ≥4 µg/ml; M100-S12, 2002).

RESULTS: The MIC90 of PEN and CTRX were 0.04 µg/ml and 2 µg/ml for PEN and 0.03 µg/ml and 1 µg/ml for CTRX, respectively. For PEN, S, and R were 59.0%, 20.4%, and 20.6% using the NCCLS BP and 79.4%, 11.3%, and 9.3% using the proposed DRSPWG BP. For CTRX, S, I, and R were 81.2%, 13.7%, and 5.1% using the previous NCCLS BP and 94.9%, 3.7%, and 1.4% using the new NCCLS BP. CTRX-R decreased from 1.9% to 0.6% for PEN and from 22.9% to 6.0% for PEN-R strains using the new NCCLS BP.

CONCLUSIONS: The percentage of NM SP isolates reported as I and R to PEN and CTRX is markedly decreased when MICs are interpreted using the new or proposed BP. However, continued surveillance of resistance trends is necessary as isolates may remain resistant to these agents despite BP changes.


BACKGROUND: Some toxicity and activity of anti-mycotics can be predicted based on changes in gene expression profiles. However, mycotic organisms alter the host cell milieu in attempts to improve pathogen survival.

OBJECTIVES: To evaluate the effects of fungal infections on anti-mycotic induced human gene expression in vivo.

METHODS: Participants with disseminated candidiasis treated with an azole, polyene or echinocand were evaluated. Total RNA was isolated from cells obtained during peripheral venipuncture using the Triazol reagent. cDNA was synthesized using anchoring primers and labeled using Cy3 or Cy5. Complementary DNA were then hybridized to a human gene array containing >12,000 known genes. The variability in gene expression could be accounted for by the potent effects of desoxycholate (DOC) alone. Calcium channel, integrin, T cell receptor and β1 integrins were considered unique to one of the treatment groups. Eighty-four percent of the product-moment analysis was performed on the two expression outcomes.

RESULTS: Three hundred forty-two up and 621 down-regulated CDAs were considered unique to the treatment groups. Eighty-four percent of the variability in gene expression could be accounted for by the potent effects of antifungal B/D."
144E. Hospital demographics and prevalence of methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus faecium. Kevin W. Garay, Pharm.D., Katie Suda, Pharm.D., Vikas Gupta, Pharm.D., Alisa Goetz, Pharm.D., Scott Larson, M.D., TX; University of Illinois, Chicago, IL; Cardinal Health Provider Pharmacy Services, Houston, TX.


145E. Regional variation in Gram-positive antimicrobial susceptibility patterns from non-teaching hospitals throughout the United States. Kevin W. Garay, Pharm.D., Katie Suda, Pharm.D., Vikas Gupta, Pharm.D., Alisa Goetz, Pharm.D., Jennetre Tran, Pharm.D.; University of Houston, Houston, TX; University of Illinois, Chicago, IL; Cardinal Health Provider Services, Houston, TX.

Presented at the 12th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America, Salt Lake City, UT, April 6-9, 2002.


147. Sequential intravenous to oral moxifloxacin monotherapy for community-acquired pneumonia. Charles Fogarty, M.D., Dimitrios P. Kontoyiannis, M.D., Sc.D.; University of Houston; University of Texas, Houston, TX.


148E. In vitro susceptibility of bloodstream candidiasis in cancer patients: correlation with outcome of antifungal therapy. Russel E. Lewis, Pharm.D., Anastasia Antonidou, M.D., Harrys A. Torres, M.D., John Thororny, Ph.D., Jeffery Tarrand, M.D., Dimitrios P. Kontoyiannis, M.D., Sc.D.; University of Houston; University of Texas, Houston, TX.

158. Relationship between antimicrobial usage and prevalence of Gram-negative bacterial resistance at a teaching hospital in southern Thailand.

Sutthiporn Pattharachayakul, Pharm.D., BCPS; Prince of Songkla University, Songkhla, Thailand.

PURPOSE: The purpose of this study was to assess the relationship between antimicrobial usage and prevalence of gram negative bacterial resistance.

METHOD: Antimicrobial usage including ceftazidime, imipenem, gentamicin, ciprofloxacin and ceftazidime/sulbactam were collected annually from 1998 to 2000. The amount of antimicrobial usage in gram was converted into defined daily dose (DDD)/1000 patient-days. Prevalence of antimicrobial resistance of 5 common hospital acquired gram negative bacteria including Acinetobacter baumanii, Pseudomonas aeruginosa, Escherichia coli, Enterobacter cloaceae and Klebsiella pneumoniae were collected from 1999-2001. Correlation between antimicrobial usage and prevalence of Gram-negative bacterial resistance were assessed statistically using the Spearman Rank Correlation Analysis (SPSS System for Windows v 7.5).

RESULTS: There was a significant correlation between ceftazidime usage and prevalence of ceftazidime resistant P. aeruginosa, E. coli, A. baumanii and K. pneumonia (r = 1, p=0.00). In addition, we found a significant correlation between ciprofloxacin usage and prevalence of ciprofloxacin resistant A. baumanii and P. aeruginosa (r = 1, p=0.00), as well as imipenem usage and the prevalence of imipenem resistant P. aeruginosa (r = -1, p=0.00).

CONCLUSION: There was a strong relationship between some antibiotic usage and the prevalence of gram negative antimicrobial resistance, the task control to use of those antimicrobial agents is needed.

159E. National survey of antifungal susceptibility testing practices in community hospitals throughout the United States.

Katie J. Suda, Pharm.D., Manjunath (Amit) P. Pai, Pharm.D., Vikas Gupta, Pharm.D., BCPS; University of Illinois at Chicago, Chicago, IL; Cardinal Health Provider Pharmacy Services, Houston, TX; University of New Mexico, Albuquerque, NM.


160E. National survey of extended-spectrum β-lactamase susceptibility testing practices in community hospitals throughout the United States.

Katie J. Suda, Pharm.D., Vikas Gupta, Pharm.D., BCPS; University of Illinois at Chicago, Chicago, IL; Cardinal Health Provider Pharmacy Services, Houston, TX.


P. David Rogers, Pharm.D., Ph.D., Katherine S. Barker, Ph.D., Vanessa Herring, B.S., Melissa Jacob, Ph.D.; University of Tennessee, Memphis, TN; University of Mississippi, Oxford, MS.


162E. Pneumolysin-dependent cytokine and chemokine production in THP-1 cells exposed to Streptococcus pneumoniae.

P. David Rogers, Pharm.D., Ph.D., Justin Thornton, B.S., Katherine S. Barker, Ph.D., Edwin Swiatek, M.D., Ph.D., Larry S. McDaniel, Ph.D.; University of Tennessee, Memphis, TN; University of Mississippi Medical Center, Jackson, MS.


163. Functional genonomic analysis of coordinate gene expression in stepwise acquisition of high level azole antifungal resistance in Candida albicans.

P. David Rogers, Pharm.D., Ph.D., Katherine S. Barker, Ph.D.; University of Tennessee, Memphis, TN.

PURPOSE: The purpose of this study was to identify genes that contribute to azole antifungal resistance by examining differential gene expression on a genomic scale throughout the stepwise acquisition of this phenotype.

METHODS: Four isogenic, serial, clinical isolates of C. albicans were obtained from an AIDS patient with oropharyngeal candidiasis who failed fluconazole therapy (isolates 2, MIC=0.25 μg/ml; 3, MIC=4 μg/ml; 15, MIC=16 μg/ml; and 17, MIC=64 μg/ml). RNA was isolated for cDNA microarray analysis. Gene expression profiles for isolates 3, 15 and 17 were compared to that of isolate 2.

RESULTS: As expected, CDR1 and CDR2 were up-regulated only in isolate 17, whereas MDR1 was up-regulated in isolates 3, 15 and 17. Among the additional genes up-regulated in isolate 17 were 4 genes coordinately regulated with CDR1/2 (ERG2, GPX1, LT1V, RTA3) and 7 coordinately regulated with MDR1 (GPR2, IFDL, IFD4, IFD5, IFD7, MAL31, IFP987). Among the 11 genes down-regulated in isolate 17 were 5 genes coordinately down-regulated with CDR1/2 (BP1, CDK2, DALS, OCD1, PFZ2, SP072, SU2, and 7 unknown) and 4 coordinately down-regulated with MDR1 (FET34, SOD1, and 2 unknown). Other down-regulated genes included glutathione pathway genes (GTH2, IFP11526), chitin synthase genes (CHS1, CHS4), and agglutinin-like protein genes (AL52, AL53, AL59).

CONCLUSIONS: These results implicate a multitude of gene products in azole resistance. Furthermore, they demonstrate the coordinate expression of the IFD family of arylic alcohol dehydrogenase enzymes with the MDR1 efflux pump, and the ergosterol biosynthesis enzyme, C-8 sterol isomerase, as well as the glutathione pathway with the CDR efflux pumps.

164. Surgical antimicrobial prophylaxis: administration timing analysis.

Eileen M. Sakai, Pharm.D.; Pharmacology Healthcare Solutions, Grapevine, TX.

PURPOSE: This study identifies the key steps that can influence the timing of the preoperative antibiotic (Pre-Op Abx.) administration in surgical patients.

METHODS: The medical records of 130 contaminated or clean-contaminated procedures in October 2000 were reviewed. The type of patient, timing of drug allergy documentation, and timing of Pre-Op Abx. administration, name/dose of Pre-Op Abx., and location/person for Pre-Op Abx. administration were documented.

RESULTS: The surgical procedures were performed in 36 In-Pt, and 64 In-Amb. Pre-Op Abx. administration timings resulted in 10.3% “Early” (>30 minutes prior to incision); 44.8% “On-Time” (30-120 minutes prior to incision); 38% “Late” (>30 minutes prior or after incision); and 6.9% “Not given”. The allergy documentation and Pre-Op Abx. ordered rates were 77.8% and 93.8% for “Early”, 64% and 67.5% for “On-Time”, 89.2% and 87.2% for “Late”, compared to 90.7% and 91.8% for Pre-Op Abx. and Pre-Op Abx. documentation, respectively. The “Late” was the highest when allergy documentation and Pre-Op Abx. ordered. On-time documentation and Pre-Op Abx. Ordering were done prior to surgery date -51.5% and 52.5% respectively. The “Late” was the highest when allergy documentation and Pre-Op Abx. Ordering were done prior to surgery date -55.6% and 54.5% respectively. The majority of “On-Time” doses were administered in the Preoperative Holding Unit; all of the “Late” doses were given in OR. The storage location of the antibiotics did not make a difference in administration timing. The antibiotics with longer required infusion time were more prone to be “Late”. Diffused responsibility for antibiotic administration in Preoperative Holding Unit added to the delay of the administration timing.

CONCLUSION: The timing of patients’ drug allergy documentation and Pre-Op Abx. administration timing being one of the key factors in preventing Surgical Wound Infections, recognition of the importance of Pre-Op Abx. administration timing by surgeons and anesthesiologists is imperative in order to make a difference in their practice pattern.


Kevin A. Enzweiler, Pharm.D., John A. Bosso, Pharm.D., Roger L. White, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To compare activity of macrolides (M), ketolides (K), azithromycin, and clindamycin (C) against S. pneumonias (SP) using an integrated database of MIC studies.

METHODS: We assessed susceptibility (S) to 6 drugs, including K (telithromycin (T) and ABT-773 (AB)) using a database of published studies (n=61). Isolates were divided into penicillin S, macrolide S, and resistance [telithromycin (T) and ABT-773 (AB)] using a database of published studies.

<table>
<thead>
<tr>
<th>Drug # isolates</th>
<th>mef E</th>
<th>mef A</th>
<th>erm B</th>
<th>ery R</th>
</tr>
</thead>
<tbody>
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<td>Clarithromycin</td>
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<td>ABT-773</td>
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</tbody>
</table>

PHARMACOTHERAPY Volume 22, Number 10, 2002
CONCLUSIONS: From this analysis utilizing a large database of 61 studies, K appear more potent against SP than the other agents evaluated, including those isolates resistant to M, A, and C.

166. Percent susceptible vs. percent resistant: should both markers be used in surveillance of susceptibility trends? Kevin A. Enzweiler, Pharm.D., John A. Bosso, Pharm.D., Roger L. White, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To determine if % resistance (%R) is a more sensitive marker than % susceptible (%S) in the assessment of susceptibility trends.

METHODS: Nine years of aggregate susceptibility data (1992-2000) for 5 Gram-positive and 8 Gram-negative organisms against 29 antimicrobials from our hospital were analyzed. Each organism was evaluated against at least 10 isolates representative of all culture sites were analyzed by linear regression. Only those data sets (same organism, same drug, same hospital area, same culture site) with relatively strong relationships (R2 > 0.5) for each %S or %R vs. time were further analyzed. To compare the strengths of the relationships, the ratio of R2 (%R value / %S value) was determined. Instances when R2 for %R vs. time was (NA), Europe (EU) and Asia (AS). Using criteria of A > S.

RESULTS: Of the 360 possible relationships involving 398,487 drug/organism pairs, 45% (n = 154) met our criteria with 65% (100/154) having pos slopes. EU had the highest rate of pos slopes (rate = 1.1), although 45% (n = 154) using Monte Carlo analysis. The subsets of pos (MICs) and steepest pos slopes (0.6) were analyzed with ANOVA for slope differences. The rate of occurrences of pos (0.6) were noted in 20% stronger or weaker (determined by the R2 ratio >1.2 or < 0.8) than that for %S vs. time were assessed.

CONCLUSIONS: In most instances, %S and %R trends agreed among the different time periods but had stronger relationships over time when considering longer time periods. The desired strength of the relationships may be the determining factor in choosing which time period to use in the analysis of susceptibility trends.

169. Moxifloxacin in the treatment of community-acquired pneumonia associated with drug-resistant Streptococcus pneumoniae, Charles Pagory, M.D., Shurjeel Choudhri, M.D., Janet Herrington, M.S., Barbara Painter, Ph.D., Renee Perroncel, B.A., Deborah Church, M.D.; Lung and Chest Medical Associates, Spartanburg, SC; Bayer Corporation, West Haven, CT.

PURPOSE: There has been a dramatic increase in infections due to penicillin resistant (PRSP) and penicillin plus macrolide resistant (DRSP) S. pneumoniae in the US. The objective of this study was to determine the efficacy of moxifloxacin (MXF) in the treatment of community-acquired pneumonia (CAP) due to PRSP and DRSP.

METHODS: Patients with CAP due to penicillin sensitive S. pneumoniae (PSSP), PRSP and DRSP were identified from an ongoing prospective, open, non-comparative, multi-center, multinational trial. All patients received oral MXF 400 mg QD for 10 days. The primary endpoint was clinical success at the test-of-cure (TOC) visit (10-14 days post-therapy) for patients who had an initial sputum or blood culture positive for S. pneumoniae, MCF, penicillin, erythromycin, clarithromycin, and azithromycin MCIs were determined by microbroth dilution.

RESULTS: The study identified 55 patients with CAP due to S. pneumoniae including 42 patients with PSSP, 3 patients with PRSP and 10 patients with DRSP. All S. pneumoniae isolates, PSSP, PRSP and DRSP were highly susceptible to MXF (MIC range: 0.06 to 0.25 mg/ml). The clinical cure rate at TOC was 98% (41/42), for PSSP, 100% (3/3) for PRSP and 100% (13/13) for DRSP.

CONCLUSIONS: Most (77%) PRSP strains were also resistant to all macrolides tested. All PSSP, PRSP and DRSP strains isolated remained highly susceptible to MXF. Moxifloxacin was highly efficacious in the treatment of CAP due to PRSP and DRSP and represents an excellent choice for the treatment of CAP due to S. pneumoniae.

170. Safety of moxifloxacin in the elderly, Vincent Andriole, M.D., Shurjeel Choudhri, M.D., Daniel Haverstock, M.S., Deborah Church, M.D.; Yale University, New Haven, CT; Bayer Corporation, West Haven, CT.


172. Pharmacodynamic evaluation of meropenem and imipenem against Pseudomonas aeruginosa and enterobacter species using Monte Carlo analysis. David S. Burgess, Pharm.D., Michael B. Keys, Pharm.D., Gerald A. Denys, Ph.D.; University of Texas Health Science Center, San Antonio, TX; Purdue University, Indianapolis, IN; Cilary Health Partners, Methodist Hospital, Indianapolis, IN.

P aeruginosa (PSA) and Enterobacter species are the most common gram-negative pathogens in hospital-acquired pneumonia. For β-lactams, treatment outcomes have been linked to the time (%) that drug concentrations remain above the MIC of a pathogen (T>MIC). PURPOSE: To compare the pharmacodynamic profiles of meropenem and imipenem against recent clinical isolates of PSA and Enterobacter species using Monte Carlo analysis.

METHODS: MICs were determined by broth microdilution (NCCLS) for 158 PSA isolates and 116 Enterobacter isolates from 4 hospitals in the US. The objective of this study was to determine the efficacy of moxifloxacin (MXF) in the treatment of community-acquired pneumonia (CAP) due to PRSP and DRSP.

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RESULTS: The study identified 55 patients with CAP due to S. pneumoniae including 42 patients with PSSP, 3 patients with PRSP and 10 patients with DRSP. All S. pneumoniae isolates, PSSP, PRSP and DRSP were highly susceptible to MXF (MIC range: 0.06 to 0.25 mg/ml). The clinical cure rate at TOC was 98% (41/42), for PSSP, 100% (3/3) for PRSP and 100% (13/13) for DRSP.

CONCLUSIONS: Most (77%) PRSP strains were also resistant to all macrolides tested. All PSSP, PRSP and DRSP strains isolated remained highly susceptible to MXF. Moxifloxacin was highly efficacious in the treatment of CAP due to PRSP and DRSP and represents an excellent choice for the treatment of CAP due to S. pneumoniae.
dosing interval were 92% and 87% for meropenem 0.5 g q6h, 94% and 88% for meropenem 1 g q8h, 75% and 63% for imipenem 0.5 g q6h, and 83% and 74% for imipenem 1 g q6h. For Enterobacter species, the probabilities of obtaining free T>MIC for 50% and 70% of the dosing interval were 96% and 92% for meropenem 0.5 g q6h, 95% and 88% for meropenem 1 g q8h, 89% and 76% for imipenem 0.5 g q6h, and 92% and 85% for imipenem 1 g q6h. CONCLUSIONS: Although the carbapenem protein exhibits similar susceptibility profiles, meropenem was the more potent agent and provided the best probability of obtaining free T>MIC for 50% and 70% of the dosing interval for both PSA and Enterobacter species. In addition, meropenem 0.5 g q6h provides the opportunity for a substantial reduction in daily drug cost compared to 1 g q8h and both imipenem dosing regimens.

173. Comparison of Vitek™ and broths microdilution methods for testing cephalosporin and ceftazidime against Pseudomonas aeruginosa and enterobacter species. Gerald A. Denys, Ph.D., Pam B. Renzi, MT(ASCP), Michael B. Kays, Pharm.D.; Clevelander Health Partners, Inc., Methodist Hospital; Purdue University, Indianapolis, IN.

Previous reports have documented high false-resistance rates for cephalosporin and Pseudomonas aeruginosa (PSA) using the Vitek™ susceptibility system. In January 1999, the manufacturer removed restrictions for testing this combination when using software version 7.01. PURPOSE: To compare Vitek and broth microdilution (BMD) susceptibility results for cephalosporin and ceftazidime against PSA and Enterobacter species.

METHODS: Clinical, non-duplicate isolates of PSA (n=158) and Enterobacter species (n=116) were randomly selected from clinical and microbiology cultures obtained at Methodist Hospital, Newark, New Jersey, and were tested on Vitek BMD using manufacturer-recommended methods. The Vitek method was performed using version 7.01. BMD MICs were performed according to NCCLS guidelines (M10-A5). After inoculation, BMD panels were incubated for 18-20 hours at 35°C, and MICs were read manually. NCCLS breakpoints were utilized, and differences between testing methods were determined by chi-square (p<0.05). RESULTS: Cephalosporin and ceftazidime susceptibility results for PSA were significantly different by Vitek and BMD, but ceftazidime resistance was the same for both methods. For Enterobacter, Vitek and BMD were significantly different for ceftazidime, with a higher resistance rate by BMD. Fifteen cefepime-resistant Enterobacter strains were reported susceptible by Vitek (very major error rate, 4.3%).

Nephrology

174. Effect of sevelamer hydrochloride and calcium acetate on the relative oral bioavailability of ciprofloxacin. Michael B. Kays, Pharm.D., Brian R. Overholser, Pharm.D., Bruce A. Mueller, Pharm.D., Sharon M. Moe, M.D., Kevin M. Sowinski, Pharm.D.; Purdue University, Indiana University, Indianapolis, IN.

PURPOSE: The purpose of this study was to determine the effects of sevelamer HCl (Renagel®) and calcium acetate on the relative bioavailability of oral ciprofloxacin in healthy volunteers.

METHODS: Fifteen healthy subjects (8M, 7F) were enrolled. They were admitted to the research unit in the morning of each study day, and were required to fast > 8 hr prior to admission. Subjects were randomly assigned to receive each of the following regimens orally: ciprofloxacin 750 mg alone (Arm A); ciprofloxacin 750 mg + sevelamer 403 mg capsules (Arm B); ciprofloxacin 750 mg + 4 calcium acetate 667 mg tablets (Arm C). The subsequent period between treatments was ≥ 7 days. Serial blood samples were obtained over a 24 hr period, and ciprofloxacin serum concentrations were determined by HPLC. Maximum serum concentrations (Cmax) and time to Cmax (Tmax) were determined by visual inspection of the concentration-time curves. The area under the serum concentration-time curve from 0 to infinity (AUC) and terminal elimination half-life (t1/2) of ciprofloxacin were estimated by non-compartmental analysis. The relative bioavailability of ciprofloxacin in Arms B and C was calculated as AUCarm B = AUCarm C/AUCarm A. Statistical analysis was performed using Friedman’s test and the Wilcoxon Signed Rank test (p<0.05) where appropriate.

RESULTS: Median (Range) data are shown below.

<table>
<thead>
<tr>
<th>Ciprofloxacin</th>
<th>Ciprofloxacin + Sevelamer</th>
<th>Ciprofloxacin + Calcium Acetate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm A</td>
<td>Arm B</td>
<td>Arm C</td>
</tr>
<tr>
<td>Cmax (mg/L)</td>
<td>2.38 (1.97-3.59)</td>
<td>2.49 (1.99-3.42)</td>
</tr>
<tr>
<td>Tmax (HR)</td>
<td>1.18 (0.50-4.00)</td>
<td>1.18 (0.50-4.00)</td>
</tr>
<tr>
<td>AUC (mg hr/mL)</td>
<td>18.55 (14.32-32.02)</td>
<td>11.27 (4.50-28.17)</td>
</tr>
<tr>
<td>T1/2 (HR)</td>
<td>5.38 (4.14-6.26)</td>
<td>5.18 (3.84-7.33)</td>
</tr>
<tr>
<td>Relative %</td>
<td>100.0</td>
<td>92.0 (52.7-131.0)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Although there was no statistically significant difference in the proportion of patients achieving adequte BPS, allowing alteplase to dwell until the next hemodialysis session appears to be technically easier and may be more effective. 175. A randomized trial comparing two modalities of alteplase administration for treatment of occluded hemodialysis catheters. Jennifer M. MacRae, M.Sc., M.D.; Gabriel Loh, B.Sc.Pharm., Stephen Shalansky, Pharm.D., Mercedes Kial, M.D.; St. Paul’s Hospital, Vancouver, BC, Canada.

PURPOSE: To compare two alteplase regimens, differing only in dwell time duration, for use in occluded hemodialysis catheters resulting from suspected thrombus.

METHODS: Patients receiving hemodialysis via catheter between Oct/01 and May/02 with a blood pump speed (BPS) > 250 mL/min after flushing and repositioning were included in the study if they had not been previously enrolled. Patients received 1 mg/ml alteplase (volume determined by the catheter lumen size) randomized to one hour dwell or dwell until the next hemodialysis session (48-72 hours). The primary endpoint was the proportion of patients achieving BPS > 250 mL/min upon alteplase aspiration, and the secondary endpoint was the same outcome assessed at two weeks after alteplase was first instilled.

RESULTS: Twenty-six patients were randomized to one hour dwell, and 34 patients to 48-72 hour dwell. The study groups were similar with respect to mean age (70 versus 67 years), gender (69% versus 56% male), and median baseline BPS (200 mL/min versus 211 mL/min). The primary endpoint was achieved in 16 (62%) of one hour dwell and 27 (79%) of 48-72 hour dwell patients (p=0.13), while the secondary endpoint was achieved in 12 (46%) and 19 (56%) patients, respectively (p=0.46). Of the catheters remaining dysfunctional at 2 weeks, dye studies indicated the cause to be persistent thrombus in 13/14 (93%) one hour dwell and 10/35 (67%) 48-72 hour dwell patients.

CONCLUSION: Although there was no statistically significant difference in the proportion of patients achieving adequate BPS, allowing alteplase to dwell until the next hemodialysis session appears to be technically easier and may be more effective.


PURPOSE: To compare the proportion of vancomycin treatment courses resulting in therapeutic steady state levels using two common dosing regimens in high flux hemodialysis patients.

METHODS: Patients received a loading dose of 25 mg/kg, then were randomized to receive a maintenance dose of either 500 mg every dialysis (q2 dialysis) or 20 mg/kg every second dialysis (q2 dialysis). The target therapeutic range was 10-20 mg/L.

RESULTS: Steady-state vancomycin serum levels were obtained in 21 of 28 dialysis treatment courses and 17 of 31 q2 dialysis treatment courses. The main reason for dropout prior to reaching steady-state was changing to a less expensive antibiotic based on culture and sensitivity results. Demographics were similar between patients in the q dialysis group (17 patients) and q2 dialysis group (16 patients), respectively, including mean weight (64 +/-9 vs. 59 +/-10 kg), sex (43% vs. 44% male) and mean age (67 +/-4 vs. 67 +/-5 years). Pre-steady state levels were more often in the target range in the q dialysis arm (99%) than the q2 dialysis arm (25%, p<0.001); however, there was no statistically significant difference in the proportion of treatment courses resulting in therapeutic steady state serum levels (95% vs. 76% respectively p=0.152). Clinical cure was eventually achieved on vancomycin in 25% (10/21) q dialysis and 94% (16/17) q2 dialysis treatment courses (p=0). CONCLUSION: Although there was no statistically significant difference in the proportion of treatment courses resulting in therapeutic steady state levels between the two regimens, maintenance therapeutic serum levels more consistently throughout the course of vancomycin therapy.


PURPOSE: Patients with end-stage renal disease often suffer from
malnutrition. One modality used to treat malnourished hemodialysis patients is intradialytic parenteral nutrition (IDPN), a multi-component nutritional supplement. The primary outcome of this trial was to determine the effects of IDPN on weight and serum albumin in a large tertiary care institution.

**METHODS:** All patients who received IDPN for greater than 1 month from program inception in June 1997 to December 2000 were analyzed. Patients received IDPN as amino acid 10% 250 ml or 500 ml, dextrose 50% 250 ml, and fat emulsion 20% 250 ml. IDPN was administered during each hemodialysis run three times weekly. Data was collected at 6 and 3 months prior to IDPN initiation as well as at 6, 9, and 12 months post-therapy. Therapeutic efficacy was assessed by percent change from baseline of dry weight and serum albumin.

**RESULTS:** Twenty-six courses of IDPN in 24 patients met inclusion criteria. The mean duration of treatment was 4.3 months. A significant decline in dry weight was observed at both 6 and 3 months prior to IDPN initiation. Dry weight increased from baseline and achieved significance at 6, 9, and 12 months post-therapy. Serum albumin also significantly improved from baseline at 3 and 9 months. Compared to baseline, there was a 3- to 4-fold increase in the percent of patients with serum albumin greater than or equal to 34 g/L. Adverse drug reactions consisted primarily of excess fluid gain and hyperglycemia.

**CONCLUSION:** IDPN significantly increases both weight and serum albumin in malnourished hemodialysis patients.


**PURPOSE:** Complications of chronic kidney disease (CKD) arise early in the course of the disease and are associated with adverse outcomes. Guidelines for management of complications in ESRD patients (pts) are generally applied to the early CKD population due to the absence of standardized guidelines. Data from adult CKD pts not requiring dialysis were evaluated to 1) evaluate management of secondary complications; 2) determine medication (MED) prescribing patterns; and 3) identify potential areas for intervention.

**METHODS:** Select laboratory data, MED profiles, and demographic information were collected for pts in an outpatient nephrology clinic by chart review and patient interviews. This information was evaluated in the context of recommendations in CKD patients to determine overall management and areas for intervention.

**RESULTS:** CKD pts = 100; Demographics: 87% black, 61% female, mean age 50.0 ± 14.1 years; cause of CKD: HD 62%, DR 26%, Lab data: Mean serum creatinine 3.0 ± 1.8 mg/dL, estimated creatinine clearance 48.2 ± 38.6 mL/min, Hct 33.4 ± 5.4%, phosphorus 3.9 ± 1.1 mg/dl, albumin 3.4 ± 0.64 g/dL. Mean systolic and diastolic BP were 136 ± 25 mm Hg and 81 ± 13 mm Hg, respectively; MED use: Diuretics 67%, CCB 50%, ACE inhibitors 41%, β-blockers 22%, ARB 3%, diuretics inhibitors 34%, phosphate binders 18%, erthropoietin 3%, iron supplements 13%, median number of MEDs/patient = 5.

**Conclusions:** Significant areas for intervention.


**PURPOSE:** Determine the safety of enalaprilat and enalapril maleate in the treatment of neonatal hypertension addressing possible anuria and renal failure reported with angiotensin converting enzyme inhibitors (hypotensive effects and alterations in renal perfusion).

**METHODS:** Records of all neonates who received enalaprilat or its prodrug, enalapril maleate, over 30 months (1999-2001) were reviewed. Demographic information, complications during pregnancy, comorbid conditions, and catheter utilization (UAC) were obtained. Dose and route of enalaprilat, concurrent medications, clinical and laboratory parameters were obtained. Data were analyzed via the proc mixed model to account for variability. Pearson's product-moment correlation coefficient was used to assess the relationship between urine output, and blood pressure.

**RESULTS:** Gestational age at admission was 294 ± 55 days and the start of therapy was 269 ± 58 days. Duration of therapy was 8 ± 11 days with an average of 8 ± 9 doses. APGAR scores were 4 ± 3 at 1 minute and 6 ± 2 at 5 minutes. Eighteen patients (n=27) had a UAC, 14 received enalaprilat, nine enalapril maleate and four both. Proc mixed model confirmed no change in urine output (F=0.26, p=0.77 with 2, 49 degrees of freedom). Urine output correlated with systolic blood pressure (r=0.42, p<0.001), and diastolic blood pressure (r=0.365, p=0.008). Urine output did not correlate with mean arterial pressure (r=0.239, heart rate (r=0.080), blood urea nitrogen (r= -0.037) or serum creatinine (r=0.035).

**CONCLUSIONS:** No difference was found in urine output during therapy when appropriate monitoring was performed. Appropriate dose adjustment and monitoring is required for the safe utilization of enalaprilat in this population.


**PURPOSE:** Alternative medicine use is widespread in all industrialized western countries. Patients with chronic and incurable diseases are particularly inclined to seek alternative treatments, as documented by previous studies. Although other investigators addressed the use of alternative medicine by ALS patients, there are no published data regarding the use of botanical or herbal supplements in ALS. Our objective was to survey patients with ALS in our clinic regarding their use of vitamins, herbal supplements, and other compounds.

**METHODS:** Study subjects were followed by the University of Utah Motor Neuron Disease Clinic. A questionnaire was mailed to subjects and was designed to assess: 1) disease progression; 2) use of herbal supplements, vitamins, herbal supplements, and other compounds; and 3) sources of information and expectations of products.

**RESULTS:** A total of 53 subjects participated; mean age 60 years old (range 39-83 years), 15 females, 38 males. Symptom duration averaged one to five years (45 limb onset, 8 bulbar onset). 32% were taking riluzole. 70% were taking vitamins, 42% were taking herbal supplements, and 21% were taking other compounds (prescription medications used for ALS, but not indicated for ALS). Information about herbal medicines was obtained mostly via friends and relatives (n=17), a physician (n=20), and the Internet (n=6). Our patients selected “improvement of general well being” and “slowing of disease progression” most often as reasons for using herbal supplements, vitamins, and other compounds.

**CONCLUSIONS:** Our study demonstrated that the majority of ALS study subjects take vitamins, herbal supplements, or unproven prescription drugs.


PURPOSE: Nitroglycerin (GTN) is widely known to induce headache and has been used as an experimental model of migraine headache in healthy volunteers. Relatively little is known about the effects of GTN on migraineurs. This study used PET to study the influence of GTN on global and regional cerebral blood flow (CBF, rCBF) in migraineurs.

METHODS: Subjects meeting IHS criteria for migraine with or without aura were studied. Subjects with significant neurologic, psychiatric, or other medical conditions were excluded. Neither prophylactic or analgesic medications were permitted at the time of study. CBF and rCBF was measured using 15O-H2O at baseline, following IV GTN infusion at 0.125, 0.25, and 0.5 µg/kg/min, and 30 and 60 minutes following discontinuation of GTN. rCBF was determined using the widely accepted approach of statistical parametric mapping (SPM).

RESULTS: Nine subjects have been scanned to date. CBF values (ml/min/100 g) are as follows.

<table>
<thead>
<tr>
<th>Baseline CBF</th>
<th>GTN 0.125</th>
<th>GTN 0.25</th>
<th>GTN 0.5</th>
<th>30 min p GTN</th>
<th>60 min p GTN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>49 (19)</td>
<td>59 (13)</td>
<td>57 (17)</td>
<td>54 (19)</td>
<td>55 (14)</td>
<td>49 (19)</td>
</tr>
</tbody>
</table>

Conclusions: Significant increases in rCBF were found in the meninges at 0.5 µg/kg/min GTN and persisted 30 and 60 minutes post GTN. Significant reductions in rCBF were identified in the left temporal and occipital lobes at 0.25 and 0.5 µg/min GTN. Occipital reductions in rCBF persisted 30 and 60 minutes post GTN.

CONCLUSIONS: In migraineurs, GTN induced expected increases in global CBF. GTN induces changes in rCBF that should be compared with spontaneous migraine headache.

187. Correlation of levetiracetam concentrations between serum and saliva.

Shellee A. Grim, Pharm.D., Melody Ryan, Pharm.D., BCPS, CGP, Michael V. Miles, Pharm.D., Peter H. Tang, Ph.D., Richard H. Strawburg, M.D., Ton J. deGrauw, M.D., Ph.D., Robert J. Baumann, M.D., M.D.; University of Kentucky, Lexington, KY; Cincinnati Children's Hospital, Cincinnati, OH.

PURPOSE: More than 100 drugs have been evaluated for salivary TDM since the 1970s; phenytoin, phenobarbital, and carbamazepine have demonstrated tight correlations between serum and saliva concentrations. There are no published data for levetiracetam. The objective of this study was to determine the correlation between levetiracetam serum and saliva concentrations.

METHODS: Investigators identified outpatients who were taking levetiracetam and for whom a serum concentration was ordered. Saliva samples were obtained by spitting into a cup. Blood samples were obtained by phlebotomy. Serum and saliva levetiracetam concentrations were determined via HPLC. Regression analysis was utilized to determine correlations.

RESULTS: Serum and saliva samples were obtained from 36 patients (21 female, 15 male) whose ages ranged from 3-57 years (mean 25.4 ± 15.6). Three patients were given one drop of lemon juice to stimulate saliva production. Saliva to serum concentration ratio ranged from 0.10 to 0.95 (mean=0.427 ± 0.176). Regression analysis showed an r-value of 0.88.

CONCLUSION: We demonstrated a positive correlation between levetiracetam serum and saliva concentrations. Our data suggest that saliva monitoring can help the clinician to monitor levetiracetam therapy. We believe that saliva monitoring will facilitate sample collection and improve the quality of life for persons with epilepsy; especially individuals with poor venous access such as children and elderly patients and persons afraid of needles.

188. Correlation of lamotrigine concentrations between serum and saliva.

Melody Ryan, Pharm.D., BCPS, CGP, Shellee A. Grim, Pharm.D., Michael V. Miles, Pharm.D., Peter H. Tang, Ph.D., Richard H. Strawburg, M.D., Ton J. deGrauw, M.D., Ph.D., Robert J. Baumann, M.D., University of Kentucky, Lexington, KY; Cincinnati Children's Hospital, Cincinnati, OH.

PURPOSE: More than 100 drugs have been evaluated for salivary TDM since the 1970s; phenytoin, phenobarbital, and carbamazepine have demonstrated tight correlations between serum and saliva concentrations. There are two published studies correlating serum and saliva concentrations of lamotrigine. However, neither study included individuals younger than 16 years. The objective of this study was to determine the correlation between lamotrigine serum and saliva concentrations for individuals of all ages.

METHODS: Investigators identified subjects at the University of Kentucky neurology clinic who were taking lamotrigine for whom a serum concentration was ordered. Saliva samples were obtained by spitting into a cup. Blood samples were obtained by phlebotomy. Serum and saliva lamotrigine concentrations were determined via HPLC and regression analysis was utilized to determine correlations.

RESULTS: Serum and saliva samples were obtained from 21 patients (12 female, 9 male). Ages of these patients ranged from 2-46 years (mean=±11 years). Saliva to serum concentration ratio ranged from 0.41 - 0.91 (mean=0.58 ± 0.12). Regression analysis showed an r-value of 0.97. For the five patients ≥12 years, the saliva to serum concentration ratio mean was 0.52 ± 0.12.

CONCLUSION: We demonstrated high correlation between saliva and serum concentrations for lamotrigine. The data suggest that saliva monitoring may play a role in the monitoring of lamotrigine for individuals of all ages. While saliva monitoring may facilitate sample collection and improve the quality of life for all patients with epilepsy; children, elderly patients, others with poor venous access, and those with fear of needles may benefit especially from this technology.

189E. A retrospective review of identifying and treating hyperglycemia in stroke patients before and after American Heart Association recommendations.

Shana L. Lettieri, Pharm.D., John J. Sieler, Pharm.D., Soo M. Ahn, M.S.; Sookmyung Women's University, Seoul, Korea.

PURPOSE: The objective of this study was to evaluate the effects of orlistat on weight reduction and parameters associated with risk factors of cardiovascular or metabolic disorders and to assess the factors affecting weight reduction in obese patients taking Orlistat.

METHODS: All adult obese patients (body mass index over 25 kg/m²) who received orlistat for 24 weeks continuously at Asian Medical Center were retrospectively evaluated for the changes in weight, waist and hip circum-
ference, body fat, serum lipid profile, fasting glucose and blood pressure. RESULTS: A total of 63 patients were included for the evaluation of changes in weight, waist and hip circumference, body fat, serum lipid profile, fasting glucose and blood pressure. After 24 weeks of treatment, mean reductions in weight, BMI (kg/m²), and waist circumference from baseline were 3.6 ± 2.9 kg (p<0.001), 1.4 ± 1.1 kg/m² (p<0.001), and 4.4 ± 3.8 cm (p<0.001), respectively. Eight percent of patients lost the weight over 10% of their initial weight. The number of patients with high risk of metabolic disorders (male >102 cm, female >108 cm) decreased to 23 from 35 patients after 24 weeks of treatment. Body fat was also reduced by 2.9 ± 2.5% from baseline (p<0.001) after 24 weeks of treatment. The mean reduction in total cholesterol level and fasting glucose level from baseline were significant with 11.4% (p<0.005), and 14.1% (p<0.029), respectively. Mean systolic and diastolic blood pressure decreased from 132.0 ± 13.1 mmHg to 124.9 ± 14.6 mmHg (p<0.001), and 75.7 ± 11.8 mmHg to 71.7 ± 11.3 mmHg (p<0.014), respectively. However, there were no significant changes in LDL cholesterol, triglyceride and HDL cholesterol levels. The side effects reported with the use of orlistat were mild gastrointestinal effects.

CONCLUSIONS: Orlistat was effective in reducing weight, abdominal fat distribution and body fat, and in improving parameters associated with risk factors of cardiovascular and metabolic disorders.

194E. Glutamine and bombesin do not regulate gut-associated lymphoid tissue via mucosal addressin cell adhesion molecule-1. Gordon S. Sacks, Pharm.D., Shigeki Ikeda, M.D., Kenneth A. Kuduk, M.D., Cheryl D. Johnson, Ph.D., Ben L. Zarzar, M.D.; University of Wisconsin, Madison, WI; University of Tennessee, Memphis, TN.

Published in Am J Clin Nutr 2002;75(suppl):345S.

195. Sterility of lipid emulsions following 24-hour infusion. Catherine M. Crill, Pharm.D., Emily B. Hak, Pharm.D., Richard A. Helms, Pharm.D.; University of Tennessee Health Science Center; Le Bonheur Children's Medical Center, Memphis, TN.

PURPOSE: Based on studies that show lipid emulsion (LE) supports microbial growth in inoculated LE, the CDC Hospital Infection Control Practices Advisory Committee recommends that LE solutions be infused within 12 hours while total nutrient admixtures may be infused over 24 hours (based on no greater microbial growth than non-LE containing parenteral nutrition (PN) solutions). Studies have not evaluated microbial growth for LE spiked under sterile conditions and infused from bottle to patient over 24 hours.

METHODS: On 2 study days (separated by 8 weeks), LE (Intralipid 20%, Baxter) bottles were spiked under laminar flow conditions and hung at pediatric patients' bedside to infuse with PN (via y-site) for 24 hours. The technician spiking and the nurses hanging the solutions had no prior knowledge of the experiment. After 24-hour infusion, 10 ml samples were withdrawn from LE bottles under aseptic conditions and refrigerated until the following morning. The hospital microbiology laboratory then inoculated the samples into blood culture bottles and incubated them (Bact/ALERT Incubator Module, Biomerieux) for 5 days. The samples were subcultured to blood agar plates with olive oil and incubated for 2 days (CO₂ incubator).

RESULTS: On each of the 2 study days, 9 bottles were sampled (n=18). None of the bottles were from ICU patients. At 7 days, all 18 LE samples showed no bacterial or fungal growth (including M. alassea furtur).

CONCLUSIONS: The practice of spiking LE bottles under sterile conditions and hanging them (not repackaging) over a 24-hour period may not increase the risk for microbial contamination.

Oncology

196. Clinical and economic outcomes of a formulary change from filgrastim to sargramostim in patients receiving myelosuppressive chemotherapy. Holly D. Chan, Pharm.D., Siu Fun Wong, Pharm.D.; University of California Irvine Medical Center, Irvine, CA; Western University of Health Sciences, Pomona, CA.

PURPOSE: Based on studies that suggest filgrastim (G-CSF) and sargramostim (GM-CSF) are therapeutically equivalent, the Pharmacy Department at UC Irvine implemented a formulary change from G-CSF to GM-CSF. This study evaluates clinical and economic outcomes of this formulary change.

METHODS: A retrospective chart review was conducted in patients ≥ 18 years old with melanoma, lymphoma, breast, ovarian and lung malignancies who received ≥ 5 days of G-CSF or GM-CSF as primary or secondary prophylaxis following conventional-dose myelosuppressive chemotherapy from Jan 1995 to March 2002. Patients treated before Jan 2000 received G-CSF whereas those treated after that date received GM-CSF. Clinical outcomes evaluated included time to ANC > 1500, time to baseline of febrile neutropenia, subsequent chemotherapy dose delay, and adverse events. Resource utilization data was collected.

RESULTS: Twenty-nine and 27 patients received G-CSF and GM-CSF, respectively. (priority 2 if number of words allowed - you may insert a sentence here to identify the number of pts with primary vs secondary prophylaxis). Time to ANC recovery in patients receiving G-CSF and GM-CSF was 16.7 days and 18.6 days (p = NS). One (3.4%) patient in G-CSF group developed febrile neutropenia, as compared with four (14.8%) in GM-CSF group. More patients treated with GM-CSF experienced dose delay (12 vs. 4, p < 0.05). Overall incidence of adverse events was similar, but more patients in the GM-CSF group had fever and fatigue. Patients treated with GM-CSF required more platelet and red blood cell transfusions, antibiotics, and hospitalizations.

CONCLUSION: The formulary change from G-CSF to GM-CSF was associated with a higher incidence of febrile neutropenia, subsequent chemotherapy dose delay, and greater resource utilization. These results suggest that G-CSF and GM-CSF are not therapeutically equivalent.


PURPOSE: This is a pilot study investigating the safety and efficacy of topical doxepin as an adjuvant analgesic in the management of chemotherapy-induced painful polyneuropathy (CIPP).

METHODS: This is a randomized, double-blind, placebo controlled study of oncology patients with CIPP. Patients were randomized to use topical doxepin hydrochloride 5% cream (Bioglan) or placebo cream. The presence of NCI grade 2 CIPP was determined through physical examination and nerve conduction studies. The study cream or placebo was applied to affected areas three times a day. Pain was assessed using neuropathic pain scales at baseline and weekly for 4 weeks. Side effects and concomitant analgesic use were closely monitored.

RESULTS: Nine patients were recruited and eight were enrolled. All enrolled patients completed the 4-week study period. Paclitaxel was the causative agent in seven patients, vinorelbine in one patient. There were no statistically significant differences between the baseline group characteristics. Using mixed model analysis of variance for repeated measures, a reduction in thermal dysesthesia was demonstrated for doxepin (p<0.05). There was a trend towards significance for reduction in pain intensity (p<0.06). No significant side effects were reported.

CONCLUSION: This pilot study suggests that topical doxepin is a safe and effective adjuvant treatment for CIPP. This result is consistent with current use of systemic tricyclic antidepressants for similar conditions. A larger study would help determine appropriate dosing, duration of therapy and magnitude of analgesic effect.

198E. Factors associated with early termination of CHOP, and its association with overall survival among patients with intermediate-grade non-Hodgkin's lymphoma. Elizabeth Chrischilles, Ph.D., Brian Link, M.D., Shane Scott, Pharm.D., David J. Delgado, Ph.D., Moshe Fridman, Ph.D.; University of Iowa, Iowa City, IA; Amgen, Thousand Oaks, CA; AMF Consulting, Los Angeles, CA.


200E. Pegfilgrastim was observed to be safe and effective as filgrastim in elderly patients with breast cancer. Jeffrey E. Shogran, M.D., Heinz Koebel, M.D., Frankie Ann Holmes, M.D., Sally Yowell, Pharm.D., et al.; University of Pittsburgh Medical Center, Pittsburgh, PA; Universitätsklinikum Halle, Halle Germany; U.S. Oncology, Huntington, TX; Amgen, Inc., Thousand Oaks, CA; Duke University Medical Center, Durham, NC.


201. Reducing anti-DT IgG concentrations to improve the efficacy of a diphtheria fusion protein in elderly patients with metastatic breast cancer. Richard E. Shegog, M.D., Dr. Farooq Usman, M.D., University of North Carolina, Chapel Hill, NC.

PURPOSE: Because of the poor survival in acute myeloid leukemia (AML), we are developing a novel fusion protein consisting of a truncated diphtheria toxin linked to human granulocyte macrophage colony stimulating factor (DT-suGMCSF). Pre-existing anti-DT IgG can bind and remove DT-suGMCSF from the circulation. In our phase I trial of DT-suGMCSF in relapsed or refractory AML, patients with high concentrations of pre-existing anti-DT IgG (> 2 µg/mL) had significantly lower DT-suGMCSF concentrations (Clin Cancer Res 2002;8:1004-13). One method to lower pre-existing anti-DT IgG
concentrations would be to bind the anti-DT IgG with DT388GMCSF. To
compare the pharmacokinetics from day 1 and day 5 of treatment in patients
with the absolute change or fold change in anti-DT IgG concentrations.

CONCLUSION: Treatment with four days of DT388GMCSF significantly
lowered anti-DT IgG concentrations and may increase the patients’ exposure
to different doses of DT388GMCSF. Based on these results, we will
compare the pharmacokinetics from day 1 and day 5 of treatment in patients
in the phase II trial.

202. Carboplatin dosing adult cancer patients: a survey of oncology
pharmacy practitioners in the United States, Robert J. Igoffo Pharm.D.,
Masha Lam, Pharm.D.; University of California, San Francisco, CA.

PURPOSE: 1) evaluate practice patterns of oncologists in the US that
prescribe carboplatin; 2) assess the impact of patient weight and serum
topography (Cr) on the adjustment.

METHODS: 1,290 surveys were e-mailed to a random selection of medical or
gynecologic oncologist members of the American Society of Clinical Oncology. Two-hundred and forty surveys were sent to oncology pharmacist
members of the American College of Clinical Pharmacy. The survey contained
14 multiple choice questions in the following categories: demographics (4);
privacy of carboplatin use (1); formulae used in dosing carboplatin (2);
impact of low serum Cr or high estimated Cr clearance on prescribers’
decision in carboplatin dosing (4); and the impact of patient weight (obesity)
in carboplatin dosing (3).

RESULTS: 75 responses were obtained; 12 from oncologists (1.2%) and 62
(24.5%) from oncology pharmacists. Eighty percent of respondents had been
practicing 3 years or longer. Sixty-three percent practiced hospital-based,
academic practice. Sixty-five percent of the group reviewed orders in 10 or
more patients a month. The Calvert Formula was used by 92% of responders.
Seventy-eight percent considered low creatinine to be 0.7 mg/dl or lower,
which was low planned dose on time (LPDOT), defined as < 85% for ESBC and <
65 years; 57.4% of elderly patients received CMF versus 43.6% overall. Older patients were more likely to receive LPDOT for CMF (27.8% vs. 20.6%)*
and AC (14.7% vs. 10.2%*) than their younger counterparts. Among NHL
patients, 49% were ≥ 65 years old compared to younger patients, they were less
likely to receive LPDOT (76% vs. 89%*) and more likely to have planned (27%
vs. 12%*) and received (42% vs. 23%*) LPDOT. Dose reductions were more
common than primary G-CSF prophylaxis, and G-CSF use was often
suboptimal (*p<0.001).

CONCLUSION: In community practice, elderly patients with ESBC and NHL
frequently receive less aggressive chemotherapy than younger patients.
Recognition and appropriate G-CSF use could improve outcomes for these
patients.

208E. Delivered dose intensity in randomized clinical trials of
chemotherapy for early-stage breast cancer and non-Hodgkin’s lymphoma:
A better reporting is needed, David C. Dale, M.D., Gordon M. Carter, Ph.D.,
Jeffrey Crawford, M.D., Gary H. Lyman, M.D.; University of Washington,
Seattle, WA; Memorial Sloan-Kettering Cancer Center, New York City, NY;
University of Rochester Medical Center, Rochester, NY.

PURPOSE: Otherwise healthy elderly cancer patients can achieve outcomes
equal to younger patients if given equal therapy and appropriate supportive
care; however, general belief is that elderly patients benefit less from
chemotherapy and suffer more toxicity. Data from two large nationwide
surveys of practice patterns of early-stage breast cancer (ESBC) and non-
Hodgkin’s lymphoma (NHL) treatment were analyzed to determine the
prevalence of undertreatment of elderly patients.

METHODS: The ESBC database contains 20,799 patient records from 1243
community practices (96% received CMF, CA, or AC). The NHL database
contains records for 3,165 patients with newly diagnosed intermediate-grade
NHL (100% CHOP, CNOP, or CVP) from 405 practices. The primary endpoint
was low planned dose on time (LPDOT), defined as ≤ 85% for ESBC and <
80% for NHL.

RESULTS: Among ESBC patients, 16.5% were ≥ 65 years; 57.4% of elderly
patients received CMF versus 43.6% overall. Older patients were more likely
to receive LPDOT for CMF (27.8% vs. 20.6%*) and AC (14.7% vs. 10.2%*) than
their younger counterparts. Among NHL patients, 49% were ≥ 65 years old compared to younger patients, they were less
likely to receive LPDOT (76% vs. 89%*) and more likely to have planned (27% vs. 12%*) and received (42% vs. 23%*) LPDOT. Dose reductions were more
common than primary G-CSF prophylaxis, and G-CSF use was often
suboptimal (*p<0.001).

CONCLUSION: In community practice, elderly patients with ESBC and NHL
frequently receive less aggressive chemotherapy than younger patients.
Recognition and appropriate G-CSF use could improve outcomes for these
patients.
were analyzed from 222 patients with stage II-IV breast cancer receiving 4 cycles of doxorubicin 60 mg/m2 plus docetaxel 75 mg/m2 every 3 weeks in two phase 3 studies. Daily subcutaneous Filgrastim 5 µg/kg was administered per approved labeling; that is, beginning on day 2 of each chemotherapy cycle (approximately 24 hours after chemotherapy) and continuing until an ANC ≥ 10 x10⁹/L, after the expected ANC nadir was documented or for up to 14 days, whichever occurred first.

RESULTS: For each of the 4 cycles, a mean of approximately 11 daily Filgrastim injections were administered. As expected with an ANC dosing target of ≥ 10 x10⁹/L, the median time to ANC ≥ 10 x10⁹/L was also 11 days. Moreover, the median time to ANC recovery to ≥ 2 x10⁹/L occurred at day 9 to 10 in cycles 1 through 4 (table).

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<tr>
<th>Kaplan-Meier median, Q1-Q3 percentile, and Q3-Q1 percentile</th>
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<tr>
<td>Cycle to ANC ≥ 10 x10⁹/L      Number of injections</td>
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CONCLUSION: Across cycles the average number of Filgrastim injections was approximately 11, consistent with median time to ANC ≥ 10 x10⁹/L, while the median time ANC ≥ 2 x10⁹/L was only 1 to 2 days fewer.


PURPOSE: Heptaplatin is a platinum derivative with antitumor activity against gastric cancer. Preclinical studies showed that it is less toxic than other platinum analogs. The purpose of this study was to evaluate the efficacy and toxicity of the combination therapy of heptaplatin and 5-fluorouracil in advanced gastric cancer patients.

METHODS: This study retrospectively investigated 65 patients who had received at least 3 cycles of combination chemotherapy for unresectable advanced gastric cancer or with gastrectomy. No patients with prior radiotherapy was allowed. Patients received heptaplatin 400 mg/m² on Day 1 and 5-FU 1000 mg/m² on Day 1 ~ Day 5. The sequent doses were adjusted according to the toxicity and courses were repeated every 28 days. The clinical objective response was evaluated using CT scan after third cycles of combination chemotherapy and hematological and nonhematological toxicity were evaluated before and after each cycle.

RESULTS: The objective response occurred in 16 patients (24.6%). Two were complete and 14 were partial responses. Median progression free survival was 32 weeks with 29% of patients progression free at 1 year. The most common hematologic toxicity was anemia. Grade 3 or 4 anemia was seen in 2.7% of treatment cycles. Greater than grade 3 leucopenia were seen in 6.1% and 1.5% of courses, respectively. The most common nonhematologic toxicity was proteinuria. Proteinuria was considerable factor for this chemotherapy although no patients experienced grade 3 or 4 proteinuria. Greater than grade 3 gastrointestinal toxicities were nausea and vomiting and diarrhea occurring in 4.6% and 1.1% of patients, respectively. The median toxicity of Grade 2 with the elevation of serum creatinine was noted in 0.3% of cycles.

CONCLUSIONS: This study shows that combination therapy of heptaplatin and 5-FU has modest antitumor activity against advanced gastric cancer and renal toxicity that is regarded less toxic than that of other platinum analogs.

Pediatrics

211. Bowel frequency in critically ill children. Karen D. Dominguez, Pharm.D., Matthew Borrego, Ph.D., Denise M. Coleman, M.D., Mark R. Crowley, M.D., Robert Katz, M.D.; University of New Mexico Health Sciences Center, Albuquerque, NM.

PURPOSE: The diagnosis of constipation in critically ill children is challenging since there is no clear definition. The purpose of this exploratory study is to determine if critical illness decreases stool frequency in children and to identify those risk factors that may affect stool frequency.

METHODS: All patients admitted to the PICU for more than 48 hours were eligible. Patients with any gastrointestinal disease known to alter stool output were excluded. The number of daily bowel movements for each patient was collected for the duration of the PICU stay. The patients’ average number of daily bowel movements while in the PICU was compared to the patients’ average number of daily bowel movements prior to illness, as reported by a parent, using a paired t-test. Predictors of stool frequency were determined by stepwise linear regression.

RESULTS: Fifty-six patients were enrolled in the study. There was a statistically significant decrease in the number of daily bowel movements during critical illness (2.0 ± 1.1 vs. 0.6 ± 0.8, mean difference -1.4, CI 1.1-1.8). The variables that best predicted a decrease in bowel movements were male gender, length of PICU stay, the use of narcotics and the presence of hypercalcemia at any time during PICU admission (r² = 0.309).

CONCLUSION: Stool output is significantly reduced during critical illness and several factors affect stool output. This preliminary study will assist with the definition of constipation at our institution and the identification of children who may require prophylaxis.

212. Treatment of non-insulin dependent diabetes mellitus in pediatric patients. Sandra Benedvides, Pharm.D., Jeffrey Striet, John Germak, M.D., Milag C. Nahata, Pharm.D.; Ohio State University, The Children’s Hospital, Columbus, OH.

PURPOSE: The purpose of the study was to determine efficacy of medications in the treatment of non-insulin dependent diabetes mellitus (NIDDM).

METHODS: All pediatric patients diagnosed with NIDDM from January 1996 to December 2001 were included in this retrospective study. Basic demographic information, presenting signs and symptoms, medication history and laboratory values were collected. The primary endpoints of the study were resolution of nocturia, polydipsia, and reduction of glycosylated hemoglobin (HbA1c). Descriptive statistics and paired two-tailed t-tests using SPSS were used in the analysis.

RESULTS: A total of 45 patients, 18(40%) males and 27 (60%) females, were included in the study. The average age at diagnosis was 14.6 (SD = 2.0) years. The signs and symptoms most commonly included polydipsia (79%), polyuria (69%), fatigue (35%) and concomitant infection (31%). Initial HbA1c was 11 (SD = 2.3). Patients treated with metformin (29%), sulfonylureas (18%), insulin (22%) or combination therapy (30%) did not have a significant decrease in HbA1c. While treating therapy, 50% of all patients still had symptoms defined as polydipsia, nocturia or glycosuria. Although 56% of patients had a decrease in HbA1c from baseline after drug therapy, only 13% reached an HbA1c < 6 %. Forty-one percent of the patients were non-compliant with therapy.

CONCLUSIONS: Pediatric patients with NIDDM have clinical features similar to adult patients. Monotherapy or combination therapy did not appear to significantly reduce HbA1c. One possible explanation for the results could be the noncompliance with medications.


PURPOSE: Medical education programs targeting underserved ethnic groups are needed to improve patient understanding and ultimately decrease medication-related hospital admissions. In 1992, the California State Council on Developmental Disabilities Statewide Epilepsy Report on the Needs Assessment for Multicultural issues stated that there were several misconceptions about their disorder, its treatment, and what to do during a seizure.

METHODS: We designed a study to evaluate the Latino caregiver’s knowledge at baseline and following a comprehensive educational program provided by a pharmacist regarding their child’s anticonvulsant medications with respect to dose, adverse effects, and storage. Caregivers were also surveyed at baseline and post education regarding their satisfaction with the information provided by all healthcare professionals as well as the amount of information the caregiver knew about proper seizure first aid and precautions.

RESULTS: Thirty Latino caregiver’s knowledge improved following the educational program provided by the pharmacists. Knowledge of anticonvulsant adverse effects and ultimate management of seizure first aid, medication storage, and seizure precaution for pre versus post pharmacist consultation improved from 0.16 to 0.93 (p<0.05), 0.47 to 0.97 (p<0.05), 0.33 to 1.0 (p<0.05), 0.30 to 1.0 (p<0.05), and 0.27 to 1.0 (p<0.05), respectively. All caregivers were also highly satisfied with the role of the pharmacist (0.36 to 0.93 (p<0.05)).

CONCLUSIONS: The pharmacist is perceived by the Latino caregiver to be a valuable medication education resource. Pharmacists can play an important role in the multidisciplinary approach to the management of pediatric patients with seizures.

215. The use of low dose Activase® for catheter clearance in pediatric patients. May Saba, Pharm.D., BCNSP, Judith Christie, R.N., MSN, Paul Munzenberger, Pharm.D.; Children’s Hospital of Michigan; Wayne State University, Detroit, MI.

PURPOSE: This study evaluated the effect of a 1 mg dose of Activase® (Alteplase, TPA) for clearance of central venous catheters in pediatric patients.
METHODS: The number of patients reviewed was 311. The average patient age was 8.13 years (2 months-18 years). The central catheters studied included 88 Peripherally Inserted Central Catheters (PICC) with the average catheter size being 4 Fr (1.9 - 5Fr). 18 Broviac and short term central venous catheters (CVC). Other central venous access: 1 Groshong venous access, internal jugulars, and 2 ports. The fill volume of the different catheter sizes were <1 mL. The average TPA dose administered was 0.9 mg (0.1-1 mg), with an average dwell time of 39 minutes (20-240 minutes).

RESULTS: With the use of 1 mg TPA dose, there were 91 out of 111 catheters that cleared (82%); 76 cleared after one dose of TPA (68%), 15 catheters cleared after a repeat dose of TPA (14%), 20 catheters failed to clear (18%); 10 catheters failed to clear after the first dose with no repeat dose given (50%) and 10 catheters failed to clear after a second dose was given (50%).

CONCLUSIONS: The fill volume of the catheters used in pediatric patients is less than 1 mL. The use of a 1 mg TPA dose for catheter clearance with the addition of a repeat dose, as needed, may be insufficient in most pediatric patients.

219. Drug shortages in pediatrics. Victoria Tutaj Lehr, Pharm.D., Robert Franczak, R.Ph., Paul J. Munzenberger, Pharm.D., Michael Forzancies, J.V. Aranda, M.D., Ph.D.; Wayne State University; Children’s Hospital of Michigan, Detroit, MI.

PURPOSE: To identify cause and alternatives for recent drug shortages at Children’s Hospital of Michigan.

METHODS: Pharmacy purchasing records (April 2000-November 2001) were reviewed to identify drugs listed as unavailable. Dosage form(s) and strength of drug, cause and projected duration of shortage were documented. RESULTS: During this period, 43 drug products became unavailable or limited in supply. Anti-infectives (ciprofloxacin injection, gentamicin injection, penicillin injection, tobramycin powder, fusonazole injection, cefopipfopin injection, ganciclovir injection, bacitracin injection) were most frequently affected (18.6% of 43), followed by vaccines (immunizations (pneumococcal conjugate, tetanus/diphtheria toxoids, influenza, hepatitis B, 19.3% (43) and opioids (fentanyl) injection, meperidine injection, codeine liquid, Viconid ES tablets). Others were barbituates (secobarbital oral, phenobarbital injection, pentobarbital injection), 7% (3/43), vasoconstrictors (norepinephrine injection and phenylpropranolamine), (2/43; 4.7%), hemotologic agents (preservative free heparin and urokinase), (2/43, 4.7%), and gastrointestinal agents (ranitidine liquid, cisapride), (2/43, 4.7%). Drug shortages were not uncommon in pediatric patients.

CONCLUSIONS: Drug shortages occur frequently. Anti-infectives, vaccines/immunizations and opioids were most affected. Systems are needed to anticipate, and prevent drug shortages, and identify therapeutic alternatives.


Inhaled corticosteroids can suppress the hypothalamic pituitary adrenal (HPA) axis resulting in adrenal insufficiency. The objective of this study was to determine the additive effect of the combination of low dose inhaled fluticasone (Flovent®) and regular dose intranasal fluticasone (Flonase ®) on HPA axis suppression and fluticasone exposure in children. There are no published data that evaluate the effect of combined low dose Flovent plus regular dose Flonase on the HPA axis in asthmatic children with allergic rhinitis.

This was a randomized, double blind, parallel, placebo controlled study. 27 asthmatic children with allergic rhinitis (4-12 years old) currently taking Flovent (88-100 µg/day), completed one month of baseline treatment with Flovent Diskus 100 µg/day, followed by randomization to treatment with Flovent Diskus 100 µg/day plus Flonase 100 µg/day or to Flovent Diskus 100 µg/day plus placebo. 28 days. HPA axis suppression was assessed by 12-hour (overnight) creatinine-corrected urine cortisol excretion (C12uth) which was quantified by HPLC and tandem mass spectrometry. The 12-hour C12uth was collected at the baseline and at the end of the treatment. Fluticasone exposure was assessed by quantifying serum concentrations of fluticasone by HPLC-MS at the end of the treatment.

RESULTS: Baseline 12-hour C12uth ± SD (mg cortisol/gm creatinine) 27.6 ± 21.6 27.3 ± 13.3 0.96 Day 28 12-hour C12uth ± SD (mg cortisol/gm creatinine) 19.3 ± 20.1 22.1 ± 17.9 0.91

CONCLUSION: Addition of regular dose Flonase to low dose Flovent does not result in HPA axis suppression, despite increased fluticasone exposure.

221. The impact of education program on pediatric drug formulations. You-Mei Lin, M.S., TSU-Han Wu, M.S., Hui-Ping Liu, B.S., Yu-Hsuan Yen, M.S., Meei Lin, M.S., Yi-Lin Chiu, Ph.D., Betsy Pilmer, BSN, David Gremse, M.D.; Primary Children’s Medical Center, Salt Lake City, UT; Abbott Laboratories, Abbott Park, IL; TAP Pharmaceutical Products Inc., Lake Forest, IL; University of South Alabama, Mobile, AL.

PURPOSE: To evaluate the pharmacokinetics, tolerability, and safety of a single oral dose of pantoprazole in pediatric patients.

METHODS: Twenty-four (24) physiologically normal children, stratified by age and sex (10 years, n=12; 11-16 years, n=12), who received a single acid suppression therapy any time during the 12 months preceding the study were randomly assigned to receive a single 20- or 40-mg pantoprazole enteric-coated tablet while fasting. Seventeen (17) patients had a previous history of dyspepsia; other gastrointestinal symptoms included gastritis (n=3), reflux (n=3), diarrhea (n=1), and colitis (n=1). Repeated venous blood samples were collected over 12 hours after drug administration. Plasma pantoprazole concentrations were measured by a HPLC-UV method and analyzed by non-compartmental methods. Pharmacokinetics were compared between age and dose groups and to adult data. Safety was monitored throughout the study.

RESULTS: Pharmacokinetic data from 3 children suggested the presence of slow metabolizer (elimination half-life > 3.5 hours) phenotype for CYP2C19. Data from the remaining subjects demonstrated dose proportionality and similarity between the two age groups. Mean pharmacokinetic data (maximum concentration of 3.8 mg/L for a 40 mg dose at 2.5 hours, terminal half-life of 0.63 h and clearance of 0.298 L/hour/kg) were similar to data obtained in adults. A significant association was observed between AUC, clearance and half-life and age. Pantoprazole was well-tolerated. There was only one mild non-drug related adverse event.

CONCLUSION: Pantoprazole pharmacokinetics in patients aged 5-16 years are similar to those in healthy adults. The pantoprazole dose for these patients may be the same as that for adults.

218. The impact of pharmacists’ interventions on the discharge medication process: a randomized controlled trial. Pierre Voriot, Ph.D., Sharon L. Youmans, Pharm.D., Chi Y. Chang, Pharm.D., Q. Laura Zhang, Pharm.D., Yih-Ping Liu, B.S., Yu-Hsuan Yen, M.S., Meei Lin, M.S., Yi-Lin Chiu, Ph.D., Betsy Pilmer, BSN, David Gremse, M.D.; Primary Children’s Medical Center, Salt Lake City, UT; Abbott Laboratories, Abbott Park, IL; TAP Pharmaceutical Products Inc., Lake Forest, IL; University of South Alabama, Mobile, AL.

PURPOSE: To evaluate the coordination of efforts of pharmacists’ interventions during the discharge process have a positive impact on patients’ outcomes. These results can be used to formalize a discharge medication service and set criteria for patients at risk for having problems with obtaining medications at discharge.

RESULTS: A total of 3278 patients were screened of whom 146 were consent were randomized to an intervention or control group. All patients assigned to receive a single 20- or 40-mg pantoprazole enteric-coated tablet were randomly March 29, 2002 were screened for inclusion into the study. Patients who met their caregivers’ ability to obtain discharge medications in a timely fashion and 2) caregivers’ knowledge of how to give the medications between the two groups.

CONCLUSION: Our results suggest that the coordinated efforts of pharmacists’ interventions during the discharge process have a positive impact on patients’ outcomes. These results can be used to formalize a discharge medication service and set criteria for patients at risk for having problems with obtaining medications at discharge.
patterns. The purpose of the study was to provide an educational program to intervene the parents' attitudes and knowledge regarding to extemporaneous formulation versus commercial solution product.

METHODS: Parents of pediatric patients admitted to Taipei Municipal Wan-Fang Hospital (TMWH) were enrolled. The patients were divided into two groups according to the age of their children. A pharmacist provided an education program to introduce the compounding process and storage method of extemporaneous powder formulations to the parents individually. The advantages and disadvantages of the compounded powder and commercial product were also presented objectively. The scores from a questionnaire included 10 attitude questions in a 5-point scale and 10 knowledge questions in a dichotomous scale was compared before and after the program.

RESULTS: One hundred and two parents were recruited from March to April 2002. The TMWH health education program, the total attitude scores of two groups were significantly improved from 30.0 to 36.5 and 30.0 to 36.0, respectively (p<0.001). The total knowledge scores of two groups were significantly increased from 4 to 9 and 5 to 9, respectively, after the education program (p<0.001).

CONCLUSION: The education program conducted by the pharmacist was associated with a change in attitudes and knowledge toward pediatric drug formulations. The change might provide further insight into behavioral adjustment.

222. Dolasetron for the prevention of postoperative vomiting in children undergoing strabismus surgery. Debrah J. War, Pharm.D., Uma Pandit, M.D., Terri Voepel-Lewis, M.S., R.N.; University of Michigan, Ann Arbor, MI.

PURPOSE: Serotonin 5-HT3 receptor antagonists' agents have been shown to effectively reduce postoperative vomiting. This study evaluated the safety and efficacy of intravenous dolasetron 12.5 mg fixed dose vs. 0.35 mg/kg vs. placebo, in children undergoing strabismus surgery.

METHODS: Federal IRB approval and informed consent, 110 patients aged 2-12 years old were randomized to receive placebo, dolasetron 12.5 mg, or 0.35 mg/kg 15 minutes prior to the end of surgery. Anesthesia was induced with halothane in N2O/O2 and maintained with isoflurane. Oral acetaminophen (15 mg/kg) was administered pre-operatively, and intravenous ketorolac (0.5 mg/kg) intraoperatively for analgesia. Post-operatively episodes of vomiting, time to awakening, PACU length of stay and agitation were recorded. Patients experiencing two or more episodes of vomiting were rescued with metoclopramide 0.05 mg/kg. Data were compared using chi-square with Fisher's exact test where appropriate.

RESULTS: Patients with an acute complete response (ACR) defined as no emetic episodes and no rescue medication within 24 hours of study drug administration were 62% (weight dose), 64% (fixed dose) and 33% (placebo, p<0.05). There was no statistical difference in ACR between the 0.35 mg/kg dose and the fixed 12.5 mg dose of dolasetron with both doses reducing the incidence of postoperative vomiting (POV).

CONCLUSION: Prophylactic administration of intravenous dolasetron reduced the incidence of postoperative vomiting following strabismus surgery. There was no statistical difference between a fixed dose and weight based dose. Prophylactic administration of dolasetron is well tolerated and effective for the prevention of POV in children.

Pharmacoeconomics


PURPOSE: Risk of cardiovascular disease in hypertensive patients with diabetes is approximately two-fold greater than in those without diabetes. Controlling blood pressure (BP) with appropriate therapy is key to improving outcomes. Our objective was to compare the level of BP control among HTN-DM patients using the 1997 JNC-VI standard of 130/85 mm Hg versus the 2002 ADA recommendation of 130/80 mm Hg.

METHODS: As part of a national hypertension quality improvement program, chart reviews for 491 randomly selected HTN-DM patients in four major health care plans were conducted (1/99 to 10/01). BP control as defined by each guideline, cardiovascular risk factors, target organ damage, and antihypertensive therapy were analyzed using descriptive statistics.

RESULTS: The HTN-DM population was predominantly female (55%) and Caucasian (55%) with a mean age of 63. Compelling risk factors included dyslipidemia (70%), CAD/angina (14%), nephropathy (10%), retinopathy (10%), CHF (9%), and stroke (18%). A majority of patients were prescribed diuretic therapy, a 48-hour stop, and a restriction to the cardiology (VENXR) and selective serotonin reuptake inhibitors (SSRIs) for major depression.

METHODS: A decision model was developed to estimate the cost and effectiveness of VENXR and SSRIs as measured by costs (pharmacy/medical) and effectiveness (patient achieving full activity/productive day). The probability of achieving full activity and number of productive days were based on pooled data from eight clinical trials comparing venlafaxine, SSRIs, and placebo over eight weeks of treatment. Medical costs over eight weeks of treatment were modeled using probabilities of symptom response from the pooled clinical trial data, associated therapy changes from an expert panel, and treatment costs from the 2002 HCFA Physician Fee and Coding Guide. Pharmacy costs and market share data were based on AWP listings from 2002 and treatment costs from the 2002 HCCA Physician Fee and Coding Guide.

RESULTS: The cost per patient achieving full activity for VENXR was $2,260.50 versus $2,786.79 for SSRIs. The cost per productive day for VENXR was $26.54 versus $28.24 for SSRIs. The costs per patient achieving

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full activity and productive day were computed using the expected mean total costs ($585.47 for VENXR; $546.21 for SSRIs), the probability of achieving full activity (25.9% for VENXR; 19.6% for SSRIs), and the expected productive days per patient (22.06 for VENXR; 19.34 for SSRIs).

CONCLUSIONS: VENXR positively impacts workplace efficiency including achievement of full activity and productive days. VENXR is a cost-effective treatment for major depression in terms of cost per patient achieving full activity and cost per productive day.

227. Impact on proton pump inhibitor utilization and costs following a pharmacy preference change and conversion. B.A. Brown, L.A. Kippley, PA; Tabor, A.K.; Thompson, Scott and White Health Plan, Temple, TX; Janssen Pharmaceuticals, Titusville, NJ.

PURPOSE: This study evaluates PPI pharmacy costs and daily tablets consumed (DACPON) before and after a pharmacy policy conversion in which the preferred PPI changed from lanzoprazole to rabeprazole.

METHODS: A retrospective claims-based analysis was undertaken in a managed care plan with approximately 167,000 members from March through December 2000. Outcomes were evaluated over two 4-month periods (pre- and post-conversion), and a 2-month conversion period. Wholesale acquisition costs were used. Paired t-tests assessed statistical significance in changes in PPI pharmacy costs and DACON among a subset of patients with equal numbers of pre/post PPI prescriptions.

RESULTS: PPI prescriptions totalled 24,873 in 6437 patients; 59% female, 63% between ages 18 and 75. Nineteen hundred nineteen patients had equal numbers of pre/post PPI prescriptions. In this subset, the average cost per prescription decreased $7.76 ± 35.86 (p<0.0001), and DACON decreased 0.02 ± 0.03 (p<0.0001) during 6437 patients, lanzoprazole market share decreased (91% to 3%), while rabeprazole increased (3% to 90%); omeprazole share remained low (~7%), and pantoprazole was limited (<1%). PPI DACON averaged (n = prescriptions): rabeprazole 1.06 (n=9854), lanzoprazole 1.08 (-14.5%), omeprazole 1.07 (n=1760), pantoprazole 1.03 (n=94).

CONCLUSIONS: Conversion from lanzoprazole to rabeprazole achieved in 90% of patients resulted in significant reductions in PPI pharmacy costs and DACON.

228E. Risk of first febrile neutropenia among patients receiving CHOP chemotherapy. Gary H. Lyman, M.D., Vicki A. Morrison, M.D., David C. Dale, M.D.; Jeffrey Dekker, M.D., David J. Delgado, Ph.D.; Mosha Fridman, Ph.D.; Albany Medical Center, Albany, NY; VA Medical Center, Minneapolis, MN; University of Washington, Seattle, WA; Duke Medical Center, Durham, NC; Amgen, Thousand Oaks, CA; AMF Consulting, Los Angeles, CA.


PURPOSE: The purpose of this analysis was to evaluate original evaluations of the economic impact of clinical pharmacy services (CPS) published from 1996-2000, and to compare these studies to future research.

METHODS: Articles identified through a literature search were blindly and randomly assigned to reviewers to confirm inclusion and abstract information. Results were compared to a similar review of literature published between 1988 and 1995.

RESULTS: A variety of practice sites (hospitals, community pharmacies and clinics, health maintenance organizations, and long-term or intermediate care facilities) and CPS (general pharmacotherapy monitoring, target drug problems, disease state management, and patient education or cognitive services) were represented in the 59 included articles. Compared to the previous review, a greater proportion of evaluations were conducted in community pharmacies, clinics and non-US sites, contained more rigorous study designs, and were more comprehensive rather than specialized services. Articles were categorized by type of evaluation: 35.5% were outcome analyses, 23.7% full economic evaluations, 16.9% outcome descriptions, 15.2% cost-outcome descriptions, and 8.5% cost analyses. Most studies reported positive financial benefits. In 16 studies a benefit-to-cost ratio could be calculated (range: 1.7:1 to 17.0:1, median 4.68:1).

CONCLUSION: While the body of literature included in this review provides evidence of the continued economic benefit of CPS, the emergence of many highly predictive characteristics, the excess of non-initiators among the eligible patients permits propensity score matching to form balanced comparison cohorts suitable for the study of drug effects.


PURPOSE: To improve coordination of care (COC) with provider and pharmacies for Medicaid fee-for-service patients at high risk for adverse events.

METHODS: Prospective pre/post study. Physicians of those patients that received more than 10 different medications, prescribed by ≥ 3 different providers, and dispensed from ≥3 different pharmacies, were notified 60 days prior to baseline. Physicians were mailed a cover letter explaining the criteria, a patient newsletter, and patient profiles. Changes in pharmacy and medical utilization from baseline to 6 months were compared for those patients continuously enrolled during the post intervention period.

RESULTS: Three thousand three hundred and seventy seven patients had COC issues at baseline while only 769 (~77%) did at 6 months (p<0.05). At baseline the average unique medications, pharmacies, and physicians per patient were 14.3, 3.6, and 5.5, respectively. At 6 months in those patients no longer had COC issues (n=2608) compared to those that did (n=769) had less unique medications (112 vs. 15.6, respectively), pharmacies (2.3 vs. 3.7), and physicians (3.7 vs. 5.5). Changes from baseline were significant (p<0.05) for all parameters except the number of unique medications in those patients that still had COC issues. Additionally, the average cost per patient per month decreased 8.5% (~$56.53) while medical costs per patient per month decreased 53.0% (~$566.4). Overall cost avoidance from baseline to 6-months was $385.61.

CONCLUSIONS: By notifying physicians of patients with potential coordination of care issues, positive clinical and economic outcomes were seen.

Pharmacoeconomics

231. Predicting initiation of statin therapy at Fallon Community Health Plan: building a propensity score-matched cohort study. John D. Seeger, Pharm.D., Dr.PH., Alexander M. Walker, M.D., Dr.PH., Paige L. Williams, Ph.D., Frank M. Sacks, M.D., Gordon M. Saperia, M.D.; Harvard University, Boston, MA; Ingenuity Epidemiology, Newton, MA; Fallon Clinic, Worcester, MA.

PURPOSE: National guidelines specify clinical characteristics that identify patients as candidates for statin therapy. We sought to identify empiric predictors of statin initiation and develop a propensity score that could be used to create matched cohorts.

METHODS: From 1993 through 1999, Fallon Community Health Plan members initiating statin therapy were compared to eligible non-initiators. Patient characteristics were compared across serial half-year blocks of calendar time both univariately (t-test or Fisher’s exact test), and multivariately (logistic regression).

RESULTS: There were an average of 504 statin initiators and 8958 non-initiators in each half-year block. Statin initiators differed significantly from non-initiators on 43 of 52 variables evaluated with statin initiators exhibiting higher cardiovascular risk. Plasma lipid values (LDL, HDL, and TG) and cardiovascular comorbidities were highly predictive of statin initiation, while other NCEP variables (age, sex, diabetes, hypertension, and smoking) were less predictive. Variables relating to health care utilization (physician visits, laboratory tests, and prescription dispensions) were more predictive than medical variables. A logistic regression including all 52 variables discriminated well between statin initiators and non-initiators (c-statistic=0.92), and matching based on this model (propensity score) created cohorts (N=9001 each) that were significantly different from each other on only one of the 52 variables.

CONCLUSIONS: Among persons eligible for statin therapy, lipoprotein concentrations and cardiovascular comorbidities are predictive of statin initiation, but measures of healthcare utilization are equally predictive. Despite the existence of many highly predictive characteristics, the excess of non-initiators among the eligible patients permits propensity score matching to form balanced comparison cohorts suitable for the study of drug effects.

232. Risk factors for drug-related Stevens-Johnson syndrome and toxic epidermal necrolysis: a case-control study in Taiwan. Mei-Shu Lin, M.S., Yang Shia Dai, M.D., Rau-Fang Puw, M.S., Yan-Hui Chen Ph.D.; National Taiwan University, National Taiwan University Hospital, Taipei, Taiwan.

PURPOSE: Stevens-Johnson syndrome (SJS) and toxic epidermal necrosis (TEN) are rare, however, life-threatening cutaneous reactions. The etiology of SJS and TEN is usually drug-related (80-95% of patients with TEN, >50% with SJS). The purpose of this study is to estimate odds ratios of suspected drugs in Taiwan.

METHODS: A case-control study was used to estimate the odds ratios of suspected drugs related to SJS/TEN. The analysis of total subjects was based (N=9001 each) that were significantly different from each other on only one of the 52 variables.

CONCLUSIONS: Among persons eligible for statin therapy, lipoprotein concentrations and cardiovascular comorbidities are predictive of statin initiation, but measures of healthcare utilization are equally predictive. Despite the existence of many highly predictive characteristics, the excess of non-initiators among the eligible patients permits propensity score matching to form balanced comparison cohorts suitable for the study of drug effects.
RESULTS: Carbamazepine has the most strong association with SS/STEN (OR=26.1, CI 3.6, 220). The odds ratios for allopurinol and phenytoin were 17.6 (CI 2.1, 149.4) and 7.4 (CI 1.5, 37.5), respectively. The death rates of SS and TEN were 10% and 40%, respectively. The average onset of these severe conditions after the first drug administration was 15 days.

CONCLUSIONS: This study, with limited sample sizes, observed that carbamazepine, allopurinol, and phenytoin increase the risk of SS and TEN. Further study with larger sample sizes is needed to confirm the results.


PURPOSE: S. pneumoniae is the leading cause of community-acquired pneumonia and pneumococcal bacteremia. Using data from the ongoing Antimicrobial Resistance Management (ARM) program, this study examined national and regional susceptibility rates of S. pneumoniae to two second-generation cephalosporins, cefotaxime and ceftriaxone, historically regarded as being therapeutically equivalent.

METHODS: The ARM program has collected nearly 15 million inpatient and outpatient isolates from 121 hospitals in five U.S. regions: north central, northeast, south central, southeast, southwest. Antibiotics and sensitivity reports of the 54 ZIP codes collected from 1995-2001 were reviewed for susceptibility to cefotaxime and ceftriaxone and compared using a Web-based analysis tool.

RESULTS: From 1995-2001 nationally S. pneumoniae isolates were more susceptible to ceftriaxone (80.9%) than to cefotaxime (71.7%; n=4366). This difference was accounted for primarily in the Southeast (cefotaxime, 65%; ceftriaxone, 77.7%). Rates were consistently lower for cefotaxime for each of the years reviewed. In 1995, susceptibility was 54.7% (n=507), compared with 72.5% (n=497) for ceftriaxone and for 2001, 73.6% (n=938) compared with 82.3% (n=499) for ceftriaxone. Regionally, this trend was seen in all areas except in Northeast, where rates were comparable, with the exception of 2001: susceptibility to cefotaxime was 70.2% (n=212), compared with 80.2% for ceftriaxone (n=2983).

CONCLUSIONS: These data suggest that cefotaxime and ceftriaxone may not be therapeutically equivalent for the treatment of S. pneumoniae. Given the recent change in recommended breakpoints for these two third-generation cephalosporins, this result may have clinical relevance.


PURPOSE: There is little data regarding adherence with dosing adjustment recommendations for renal insufficiency (RI) in the ambulatory setting. This study describes adherence to medication dosing recommendations in ambulatory patients with renal insufficiency in a group HMO.

METHODS: Medications requiring dose adjustment in RI were identified. Occurrences of prescribing for these medications in RI were then defined using a CRI <50 (Crockcroft and Gault). In cases where a medication was prescribed in RI, the actual dose used was compared to the recommended adjusted dose (based on the patient's creatinine clearance). A subset of 20 select medications requiring dosage adjustment for patients with RI were identified by an expert panel for further intervention, based on frequency of use and perceived potential for adverse clinical outcomes.

RESULTS: One hundred thirty-three medications requiring renal dosing adjustment were identified. Over a three-month period, 64 of those medications (a total of 2134 occurrences) were prescribed in a renal insufficiency patient within our system. Overall, 1098 (31.4%) of the prescriptions were potentially dosed excessively. Of the 20 select medications, there were 514 occurrences of prescribing in a patient with RI. In 358 (69.6%) of those cases, the medication was dosed higher than recommended based on the patient's creatinine clearance. Medications dispensing more frequently and potentially dispensed inappropriately include allopurinol, ranitidine, metformin, gabapentin, nitrofurantoin, and glyburide.

CONCLUSIONS: Our study shows ambulatory care physicians often fail to adjust medications dosages for patients with renal insufficiency. The clinical implications of this excessive dosing should be further explored.

235. Antidepressant adherence in the Iowa Medicaid pharmaceutical case management population. John G. Gums, Pharm.D.; Ryan M. Carnahan, Pharm.D., M.S., BCCP; University of Iowa, Iowa City, IA.

PURPOSE: To describe the extent of and factors related to medication adherence among patients treated with antidepressants in the Iowa Medicaid Pharmaceutical Case Management Program.

METHODS: Fills for antidepressant medications and a selected group of chronic non-antidepressant medications (e.g. antihypertensives, lipid-lowering agents, etc.) were identified from electronic pharmacy claims over a one-year period. Adherence was measured using a standardized method and defined as the number of days during the treatment period that the patient was observed to be without a supply of medication (MED-OUT).

RESULTS: This analysis included 2200 patients who received either an antidepressant or one of the selected chronic medications. Of the 1210 antidepressant users, 75% were adherent as defined by a threshold MED-OUT value of ≤ 0.20 (80% confidence). Antidepressant adherence did not differ across pharmacologic class (p=0.23) or gender (p=0.22), but improved significantly with increasing age (p=0.006). Furthermore, adherence did not differ between antidepressants and chronic medications among patients receiving both (p=0.14 vs. 0.12, respectively; p=0.56).

Finally, adherence to chronic medications was compared between antidepressant users and non-users. While adherence was impaired among antidepressant users (p=0.023), this effect was significantly dependent on age (p=0.02). In other words, higher antidepressant use was associated with better medication compliance in younger patients (≤ 55 years), but worse medication compliance among older patients.

CONCLUSIONS: Prior research suggests that patients with depression are at risk for non-compliance. While this finding was supported in the current study among the elderly, younger patients treated with antidepressants actually displayed better overall medication adherence. This observation has important implications for future compliance research in depression.


PURPOSE: Describe differences in the time to discontinuation for various nonsteroidal anti-inflammatory drugs among patients with rheumatoid arthritis and osteoarthritis. Kristian H. Kahler, R.Ph., S.M.; Douglas Gause, M.S., Dr.P.H.; Winnie Zhang, M.D., M.S.; Novartis Pharmaceuticals, East Hanover, NJ.

METHODS: Data were extracted from Medstat's MarketScan, a proprietary claims database. From those continuously enrolled and with an RA or OA claim between July 1997 and December 1999, 32,807 patients were identified with an initial prescription for an NSAID during 2000 with the last six months of 1999. Kaplan-Meier curves were created to assess the time to discontinuation for the following drug groups: rofecoxib®, celecoxib (C), meloxicam (M), diclofenac plus misoprostol (A), and all others (O).

RESULTS: This analysis consisted of 32,807 patients with RA or OA starting an NSAID therapy. The COX-2 selective inhibitors, rofecoxib and celecoxib accounted for 59.7% of initial prescriptions. The median time to discontinuation was greatest for R at 65 days, and for M, C, A, and O was 60, 57, 47, and 42, respectively. Rofecoxib, celecoxib, and to a lesser extent, meloxicam appeared to have better persistence than the traditional NSAIDs. There was a sharp increase in discontinuation after the initial 30 day supply of medication for all products.

CONCLUSION: The COX-2 selective agents appear to offer improvements over the traditional NSAIDs with regard to persistence, however, compared to other maintenance medication classes, the time to discontinuation for NSAIDs is still low. There is a need for medications that offer improved tolerability or efficacy, or both.


PURPOSE: To evaluate geospatial relationships of appropriate and inappropriate antibiotic use for acute sinusitis in one state's Medicaid population.

METHODS: A Medicaid database was queried over a one-year timeframe to identify cases of acute sinusitis with an antibiotic dispensed within two days of diagnosis. Prescription claims data were gathered including name and address for patient and provider, diagnosis code, antibiotic name, and cost of therapy. Each case was classified as appropriate or inappropriate according to sinusitis's recommendations from a 2001 clinical practice guideline from the American College of Physicians – American Society of Internal Medicine. Amoxicillin, doxycycline, and sulfamethoxazole/trimethoprim were the three antibiotics considered as being therapeutically equivalent.

RESULTS: A map was created to provide a visual representation of sinusitis prescribing (2036 cases) across the state. Fifty-four of 293 ZIP codes contained at least ten cases each. Within those 54 ZIP codes, 2918 cases
### Pharmacogenomics/Pharmacogenetics

#### 239. The effect of CYP3A4*1B 5'-promoter region polymorphism on cyclosporine pharmacokinetics among healthy volunteers.

David L. Win, Pharm.D., FCCP; Vicki L. Ellingrod, Pharm.D., BCPS; University of Iowa, Iowa City, IA.

Cyclosporine (CsA) is a substrate for CYP3A4 and MDR1 gene product. Cyclosporine (P-gp) and its pharmacokinetics is influenced by various factors including these genotypes. Recently, functional polymorphisms of the CYP3A4/1B 5'-promoter region and C3435T of MDR1 gene have been reported.

**PURPOSE:** To determine the effect of CYP3A4*1B 5'-promoter region polymorphism on CsA pharmacokinetics among healthy volunteers.

**METHODS:** CsA pharmacokinetics were performed in 14 healthy subjects. Blood cyclosporine concentrations were measured by high performance liquid chromatography. Concentration versus time data were analyzed by non-compartmental method using WinNonLin, and the blood sampling was performed for the CYP3A4 and MDR1 polymorphism using the polymerase chain reaction and a restriction digest. Each CsA pharmacokinetic parameter was compared using one-way ANOVA test.

**RESULTS:** There were four (4) homoyzous A/A (wild type), four (4) homoyzous G/G (variant) and six (6) heterozyzous A/G genotypes for CYP3A4 in these 14 healthy volunteers. For MDR1 genotype, there were seven (7) homoyzous C/C, six (6) C/T and one (1) homoyzous T/T genotypes in these 14 healthy volunteers. All of subjects with homozous A/A genotype of CYP3A4 were MDR1 C/T heterozyzous and most of subjects with CYP3A4 homozous G/G genotypes were MDR1 C/C homozyzous genotype. According to the genotypes of CYP3A4, the mean pharmacokinetic parameters (± SD) of oral cyclosporine are as follows.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CL/F (l/hour)</td>
<td>49.4 ± 13.9</td>
</tr>
<tr>
<td>Vss (l)</td>
<td>83.5 ± 16.0</td>
</tr>
<tr>
<td>T1/2 (hour)</td>
<td>7.6 ± 4.3</td>
</tr>
<tr>
<td>AUC (ng•hour/ml)</td>
<td>6989 ± 1945</td>
</tr>
<tr>
<td>ED50 (µg/kg/min)</td>
<td>17 ± 6</td>
</tr>
<tr>
<td>Emax (µg/kg)</td>
<td>6886 ± 1619</td>
</tr>
<tr>
<td>Emax (%)</td>
<td>4634 ± 1022</td>
</tr>
<tr>
<td>CL/F (l/hour)</td>
<td>83.5 ± 16.0</td>
</tr>
<tr>
<td>Vss (l)</td>
<td>52.5 ± 5.6</td>
</tr>
<tr>
<td>T1/2 (hour)</td>
<td>5.9 ± 0.9</td>
</tr>
<tr>
<td>AUC (ng•hour/ml)</td>
<td>6886 ± 1619</td>
</tr>
<tr>
<td>ED50 (µg/kg/min)</td>
<td>21 ± 5</td>
</tr>
<tr>
<td>Emax (µg/kg)</td>
<td>21 ± 5</td>
</tr>
<tr>
<td>Emax (%)</td>
<td>0.0024*</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** The CYP3A4*1B 5'-promoter region polymorphism appears to influence AUC and CL/F of oral CsA significantly in healthy subjects. Further study with larger sample size may be needed to confirm these results.

#### 240. Adrenergic receptor polymorphisms and response to dobutamine.


**PURPOSE:** To assess the impact of variation in pharmacokinetic (PK) parameters in the pharmacodynamic (PD) of dobutamine among healthy volunteers. Dobutamine (1AAR) agonists used for stress testing and inotropic support.

**METHODS:** Genomic DNA was obtained from 38 children. As topotecan is a substrate for ABCG2, we examined SNPs in exon 2 in 35 children and exon 5 in 18 children. Four of five patients which had an exon 2 SNP at amino acid 12 (V12M) were heterozygous. Each of three patients which had an exon 5 SNP at amino acid 141 (N141K) were heterozygous.

**CONCLUSION:** Our patients had a 8.6% allele frequency of the exon 2 SNP and 8.3% allele frequency of the exon 5 SNP which is comparable to literature values. Comparison of these genotypes with topotecan pharmacokinetic phenotype is underway. Also, we continue to collect genomic DNA from additional children treated with topotecan. SNP genotyping is also being performed for the CYP3A4/5 gene as well as other drug transporters, such as ABCC4 and ABCB1.


Yuchi Ando, M.D., Ph.D., Doug K. Price, Ph.D., William L. Dabah, M.D., Michael C. Cox, Pharm.D., Eddie Reed, M.D., William D. Figg, Pharm.D.; National Cancer Institute, Bethesda, MD.

**PURPOSE:** It has been known that thalidomide requires microsomal cytochrome P450 (CYP)-catalyzed biotransformation for its pharmacological activities, including antiangiogenic effect. It has been found that CYP2C19 is primarily responsible for 5- and 5'-hydroxylation of thalidomide. Because CYP2C19 is polymorphic enzyme, genotyping CYP2C19 gene of each patient might segregate the patient population into subgroups that differ in their ability to respond to thalidomide. This study was conducted to investigate the associations between the CYP2C19 genotype and clinical outcomes of thalidomide therapy.

**METHODS:** A case-control study of 63 patients with prostate cancer who were entered in the recent thalidomide phase II study at the NCI was explored. The genotype was preserved by PCR-RFLP and the metabolite concentrations in plasma were measured by HPLC.

**RESULTS:** Two of the 63 patients were homozygous for the variant CYP2C19*2 allele and were considered as poor metabolizers. Both the patients were included in the 25 patients whose CYP2C19 (M) were associated with topotecan clearance were analyzed for commonly associated drug transporters, such as ABCC4 and ABCB1.

### Pharmacokinetics/Pharmacodynamics

#### 244. Carbapenem pharmacodynamics against common pathogens utilizing variability in pharmacokinetic parameters.

Kevin A. Enzweiler, Pharm.D., Roger L. White, Pharm.D.; Medical University of South Carolina, Charleston, SC.

**PURPOSE:** To assess the impact of variability in pharmacokinetic (PK) parameters on the pharmacodynamics (PD) of carbapenems (CP) against various organisms.

**METHODS:** PK parameters obtained from 27 studies involving 220 subjects in peer-reviewed publications were used to simulate unbound serum concentration-time profiles in a 70 kg adult for IV imipenem (I), meropenem (M), and ertapenem (E). Variability in CI was accounted for using published CI vs. CrCl relationships; variability in Vss was accounted for with use of values from normal volunteer data reflecting mean ± 1 SD. MIC50 and MIC90 values were obtained from N. American studies published from 2000-2002 for...
2. Gram-positive and 5 Gram-negative aerobes, and 8. fragilis (13,060 drug-resistant isolates). Weighted (based on # of isolates) geometric mean MICs were used for subsequent PD calculations. Using manufacturer-recommended and non-approved regimens (1 at approved doses of M and M at approved doses of I) with recommended dosage adjustments for renal failure, simulations were performed at CrCl of 100, 75, 50, and 25 ml/min (51 regimens). Regimens were categorized as acceptable or optimal for all bacteria if the % T > MIC was ≥ 25 and 50, respectively.

RESULTS: Over the studied CrCl range using mean Vss, the % acceptable rank order was M = I > E for both MIC50 and MIC90, M was 100% optimal for all organisms except P. aeruginosa and was differentiated from both I and E (M = 45%, I = 0%, E = 100% acceptable). Although simulations utilizing variations in Vss resulted in differences in % T > MIC, PD categorical results were consistent between I and E. Throughout there was a trend towards increasing % T > MIC as CrCl declined, the categorical results were similar to those found in simulations at CrCl = 100 ml/min.

CONCLUSION: With the exception of P. aeruginosa, these CP exhibited similar PD profiles even when considering variability in renal function and Vss.

245. Murine pharmacokinetics and metabolism of oleandrin, a cytotoxic component of Nerium oleander. Dan Ni, M.D., Timothy L. Madden, Pharm.D., Mary Johansen, Pharm.D., Edward Felix, M.S., Dah H. Ho, Ph.D., Robert A. Newman, Ph.D., University of Texas, Houston, TX.

PURPOSE: To evaluate the pharmacokinetics and metabolism of oleandrin in mice after intravenous (IV) and oral (PO) administrations of H. oleanderin.

METHODS: To investigate the brain tissue distribution of oleandrin after intraperitoneal (i.p.) injection of either oleandrin or oleander extract.

RESULTS: Oleandrin was rapidly absorbed after oral dosing with T<sub>max</sub> at 20 min. The elimination half-life was longer (2.3 ± 0.5 h) than that after IV dosing (0.4 ± 0.1 h). An oral bioavailability of oleandrin was approximately 30%. After IV, the concentration of oleandrin in liver was approximately twice that measured in heart and kidney tissue. A major metabolite, oleandrigenin was found in these tissues. At 5 min after IV dosing, more than 60% of the total radioactivity in liver was oleandrin, while 28% of the given dose was present as oleandrigenin. Only oleandrin, but no oleandrigenin, was found in brain. Twenty-four hours following injection, 66% of the total injected radioactivity was found in feces. About 8% of total radioactivity were excreted in the urine.

CONCLUSION: Oleandrin was rapidly absorbed and distributed in mice. The major metabolite of oleandrin was oleandrigenin. Oleandrin was mainly eliminated by the liver and there were higher excretion in feces than in urine. The amount of oleandrin in brain tissue was higher after i.p. injection of oleander extract than that after injection of oleandrin.

246. Effect of ethanol on oral cocaine pharmacokinetics. Robert B. Barker, Pharm.D., Naomi Gadis, D.V.M., Timothy Mandrell, D.V.M., S. Casey Laizure, Pharm.D., University of Tennessee; St. Jude Children's Research Hospital, Memphis, TN.

PURPOSE: Cocaine (C) is frequently ingested by nasal insufflation. However, only a small fraction of the dose is absorbed nasally with most of the drug being swallowed and then absorbed in the GI tract. Most cocaine users co-ingest ethanol (EtOH) which has been shown to inhibit hepatic carboxylesterase-mediated cocaine metabolism to benzoylecgonine (BE), and result in formation of the active metabolite, cocaethylene. Therefore, the purpose of this study was to determine the effect of EtOH on oral C pharmacokinetics in conscious dogs.

METHODS: Five adult, conditioned mongrel dogs received 4 mg/kg oral C, 4 mg/kg oral C + EtOH, and 3 mg/kg IV C on different study days separated by at least 48 hours. C and metabolite concentrations were analyzed by LC/MS/MS for oleandrin content after i.p. of drugs. Pharmacokinetic parameters were estimated by WinNonlin 3.1.

RESULTS: Oleandrin was rapidly absorbed after oral dosing with T<sub>max</sub> at 20 min. The elimination half-life was longer (2.3 ± 0.5 h) than that after IV dosing (0.4 ± 0.1 h). An oral bioavailability of oleandrin was approximately 30%. After IV, the concentration of oleandrin in liver was approximately twice that measured in heart and kidney tissue. A major metabolite, oleandrigenin was found in these tissues. At 5 min after IV dosing, more than 60% of the total radioactivity in liver was oleandrin, while 28% of the given dose was present as oleandrigenin. Only oleandrin, but no oleandrigenin, was found in brain. Twenty-four hours following injection, 66% of the total injected radioactivity was found in feces. About 8% of total radioactivity were excreted in the urine.

CONCLUSION: Oleandrin was rapidly absorbed and distributed in mice. The major metabolite of oleandrin was oleandrigenin. Oleandrin was mainly eliminated by the liver and there were higher excretion in feces than in urine. The amount of oleandrin in brain tissue was higher after i.p. injection of oleander extract than that after injection of oleandrin.


PURPOSE: M100240, a thioester of MDL100,173, is a dual ACE/NEP inhibitor currently in Phase II development. This study evaluated the relative bioavailability of M100240 in various regions of the gastrointestinal tract using the Enterion™ capsule in order to explore the absorption characteristics of M100240. The absolute bioavailability of M100240 was also assessed.

METHODS: Pharmacokinetic data were obtained from 13 healthy subjects in an open-label, single-dose, randomized, 5-period crossover study. Treatments included 25 mg M100240 via short intravenous infusion, oral immediate release tablet, and oral Enterion capsule delivery of drug substance to the proximal small bowel, distal small bowel, and ascending colon. Each treatment was separated by a 14-day washout period. The Enterion capsule was monitored throughout the gastrointestinal tract using scintigraphic imaging. M100240 and MDL100,173 plasma concentrations were quantified using validated LC/MS/MS method and pharmacokinetic parameters were calculated using non-compartmental methods.

RESULTS: MDL100,173 C<sub>max</sub> and AUC<sub>0-24h</sub> following release in the proximal and distal small bowel were similar to estimates for the immediate release tablet. However, after release in the ascending colon, C<sub>max</sub> and AUC<sub>0-24h</sub> were decreased to approximately 13% and 41% of the corresponding estimates for the immediate release tablet. The estimates of relative bioavailability in the proximal small bowel, distal small bowel, and ascending colon relative to the oral immediate release tablet were 94%, 97%, and 41%, respectively. The absolute bioavailability estimate of M100240 is 49%.

CONCLUSION: M100240 is well absorbed throughout the proximal and distal small bowel with modest absorption in the ascending colon.

248. Effect of capsaicin on the pharmacokinetics and pharmacodynamics of warfarin in rats. Hsiang-Chin Chen, M.S., Pharm.D., Shih-Hein Chang, B.S., Chi-Chung Lai, M.S., Chi-Chun Chang, B.S., Fel-Yuan Hisao, M.S. candidate; Taipei Medical University; Taipei Municipal Wan-Fang Hospital, Taipei, Taiwan.

PURPOSE: To evaluate the possibility of interaction between capsaicin and warfarin, the influence of capsaicin on the pharmacokinetic and pharmacodynamic parameters of warfarin was studied in Sprague Dawley rats.

METHODS: The pharmacokinetic study included a single dose model using an oral dose of warfarin at 2 mg/kg with placebo or an oral dose of capsaicin at 50 mg/kg, and a multiple dose model using warfarin at 0.2 mg/kg once daily with placebo or capsaicin at 50 mg/kg daily for 6 days. The plasma concentrations of warfarin were compared by a validated HPLC assay. The pharmacokinetic study used a single dose of warfarin (0.8 mg/kg) at day 4, with placebo or capsaicin at 50 mg/kg for 6 days. The levels of international normalized ratio (INR), employed as a pharmacodynamic index, were measured at day 1, 4, 5, 6.

RESULTS: Single dose of capsaicin resulted in 50% increase in the peak plasma concentration (C<sub>max</sub>) of warfarin from 5.00 ± 2.14 to 7.31 ± 2.02 µg/ml, and area under concentration-time curves (AUC) from 97.66 ± 38.65 to 152.93 ± 33.52 µg·h/ml (all p < 0.05). In the multiple dosing model, significantly increased C<sub>max</sub> and decreased clearance were also observed in the presence of capsaicin. Additionally, capsaicin significantly increased maximal INR from 2.66 ± 1.30 to 3.46 ± 1.44.

CONCLUSIONS: The significant pharmacokinetic and pharmacodynamic findings in rats highlight the possibility of interactions in human. Careful monitoring of PT with appropriate dose titration with warfarin may be needed with oral intake of capsaicin.

249E. Bioavailability of intranasal butorphanol using unit-dose sprayers in healthy volunteers. George A. Davis, Pharm.D., Anita C. Rudy, Ph.D., Sanford M. Archer, M.D., Daniel P. Wermeling, Pharm.D.; University of Kentucky; Intranasal Technology, Inc., Lexington, KY.


250E. Pharmacokinetic comparison of oxcarbazepine oral suspension formulation versus film-coated tablets. J. D. Souza, Ph.D., G. Flesch, M.D.; Novartis Pharmaceuticals, East Hanover, NJ; Novartis Pharmaceuticals, Basel, Switzerland.


252E. Consistent pharmacokinetics of ximelagatran, an oral direct thrombin inhibitor, in patients with non-valvular atrial fibrillation and age and gender-matched controls. Maria Wolfflatt, M.Sc., Ulf G. Eriksson, Ph.D., Michael Wolzt, Ph.D., Mia Svensson, M.Sc., Karin Wahlander, M.D., Ph.D., Margaretha Grind, M.D., Ph.D.; AstraZeneca R&D, Molndal, Sweden; University of Vienna, Vienna, Austria; AstraZeneca R&D & D, Loughborough, United Kingdom.


253. Eye movements during same day repeated testing. M. Maggie Folan, R.N., B.S.N., Patricia D. Kroboth, Ph.D., Tanya J. Fabian, Pharm.D., Frank J. Kroboth, M.D., Gretchen Haas, Ph.D., Roslyn A. Stone, Ph.D., Kristin L. Biggs, B.S., John A. Sweeney, Ph.D.; University of Pittsburgh, Pittsburgh, PA; University of Illinois at Chicago, Chicago, IL.

PURPOSE: Saccadic eye movements (SEMs) are frequently used as measures of central nervous system activity as a quantitative indicator of drug response. This study evaluated the influence of time on SEM dynamics (velocity, amplitude, latency, gain) in healthy young and elderly women and men.

METHODS: The 66 volunteers were medically and psychiatrically healthy women (18 young and 14 older) and men (22 young and 12 older). Ages ranged from 21 to 26 years (young) and 65 to 78 years (older). Visually guided SEM recordings to multiple targets (8° and 16° of vision to the right and left of center fixation) were obtained using an infrared reflection technique at 10 testing sessions over 12.5 hours. A repeated measure ANOVA was used to assess differences in SEM dynamics across time.

RESULTS: Latency was stable over 12.5 hours for both groups. In the young, velocity was stable over time, while amplitude (to 16° targets) and gain (to 8° and 16° targets) improved (p<0.03). In the older group, velocity to 8° targets varied over time (p=0.04). For all target locations, velocity, amplitude, and gain were greater and latency was lower in the young (p<0.02).

CONCLUSIONS: SEM dynamics are relatively stable for ten repeated testing sessions during 12.5 hours. However, when used as a measure of drug response, inclusion of a placebo run-in time is necessary to account for time associated learning, especially in the young. When SEM dynamics differed statistically across time, the young group showed improvement while the older group was more variable.


PURPOSE: The pharmacokinetic profiles of tazarotene and its primary active metabolite, tazarotenic acid, were evaluated following multiple single and multiple doses of oral tazarotene.

METHODS: This was a single-center, open-label, stratified, randomized, two-period, parallel design trial. Single- and multiple-dose, dose-proportionality pharmacokinetic study in which 41 healthy volunteers were assigned to received 3 mg, 6.3 mg, 6.3 mg with food, 9 mg, or 12 mg tazarotene. After a single dose and after 7 days of dosing; plasma samples (and skin at one time-point) were collected over a 72-hour period for determination of drug concentrations using a validated LC-MS/MS method. Pharmacokinetic parameters were calculated using a non-compartmental approach. Effect of drug, food, and gender on the pharmacokinetics of tazarotene and tazarotenic acid were evaluated.

RESULTS: Tazarotene was present only in minute quantities, with the major drug related species being tazarotenic acid. Following multiple doses, tazarotenic acid AUC values were similar to single dose values and increased approximately proportionally to dose (p=0.08). Tazarotenic acid Cmax and pantoprazole AUC values were similar to single dose values and increased approximately proportionally to dose (p=0.0129, 0.0234 and 0.0472, respectively).

PURPOSE: The primary objective of this analysis was to identify covariates that influence serum cortisol levels following fluticasone propionate. Sharon C. Murray, Ph.D., Rashmi S. Mehta, Ph.D., Robert L. Kunka, Ph.D., Shuchung Shaw, M.S., Yonghua Wang, Ph.D.; GlaxoSmithKline, Research Triangle Park, NC.

METHODS: The data used in this meta-analysis comes from 182 subjects in five Phase III/III/IV studies: FLTA2001, FLTD230, FLT0325, FAS04022, and FM450243. Serum cortisol was used as a measure of the pharmacodynamics (PD) of FP. The effects of fluticasone propionate covariates were investigated on the PD of FP: Demographic data [age, gender, body mass index (BMI)], baseline cortisol, percent predicted FEV1, disease category (healthy, asthma or COPD)).

RESULTS: Adjusted mean differences (95% CI) in serum cortisol AUC between females and males for the placebo, 100 µg, 250 µg, and 500 µg groups, respectively, were 814.5 (180.0, 1610.9), 697.6 (-1137.7, 2532.8), 793.3 (1171.4, 1941.3), and 403.5 (-268.4, 833.8). Gender, formulation and percent predicted FEV1 had statistically significant effects on serum cortisol (p=0.0129, 0.0234 and 0.0472, respectively).

CONCLUSIONS: Meta-analysis showed that cortisol levels are higher in females compared to males. This difference is independent of FP formulation and was also observed after placebo treatment. Serum cortisol levels were also affected by formulation and pulmonary function. Disease category (asthma, COPD, or healthy), age, and body mass index did not affect cortisol.

257E. Cantharidin-induced inflammatory blister technique: focus on healing and blister resolution. Dana Maglio, Pharm.D., Charles H. Niggliegle, Ph.D., David P. Nicolau, Pharm.D., FCCP; Hartford Hospital, Hartford, CT.


258. The pharmacokinetics of pantoprazole and omeprazole in patients with erosive gastroesophageal reflux disease. Vijaya S. Pratha, M.D., Robyn G. Karlstad, M.D., Richard B. Lynn, M.D., Michael S. Burton, B.S., Daniel L. Hogan, Ph.D.; Clinical Applications Laboratories, San Diego, CA; Wyeth Pharmaceuticals, St. Davids, PA.

PURPOSE: Pharmacokinetics (PK) of pantoprazole and omeprazole are well described in healthy subjects. In a previous study in healthy subjects, pantoprazole 40 mg demonstrated greater acid inhibition than omeprazole 20 mg (Pratha et al. Otalaryngology Head Neck Surg. 2002;in press). The purpose of this study was to characterize the PK of these proton pump inhibitors in patients with erosive gastroesophageal reflux disease (GERD).

METHODS: 35 patients (23 M,12 F) with documented GERD who received 3 mg, 6.3 mg, 6.3 mg with food, 9 mg, or 12 mg tazarotene. After a single dose and after 7 days of dosing; plasma samples (and skin at one time-point) were collected over a 72-hour period for determination of drug concentrations using a validated LC-MS/MS method. Pharmacokinetic parameters were calculated using a non-compartmental approach. Effect of drug, food, and gender on the pharmacokinetics of tazarotene and tazarotenic acid were evaluated.

RESULTS: Tazarotene was present only in minute quantities, with the major drug related species being tazarotenic acid. Following multiple doses, tazarotenic acid AUC values were similar to single dose values and increased approximately proportionally to dose (p=0.08). Tazarotenic acid Cmax and pantoprazole AUC values were not different between fasted and fed treatments (90% confidence interval) or between genders (p=0.11 - 0.25). Tazarotenic acid in skin biopsy samples collected from volunteers ranged from 21 to 40 ng/g. CONCLUSIONS: The pharmacokinetics of tazarotenic acid after a single dose was predictive of steady-state kinetics, and systemic exposure was approximately proportional to dose. Neither food nor gender affected pharmacokinetics. Tazarotenic acid reached therapeutic levels in skin and was more rapidly eliminated from the systemic circulation than other approved retinoids.

255. Markers of inflammation in brain endothelium after exposure to three forms of amphotericin: potential mechanism of infusion reactions. Timothy R. McGuire, Pharm.D., William J. Trickler, Eric B. Haie, Pharm.D., Donald W. Miller, Ph.D.; University of Nebraska Medical Center, Omaha, NE.

Common formulations of amphotericin include a deoxycholate colloidal suspension (d-Amph), an amphotericin-B lipid complex (Abic), and a liposomal product (i-Amph). The clinical incidence of infusion related fever is highest with d-Amph, intermediate with Abic, and lowest with i-Amph. In the present study, we measured the activation of cyclooxygenase-2 (COX-2) and release of TNF-α and IL-1β from brain microvascular endothelium treated with these three formulations of amphotericin. Primary culture provided brain microvascular endothelial cells (PBMEC) were exposed to d-Amph, Abic and i-Amph at clinically relevant concentrations. Media samples from the cells were collected and analyzed for TNF-α and IL-1β. Release of these cytokines from PBMEC monolayers treated with i-Amph were similar to cells receiving culture media alone. In contrast, Abic and d-Amph caused significantly greater release of both TNF-α and IL-1β. Compared to conventional wisdom TNF-α was the initial inflammatory cytokine released with IL-1β being released later. In previously presented data we demonstrated a rise in PGE-2 within 1 hour of treating endothelium with amphotericin. We confirmed by Western blot analysis an induction of COX-2 expression in BMEC following LPS, Abic or d-Amph treatment. These studies indicate that amphotericin induces COX-2 expression in brain microvascular endothelium which is responsible for PGE-2 release and fever. TNF-α is released early from endothelium and is more likely than IL-1β to mediate amphotericin induced infusion reactions. The signal transduction pathways involved in amphotericin induced fever are under investigation.

256. Meta-analysis to evaluate factors affecting serum cortisol following fluticasone propionate. Charles H. Niggliegle, Ph.D., David P. Nicolau, Pharm.D., FCCP; Hartford Hospital, Hartford, CT.

259. Oral telithromycin for 7 to 10 days is as effective as standard comparators for the treatment of community-acquired pneumonia. John Pullman, M.D., Bruno Leroy, M.D.; Mercury Street Medical, Butte, MT; Aventis Pharmaceuticals, Bridgewater, NJ.

Hypothesis: Telithromycin, a ketolide antibacterial, is equivalent to standard comparators in the treatment of community-acquired pneumonia (CAP), including infections causing by atypical/intracellular pathogens. METHODS: The efficacy of telithromycin 800 mg QD for 7 to 10 days in 503 adult patients with symptoms of CAP (radiologically confirmed) and stratified according to Fine score, was assessed in three randomized, double-blind, multicenter Phase III studies. Comparator groups (+n21) received either amoxicillin/clavulanate 500 mg TID or clarithromycin 500 mg BID for 10 days, or trovafloxacin 200 mg QD for 7 to 10 days. RESULTS: The clinical cure rate for telithromycin post-therapy (Days 17 to 24) was 91.0% (356/391) in the per-protocol (PPc) population vs. 90.4% (356/391) for pooled comparators. In patients at increased risk of morbidity and mortality, clinical cure with telithromycin vs. comparators was 91.8% (56/61) vs. 83.3% (65/78) in those with a Fine score ≥ II, 88.3% (53/60) vs. 84.6% (56/66) in subjects aged ≥65, and 93.8% (15/16) vs. 84.6% (11/13) in patients with pneumococcal bacteremia. Among the PPC group for whom a pretreatment causative pathogen was identified, bacteriologic outcome was satisfactory in 90.2% (74/82) of telithromycin-treated patients compared with 93.3% (84/90) of comparator-treated patients. Clinical cure rates for patients infected with pneumococcal pathogens were 90.0% (198/220) of the telithromycin group vs. 88.3% (181/205) of comparator groups.

CONCLUSIONS: Telithromycin 800 mg once daily for 7 to 10 days offers a convenient first-line therapy, equivalent to comparators, for empiric treatment of CAP; providing higher rates of clinical and bacteriologic efficacy.

260. Effect of high-fat breakfast and moderate-fat evening meal on the pharmacokinetics of vardenafil, a potent, selective PDE-5 inhibitor for the treatment of erectile dysfunction. R. Prabhajyapalan, Ph.D., D. Mazzu, Ph.D., Chenghua Xia, Ph.D., Ray Dawkins, M.D., Pavur Sundaresan, M.D., Ph.D.; Bayer Corporation, West Haven, CT; PDD Development, Morrisville, NC.

PURPOSE: To assess the effects of a high-fat breakfast and a typical moderate-fat evening meal on the pharmacokinetics of vardenafil, a potent, selective PDE-5 inhibitor for the treatment of erectile dysfunction. METHODS: In this randomized crossover study, vardenafil 20 mg was administered to 25 healthy males (mean age 29 years, mean BMI 25 kg/m²) after an overnight fast or immediately after consumption of a high-fat breakfast (57% fat), at 6 PM on an empty stomach or after consumption of a moderate-fat meal (30% fat). Blood samples were analyzed for vardenafil and metabolite M1 levels; pharmacokinetic parameters were determined using non-compartmental methods.

RESULTS: High and moderate fat meals did not alter vardenafil pharmacokinetic parameters [geometric mean (CV%)] shown in Table to clinically significant degree. Moderate-fat meal did not alter Tmax and high-fat meal delayed median Tmax by an hour.

<table>
<thead>
<tr>
<th>AM Moderate Fat meal</th>
<th>Geometric mean ratio (90% CI)</th>
<th>AM High Fat meal</th>
<th>Geometric mean ratio (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tmax, h</td>
<td>3.3</td>
<td>0.99</td>
<td>3.8</td>
</tr>
<tr>
<td>AUC, µg•h/L</td>
<td>61.78</td>
<td>67.09</td>
<td>1.01</td>
</tr>
<tr>
<td>Cmax, µg/L</td>
<td>2.6</td>
<td>0.52</td>
<td>3.0</td>
</tr>
<tr>
<td>Half-life, h</td>
<td>3.3</td>
<td>0.99</td>
<td>3.8</td>
</tr>
</tbody>
</table>

A similar observation was made for metabolite M1. Treatments were well tolerated. No serious adverse events were reported. Headache (most common treatment-related adverse event) was reported in 1-3 subjects per treatment.

CONCLUSION: Vardenafil pharmacokinetics are largely unaffected by food containing high or moderate amounts of fat.
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265. Pharmacokinetic variability in patients receiving large dose-extended interval aminoglycosides. Jennifer M. Sickels, Pharm.D., Maryann Hawes, Pharm.D., candidate, Northeastern University, Boston, MA.

PURPOSE: Administering large dose-extended interval (LDEI) aminoglycosides to patients with variable pharmacokinetics could result in prolonged drug-free periods resulting in decreased efficacy. The purpose of this study was to identify characteristics and evaluate clinical outcomes of patients who received LDEI aminoglycosides and had low random serum concentrations.

METHODS: Medical records of patients who received LDEI aminoglycosides from 8/95-3/01 were reviewed. Patients with random concentrations ≤ 2 mg/dL (within 12 hours post-dose) were enrolled in the study group; patients with random concentrations > 2 mg/dL were enrolled in the control group. Demographic data, factors that could affect pharmacokinetics, and clinical outcomes were documented.

RESULTS: A total of 278 patients were evaluated. Compared to controls (n=193), study patients (n=85) were younger (43.39 years vs. 58.71 years, p=0.0001); had better renal function (Ccr 68.34 ml/min vs. 71.39 ml/min, p=0.0001); and lower actual body weight (72.54 kg vs. 78.59 kg, p=0.0001). No association was identified between low random concentrations and critical illness, neutropenia, quadruplegia, or ascites. Clinical cure or improvement rates were similar between groups (85% vs. 91%, p=0.2016). No significant differences were found between groups in rates of dosage changes (30% vs. 30%, p=0.17), duration of therapy (5.25 days vs. 5.88 days, p=0.09), or number of concentrations drawn per patient (1.67 vs. 1.70, p=0.65). Neutropenia was less common in the study group (RR=0.33; 95% CI=0.16-0.682).

CONCLUSION: Characteristics associated with low random concentrations included decreased age, increased renal function, and decreased weight. Low random concentrations did not result in decreased efficacy in our study population.


267. Effect of sex on the pharmacokinetics of ciprofloxacin. Brian R. Overholser, Pharm.D., Michael B. Kays, Pharm.D., Kevin M. Sowinski, Pharm.D.; Purdue University; Indiana University, Indianapolis, IN.

Two previous studies showed no differences in oral ciprofloxacin pharmacokinetics between males and females. PURPOSE: To assess the influence of sex on the pharmacokinetics of oral ciprofloxacin.

METHODS: Fifteen healthy subjects (8 males, 7 females) were enrolled. They were admitted to the research unit in the morning of the study day and were required to fast ≥ 8 hour prior to admission. Each subject received a single oral dose of ciprofloxacin 750 mg. Serial blood samples were collected immediately before and 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hour after administration. Ciprofloxacin serum concentrations were determined by HPLC, and pharmacokinetic models were fit to the data using ADAPT II software. Initially, models were fit to the data with a weighted (inverse of observation variance) least squares estimator. These estimated parameters were used to compute maximum a posteriori Bayesian priors, and the data were reanalyzed using the maximum a posteriori procedure. In all subjects, a two-compartment open model with two parallel first-order inputs and elimination from the central compartment was chosen as the model of best fit by Akaike’s Information Criterion and visual inspection. Differences in pharmacokinetic parameters between males and females were determined using the Student’s t-test.

RESULTS: The average ages of males and females were not significantly different, 31.8 ± 6.4 vs. 28.0 ± 5.3 years. The average weights were 87.2 ± 14.1 and 58.4 ± 7.3 kg (p<0.05) for males and females, respectively. Estimated pharmacokinetic parameters and calculated secondary parameters (mean ± SD) are shown in the table below.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cl/F (L/hour)</th>
<th>CL/F (L/hour/kg)</th>
<th>CLd (L/hr)</th>
<th>Vc/F (L)</th>
<th>Vp/F (L)</th>
<th>Vss/F (L/kg)</th>
<th>t1/2 (hr)</th>
<th>Cmax (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>55.3 ± 4.4*</td>
<td>0.94 ± 0.09</td>
<td>27.6 ± 1.6</td>
<td>12.8 ± 15.0</td>
<td>88.2 ± 10.1</td>
<td>49.2 ± 11.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rofecoxib 50 mg QD</td>
<td>76.6 ± 2.6*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Celecoxib 200 mg BID</td>
<td>46.91 (4.58)</td>
<td>10.44 (14.26)</td>
<td>63.24 (3.93)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>64.63 (2.99)</td>
<td>32.64 (3.93)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS: Differences exist in ciprofloxacin pharmacokinetics between males and females due to differences in body weight. Fixed doses of ciprofloxacin given without regard to body weight will lead to higher drug exposure in females compared to males.

268. Herbal teas and their effect on hepatic drug metabolizing enzymes in rats. Sompon Wanwimolruk, Pharm.D., Pius F. Malilakal, Ph.D.; Western University of Health Sciences, Pomona, CA; University of Otago, Dunedin, New Zealand.

PURPOSE: The present study was conducted to determine the effect of herbal teas (Peppermint, Chamomile and Dandelion tea) on the activity of hepatic phase I and phase II metabolizing enzymes using rat liver microsomes.

METHODS: Female Wistar rats were divided into 6 groups (n = 5 each). Three groups had free access to tea solutions (2%) while the control group had water. Two groups received either green tea extract (0.1%) or aqueous caffeine solution (0.0625%). After 4 weeks of pretreatment, different cytochrome P450 (CYP) isomers and phase II enzyme activities were determined by incubation of liver microsomes or cytosols with appropriate substrates.

RESULTS: Activity of CYP1A2 in liver microsomes of rats receiving Dandelion, Peppermint and Chamomile tea were significantly decreased (p < 0.05) to 15%, 24% and 39% of the control value, respectively. CYP2A1 activity was significantly increased by pretreatment with caffeine solution. No alterations were observed in the activities of CYP2D and CYP3A in any groups of pretreated rats. Activity of CYP2E in rats receiving Dandelion and Peppermint tea was significantly lower (p < 0.05) than in the control group, i.e. 48% and 60% of the control. There was a dramatic increase (244% of control) in the activity of phase II detoxifying enzyme UDP-glucuronosyltransferase in Dandelion tea pretreated group. There was no change in the activity of glutathione-S-transferase.

CONCLUSION: The results suggest that green and black teas, certain herbal teas can cause modulation of phase I and phase II drug metabolizing enzymes.

269E. Pharmacokinetic comparison of five proton pump inhibitors. Lynda S. Welage, Pharm.D., Robyn G. Karlstadt, M.D., Michael S. Burton, B.S., Richard B. Lyon, M.D.; University of Michigan, Ann Arbor, MI; Wyeth-Ayerst Pharmaceuticals, St. Davids, PA.


PURPOSE: This study examines whether olanzapine co-therapy with lithium affects the pharmacokinetics of valproic acid in patients with bipolar or schizoaffective disorder. METHODS: Patients who were in symptomatic remission of mania and depression (HAMD-21 ≤ 12) the olanzapine treated-treated patients (n=46) had a significantly lower (p<0.05) valproate monotherapy in patients suffering from bipolar disorder. RESULTS: Among patients who were symptomatic remission of mania (Y-MRS ≤ 12) the olanzapine-treated patients (n=46) had a significantly longer time to recurrence in patients suffering from bipolar disorder than the monotherapy-treated patients (n=48; estimated 25th percentile: 362 vs. 63 days, respectively; P=0.005).

Rates of recurrence into mania also significantly favored olanzapine-treated patients (monotherapy, 37.5% vs. olanzapine, 17.5%; P=0.033). Recurrence into depression was decreased (p < 0.05) in patients who were in symptomatic remission of mania and depression (HAMD-21 ≤ 8) following acute therapy. Time to and rates of recurrence into depression were not significantly different between treated (n=96) and monotherapy (n=98) groups, but were numerically favorable for the olanzapine treated group (135 vs. 27 days, respectively).
271. Telithromycin is as effective as standard comparators in the treatment of community-acquired respiratory tract infections. Marcus Zervos, M.D., James T. Hawa, D.D.; William Beaumont Hospital, Royal Oak, MI; Benbrook Family Practice, Benbrook, TX.

HYPOTHESIS: telithromycin (TEL), a ketolide antibacterial, is equivalent to standard comparators (CMPs) in the treatment of community-acquired respiratory tract infections. METHODS: In seven Phase III randomized, double-blind, active-controlled studies, patients with community-acquired pneumonia (CAP), acute exacerbation of chronic bronchitis (AECB), and acute maxillary sinusitis (AMS) were treated with TEL or CMP. RESULTS: In three studies, patients received 7 to 10-day TEL 800-mg QD, 10-day amoxicillin 1000-mg TID, 10-day clarithromycin 500-mg BID, or 7 to 10-day trovafloxacin 200 mg QD. In 2 studies, patients received 5-day TEL 800-mg QD, or 10-day amoxicillin/clavulanate (A/C) 500/125-mg TID or cefuroxime axetil (CEF) 500-mg BID. In 2 studies, patients received 5- or 10-day TEL 800-mg QD, or 10-day A/C 500/125-mg TID or CEF 250-mg BID. RESULTS: In the pooled, modified, intent-to-treat population (N=6800), patients treated with TEL vs. A/C (1190 CMPs) vs. CEF (1190 CMPs) at post-therapy/bed-of-care (Days 17 to 24): TEL and A/C achieved comparable clinical cure rates in protocol patients with CAP (91.0% TEL vs. 90.4% CEF), AECB (86.3% TEL vs. 82.7% CEF), and AMS (78.5% TEL vs. 77.4% CEF). Similar clinical cure rates at late post-therapy (Days 31 to 45) were also seen with TEL compared with CMP in treating CAP (88.3% TEL vs. 86.8% CEF), AECB (78.4% TEL vs. 75.8% CEF), and AMS (73.1% TEL vs. 73.6% CEF). Telithromycin also achieved high rates of bacterial eradication.

CONCLUSIONS: Once-daily TEL achieves clinical cure rates equivalent to CMPs in treating community-acquired respiratory tract infections.

Pharmacy Practice

272. A comparison of the responsibilities of tenure versus non-tenure track pharmacy practice faculty. Mark L. Glover, Pharm.D., Lisa Dzeliz-Evans, Pharm.D., Ph.D., Nova Southeastern University, Ft. Lauderdale, FL.

PURPOSE: To determine if tenure and non-tenure track pharmacy practice faculty differ with respect to their involvement with teaching, research, and service activities. METHODS: A survey identifying the teaching, research, and service activities of faculty was mailed to the respective chair within the division of pharmacy practice of 82 United States Schools of Pharmacy. Responses to each of the survey questions were compared between tenure and non-tenure faculty and between those schools who employ both tenure and non-tenure track faculty. Comparisons included: 1) the number of weeks per year precepting students, 2) the number of research students precepted per year, 3) the number of didactic hours taught per year, 4) the number of peer-reviewed articles published per year, and 5) the number of committee assignments per year. RESULTS: A total of 71 (87%) surveys were returned with two being excluded due to incomplete data. Of the 69 pharmacy practice departments represented, analysis of all responses indicated tenure track faculty publish more articles per year (1.5 vs. 0.6) and serve on more committees (2.1 vs. 1.8) while non-tenure track faculty precept more students per year (16.8 vs. 13) and for more weeks during the year (33.4 vs. 27.6). There was no significant difference regarding the number of didactic hours taught per year between tenure and non-tenure track faculty (36.1 vs. 29.2). Those departments that employ both tenure and non-tenure track faculty indicated a significant difference between the two groups for all questions. CONCLUSION: Tenure and non-tenure track pharmacy practice faculty differ in terms of their required teaching, research, and service activities.

273. Clinical pharmacist staffing in United States hospitals. C.A. Bond, Pharm.D., FASHP, FCPP, Cynthia L. Rael, Pharm.D., FASHP, FCPP, Todd Franke, Ph.D., Texas Tech University Health Sciences Center, Amarillo, TX.

This study evaluated hospital demographics (census regions, size, teaching affiliation, hospital ownership, hospital pharmacy director’s degree, and pharmacist’s drug–drug interactions within the hospital) and clinical pharmacy staffing/occupied beds in United States hospitals. A database was constructed from the 1992 American Hospital Association’s Abridged Guide to the Health Care Field and the 1992 National Clinical Pharmacy Services Database. Simple statistical tests and a multiple regression analysis were employed. The study population consisted of 1391 hospitals that reported information on clinical pharmacist staffing. The mean number of clinical pharmacists/occupied bed was 0.51 clinical pharmacists/100 occupied bed. Factors associated increased clinical pharmacist staffing/occupied bed were West North Central region (slope = 0.0029439, p=0.002), Pacific region (slope = 0.0032089, p=0.004), hospitals affiliated with a pharmacy teaching program (slope = 0.0025330, p=0.001), teaching hospitals (slope = 0.0028122, p=0.001), federal government hospitals (slope = 0.0029697, p=0.002), directors with the M.S. Pharmacy degree (slope = 0.0032080, p=0.002), directors with the M.S. Pharmacy degree (slope = 0.003), pharmacists in a decentralized location (slope = 0.0035393, p=0.001), and pharmacy technician staffing (slope = 0.0317173, p=0.001). Statistically significant associations between demographic variables and decreased clinical pharmacist staffing/occupied bed were Midwest, South Central, and the Atlantic region (slope = 0.0028237, p=0.002), small hospitals (slope = 0.0028894, p=0.001), and hospital pharmacy administrator staffing (slope = 0.0184513, p=0.042). Significant differences were observed between clinical pharmacists staffing and hospital demographic factors. Future research will help determine the reasons for these differences and help future clinical pharmacy administrators in the staffing of their hospitals.

Psychiatry

274. The effect of levofloxacin coadministration on international normalized ratio monitoring of warfarin therapy. Weeranuj Yamreum deong, Pharm.D., BCPs, CACP, Dennis L. Lower, M.D., David M. Kilpatrick, M.D., Ann M. Enlow, F.N.P., Margo M. Burrows, F.N.P.; Cheyenne Veterans Affairs Medical Center, Cheyenne, WY.

PURPOSE: To evaluate the effect of levofloxacin coadminstration on international normalized ratio (INR) monitoring in patients receiving warfarin therapy. METHODS: A total of eighteen patients who were receiving stable doses of warfarin therapy participated in this study. Levofloxacin was prescribed for treatment of different types of infection in these patients based on appropriate diagnoses of the health care providers. The study began after obtaining written informed consent form from the patient. The INR values of each patient were measured before and after levofloxacin initiation. Each study patient was asked to return to the clinic twice weekly for INR monitoring during levofloxacin coadministration. The INR values were also measured after the completion of levofloxacin therapy. Dosages of other concurrent medications that might interact with warfarin were kept constant during the study period. Each patient was asked if any adverse effects had occurred at each clinic visit. After levofloxacin initiation, warfarin doses were adjusted as necessary in patients with the first INR values that were higher or lower than therapeutic ranges. RESULTS: In some patients, warfarin doses were changed after the first nontherapeutic INR values post levofloxacin administration, therefore only the INR values before and the first INR values after starting levofloxacin therapy were compared. Using the two-tailed paired t-test statistical analysis, results of this study revealed no significant difference in INR values before and after levofloxacin coadministration (p=0.42). CONCLUSION: The results of this study revealed no significant effect of levofloxacin coadministration on INR monitoring of warfarin therapy.

277. Olanzapine and olanzapine-fluoxetine combination in the treatment of bipolar depression. Mauricio Tohen, M.D., Ph.D., Eduard Vieta, M.D., Ph.D., Terence Ketter, M.D., Franca Centorrino, M.D., Joseph Calabrese, M.D., Gary Sachs, M.D., Charles Bowden, M.D., Richard Risser, M.S., Robert W. Baker, M.D., Angela R. Evans, Ph.D., Virginia L. Stauffer, Pharm.D., Sanjay Dube, M.D., Gary Tolleson, M.D., Ph.D., Alan Breier, M.D.; Eli Lilly & Company; Indianapolis, IN; Harvard Medical School/McLean Hospital, Belmont, MA; DIBAPS, Barcelona, Spain; Stanford University, Stanford, CA; Case Western Reserve University, Cleveland, OH; University of Texas Health Science Center, San Antonio, TX. Presented at the International Conference of the American Psychiatric Association, Philadelphia, PA, May 18, 2002.


PURPOSE: The purpose of this study was to examine the prescribing patterns of commonly used atypical antipsychotics by physician type and patient age group. METHODS: From 1/1/97 to 8/1/98, a total of 5,907 prescriptions were written for olanzapine (n=2429), quetiapine (n=474), and risperidone (n=2521) in the National Disease and Therapeutic Index™ database. Physician specialty type was categorized into two groups: primary care physicians (PCP), which included Internists, Family Medicine, General Medicine, Geriatrics and Pediatrics, and non-primary care physicians (non-PCP), which included Psychiatry and other specialists. Patient age was divided into three categories: Child/Adolescent (age 0-19), Adult (age 20-59), and Geriatric (age 60 and above).

RESULTS: Across atypical antipsychotics, 83.8% of all prescriptions were written by non-PCPs (mostly psychiatrists). One-quarter (25.3%) of all atypical antipsychotic prescriptions were for geriatric individuals, while 60.2% and 14.5% were written for Adult and Child/Adolescent patients, respectively. Pediatric was the most commonly prescribed for Child/Adolescent patients, representing 62.8% of all Child/Adolescent prescriptions. Nearly half (47.5%) of atypical antipsychotic prescriptions written by PCPs were for the Geriatric population. Of the Geriatric prescriptions, a significantly larger proportion of risperidone prescriptions (36.8%) were written by PCPs versus non-PCPs than olanzapine (26.9%, p<0.001) or quetiapine (13.4%, p<0.0001).

CONCLUSIONS: Across physician specialty, differences exist in prescribing patterns for atypical antipsychotics particularly within Geriatric and Child/Adolescent populations. Further research is needed to examine the reasons for the atypical antipsychotic prescribing differences between PCP and non-PCPs.

279. The effects of ethnicity and antipsychotic type on medication adherence. In the Medicaid population, Jayne L. Opolka, M.S., Karen L. Raschi, Ph.D., Carolyn B. Bowden, P.J. Joseph Gibson, Ph.D.; University of Texas at Austin, Austin, TX; Eli Lilly & Company, Indianapolis, IN.

PURPOSE: Clinicians treating schizophrenia face increasingly diverse populations. Different ethnic groups have different approaches to medication adherence. The purpose of this study was to examine the association between antipsychotic medication adherence and ethnicity or the specific medication used, after controlling for other factors. METHODS: Texas Medicaid claims were reviewed for persons, age 21 to 65, diagnosed with schizophrenia or schizoaffective disorder, initiating treatment with olanzapine (n = 1875), risperidone (n = 982), or haloperidol (n = 279) between 1/1997 and 8/1998. For each of the three pairings of these medications, the association between ethnicity (African American, Mexican American, or White) and medication and days of medication in the year following initiation was assessed using multivariate linear regression. Covariates included other patient demographics, region, comorbid health conditions, and prior medication and health care resource use.

RESULTS: Overall mean adherence was 177 of 365 days (48.5%). African Americans and Mexican Americans were significantly less than Whites in the haloperidol versus olanzapine and risperidone versus olanzapine comparisons (p=0.05 for each comparison). For patients of all ethnicities, olanzapine was associated with 19 more adherent days than risperidone and 56 more adherent days than haloperidol (p<0.001 for each pair-wise comparison).

CONCLUSION: When other factors were controlled for 1) ethnicity was a significant predictor of adherence following initiation on an antipsychotic medication and 2) patients of all ethnicities were most adherent when taking olanzapine, least adherent when taking risperidone, and least adherent when taking haloperidol.


PURPOSE: This initiative was designed to promote the selection of fluoxetine as the SSRI of choice in patients new to SSRI therapy at Group Health Cooperative. This report examines 1) success of the initiative in establishing fluoxetine as first-line therapy 2) maintenance of new patients on fluoxetine over time.

METHODS: Educational efforts including newsletters, electronic communications, and academic detailing were begun to support the initiative. Prescription data was then examined monthly to determine percentage of SSRI new starts on fluoxetine and maintenance of these patients on fluoxetine. Monthly reports were developed to provide continual feedback on compliance with the initiative at various levels, including providers.

RESULTS: 1) Fluoxetine was prescribed in 17% of patients new to SSRI therapy before the initiative began. It was prescribed as follows after introduction of the initiative: January- 49%; February- 55%; March- 62%; April- 67%; May- 72%. 2) As of May 31, 67% (n=1664) of patients started on fluoxetine since January 1 had received another SSRI prescription. 99% of those patients continued on fluoxetine; 5% subsequently received paroxetine; 4% sertraline, and 2% citalopram.

CONCLUSION: Despite initial resistance based on unestablished mythology that fluoxetine is less well-tolerated than other SSRIs, the Fluoxetine First Initiative has been very successful in establishing fluoxetine as SSRI of choice without adding formulary restrictions on other SSRIs. Furthermore, the great majority of patients who were started on fluoxetine have continued on fluoxetine. These continuation rates do not differ from that of the other SSRIs within our organization.

281. An open trial of quetiapine for aggression in children and adolescents with attention deficit hyperactivity disorder. William A. Kehoe, Pharm.D., M.A., Robert B. Schorr, D.O.; University of the Pacific, Stockton, CA; Psychiatric Medical Group, Modesto, CA.

PURPOSE: Aggression is common in children with ADHD. Psychostimulants often do not provide adequate treatment, and antipsychotics have been used. This study evaluated the impact on aggression of the addition of quetiapine to psychostimulants.

METHODS: Ten children and adolescents aged 6-14 years with ADHD and aggression that inadequately responded to a psychostimulant were given quetiapine in an open, uncontrolled, prospective trial. The initial dose was 25 mg q HS and titrated as tolerated to a maximum of 200 mg per day. The primary outcome variable was the change in the “aggression” score on the Child Behavior Checklist (CBCL) after a minimum of 4 weeks of treatment. Secondary outcomes included changes in the “externalizing” and “internalizing” scores on the CBCL. Data were analyzed using two-tailed t-tests. Side effects were monitored using the Treatment Emergent Side Effects Scale.

RESULTS: The addition of quetiapine to psychostimulant therapy resulted in significant reductions in aggression scores (25%, p<0.033). Externalizing behaviors (aggression and delinquency) were significantly reduced (27%, p<0.015). Internalizing behaviors (withdrawal, social and attention problems) were also significantly reduced (23%, p=0.012). No serious side effects requiring discontinuation of therapy were observed. The most common ones included sedation and fatigue observed in 3 patients.

CONCLUSIONS: Quetiapine was effective for reducing aggression in children and adolescents with ADHD when psychostimulants were inadequate. It was well tolerated with no serious side effects noted. Further randomized, controlled trials are warranted.

282E. Meta-analysis of weight effects with aripiprazole. Lyle K. Laird, Pharm.D., BCPP, Darlene Jody, M.D., Anutosh R. Saha, Ph.D., Taro Iwamoto, Ph.D., Debjit Biswas, Ph.D., Chin-Yu Lin, Ph.D., Ronald Marcus, M.D., Robert D. McQuade, Ph.D., Bristol-Myers Squibb Company, Denver, CO; Bristol-Myers Squibb Company, Lawrenceville, NJ; Otsuka Maryland Research Institute, LLC, Rockville, MD; Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan; Bristol-Myers Squibb Company, Wallingford, CT.

Presented at the 23rd Congress of the Collegium Internationale Neuro-Psycho Phar macologicum, Montreal, Canada, June 27, 2002.

283E. Safety and tolerability meta-analysis of aripiprazole in schizophrenia. Robert D. McQuade, Ph.D., Elyse Stock, M.D., Stephen R. Marder, M.D., Anutosh R. Saha, Ph.D., Donald G. Archibald, M.Phil., Taro Iwamoto, Ph.D., Bristol-Myers Squibb Company, Lawrenceville, NJ; Bristol-Myers Squibb Company, Wallingford, CT; University of California, Los Angeles, CA; Otsuka Maryland Research Institute, LLC, Rockville, MD; Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan.

Presented at the 23rd Congress of the Collegium Internationale Neuro-Psychopharmacologicum, Montreal, Canada, June 27, 2002.

284E. Switching to aripiprazole monotherapy. John M. Petrias, Pharm.D., Robert D. McQuade, Ph.D., Daniel E. Casey, M.D., Anutosh R. Saha, Ph.D.,

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285E. Aripiprazole vs. placebo in the treatment of stable, chronic schizophrenia. Ronald Marcus, M.D., Neven Abou-Gharbia, Pharm.D., Mary J. Kujawa, M.D.; Bristol-Myers Squibb Company, Plainsboro, NJ; Bristol-Myers Squibb Company, Wallingford, CT.


287E. Effect of olanzapine and risperidone on glycose, lipids, and body mass. Robert E. Litman, Georgetown University, Rockville, MD.

288E. Long-acting injectable risperidone: efficacy and safety. John Kane, M.D.; Marielle Eerdekens, M.D., M.B.A., Samuel Keith, M.D., Michael Lesem, M.D., Keith Karcher, M.S., Jean-Pierre Lindenmayer, M.D.; Hillside Hospital, Glen Oaks, NY; Janssen Research Foundation, Beerse, Belgium; University of New Mexico, Albuquerque, NM; Claghnor-Lesem Research Clinic, Belfare TX; Janssen Research Foundation, Titusville, NJ; Manhattan Psychiatric Center, New York, NY.

289E. Clozapine augmentation with risperidone in refractory schizophrenia. Marielle Eerdekens, M.D., M.B.A., W. Wolfgang Fleischacker, M.D., Linda Beauchair, M.D., Stephen Martin; Janssen Research Foundation, Beerse, Belgium; Innsbruck University Clinics, Innsbruck, Austria; Clinic – Allan Memorial Institute, Montreal, Canada; Middleton St. George Hospital, Darlington County, Durham, United Kingdom.

290E. Long-term safety and efficacy of long-acting injectable risperidone. Marielle Eerdekens, M.D., M.B.A., W. Wolfgang Fleischacker, M.D., Linda Beauchair, M.D., Stephen Martin; Janssen Research Foundation, Beerse, Belgium; Innsbruck University Clinics, Innsbruck, Austria; Clinic – Allan Memorial Institute, Montreal, Canada; Middleton St. George Hospital, Darlington County, Durham, United Kingdom.

291E. Olanzapine combined with mood stabilizers in prevention of recurrence in bipolar disorder: an 18-month study. Mauricio Tohen, M.D., Ph.D., Roy Chengappa, M.D., Trisha Suppes, M.D., Ph.D., Robert W. Baker, M.D., Richard C. Riser, M.S., Angela R. Evans, Ph.D., Joseph R. Calabrese, M.D., Heidi Wirts, Pharm.D.; Eli Lilly & Company, Indianapolis, IN; Harvard Medical School, McLean Hospital, Belmont, MA; Western Psychiatric Institute & Clinic, University of Pittsburgh Medical Center, Pittsburgh, PA; University of Texas Southwestern Medical Center, Dallas, TX; Case Western Reserve University, Cleveland, OH.

Pulmonary


294. Patient satisfaction, switching, therapy modifications, and GI medication use with celecoxib compared to traditional NSAIDs in “usual” rheumatology clinical practice: the SUCCESS-IV Trial. Eric A. Schoen, M.D., Michael Moriarty, M.D., Michael O’Connell, Ph.D., Dan Pettitt, DVM, M.Sc., Thomas A. Burke, Pharm.D., John G. Fort, M.D.; Kaiser Permanente Mid-Atlantic, Washington, DC; Waratah Corp, Durham, NC; Pfizer Inc., New York, NY; Pharmacia Corp, Peapack, NJ.


297. Effect of olanzapine and risperidone on glycose, lipids, and body mass. Robert E. Litman, Georgetown University, Rockville, MD.

298. Long-acting injectable risperidone: efficacy and safety. John Kane, M.D.; Marielle Eerdekens, M.D., M.B.A., Samuel Keith, M.D., Michael Lesem, M.D., Keith Karcher, M.S., Jean-Pierre Lindenmayer, M.D.; Hillside Hospital, Glen Oaks, NY; Janssen Research Foundation, Beerse, Belgium; University of New Mexico, Albuquerque, NM; Claghnor-Lesem Research Clinic, Belfare TX; Janssen Research Foundation, Titusville, NJ; Manhattan Psychiatric Center, New York, NY.

299. Clozapine augmentation with risperidone in refractory schizophrenia. Marielle Eerdekens, M.D., M.B.A., W. Wolfgang Fleischacker, M.D., Linda Beauchair, M.D., Stephen Martin; Janssen Research Foundation, Beerse, Belgium; Innsbruck University Clinics, Innsbruck, Austria; Clinic – Allan Memorial Institute, Montreal, Canada; Middleton St. George Hospital, Darlington County, Durham, United Kingdom.

300. Long-term safety and efficacy of long-acting injectable risperidone. Marielle Eerdekens, M.D., M.B.A., W. Wolfgang Fleischacker, M.D., Linda Beauchair, M.D., Stephen Martin; Janssen Research Foundation, Beerse, Belgium; Innsbruck University Clinics, Innsbruck, Austria; Clinic – Allan Memorial Institute, Montreal, Canada; Middleton St. George Hospital, Darlington County, Durham, United Kingdom.

301. Olanzapine combined with mood stabilizers in prevention of recurrence in bipolar disorder: an 18-month study. Mauricio Tohen, M.D., Ph.D., Roy Chengappa, M.D., Trisha Suppes, M.D., Ph.D., Robert W. Baker, M.D., Richard C. Riser, M.S., Angela R. Evans, Ph.D., Joseph R. Calabrese, M.D., Heidi Wirts, Pharm.D.; Eli Lilly & Company, Indianapolis, IN; Harvard Medical School, McLean Hospital, Belmont, MA; Western Psychiatric Institute & Clinic, University of Pittsburgh Medical Center, Pittsburgh, PA; University of Texas Southwestern Medical Center, Dallas, TX; Case Western Reserve University, Cleveland, OH.

302. Long-acting injectable risperidone: efficacy and safety. John Kane, M.D.; Marielle Eerdekens, M.D., M.B.A., Samuel Keith, M.D., Michael Lesem, M.D., Keith Karcher, M.S., Jean-Pierre Lindenmayer, M.D.; Hillside Hospital, Glen Oaks, NY; Janssen Research Foundation, Beerse, Belgium; University of New Mexico, Albuquerque, NM; Claghnor-Lesem Research Clinic, Belfare TX; Janssen Research Foundation, Titusville, NJ; Manhattan Psychiatric Center, New York, NY.

303. Effect of olanzapine and risperidone on glycose, lipids, and body mass. Robert E. Litman, Georgetown University, Rockville, MD.

304. Long-acting injectable risperidone: efficacy and safety. John Kane, M.D.; Marielle Eerdekens, M.D., M.B.A., W. Wolfgang Fleischacker, M.D., Linda Beauchair, M.D., Stephen Martin; Janssen Research Foundation, Beerse, Belgium; Innsbruck University Clinics, Innsbruck, Austria; Clinic – Allan Memorial Institute, Montreal, Canada; Middleton St. George Hospital, Darlington County, Durham, United Kingdom.

305. Olanzapine combined with mood stabilizers in prevention of recurrence in bipolar disorder: an 18-month study. Mauricio Tohen, M.D., Ph.D., Roy Chengappa, M.D., Trisha Suppes, M.D., Ph.D., Robert W. Baker, M.D., Richard C. Riser, M.S., Angela R. Evans, Ph.D., Joseph R. Calabrese, M.D., Heidi Wirts, Pharm.D.; Eli Lilly & Company, Indianapolis, IN; Harvard Medical School, McLean Hospital, Belmont, MA; Western Psychiatric Institute & Clinic, University of Pittsburgh Medical Center, Pittsburgh, PA; University of Texas Southwestern Medical Center, Dallas, TX; Case Western Reserve University, Cleveland, OH.

306. Long-acting injectable risperidone: efficacy and safety. John Kane, M.D.; Marielle Eerdekens, M.D., M.B.A., W. Wolfgang Fleischacker, M.D., Linda Beauchair, M.D., Stephen Martin; Janssen Research Foundation, Beerse, Belgium; Innsbruck University Clinics, Innsbruck, Austria; Clinic – Allan Memorial Institute, Montreal, Canada; Middleton St. George Hospital, Darlington County, Durham, United Kingdom.
5 mg daily for at least 6 months. These charts were reviewed. However, only 132 patients were verified to be on long-term prednisone. The following interventions were recorded: otc and prescription medications for osteoporosis prevention or treatment and DEXA scans. Fracture history and other interventions were also documented. Paired t-tests were used to analyze differences in average weight, daily dose (mg/kg), serum tacrolimus level, and ratio of mean daily dose (mg/kg)/mean serum tacrolimus level before and during tacrolimus use with H2RA, PPI, SB or MO therapy.

RESULTS: The study population consisted of 12 males (66.7%), 6 females (33.3%), 11 African-Americans (61.1%) and 7 whites (38.9%). The mean age in years was 47 ± 9.6. Three patients were taking a PPI, 15 patients were taking an H2RA, 2 patients were taking MO, and 2 patients were taking SB with tacrolimus. All patients were taking MO and SB were on H2RA therapy. There were no differences in mean weight (86.3 kg ± 22.97 vs. 85.4 kg ± 22.1, p=0.62), daily dose (15.3 mg ± 7.1 vs. 15.4 mg ± 7.6, p=0.93), serum tacrolimus level (11.4 ng/ml ± 3.9 vs. 10.8 ng/ml ± 3.3, p=0.56), and ratio of mean daily dose (mg/kg)/average serum tacrolimus level (0.018 ± 0.010 vs. 0.020 ± 0.013, p=0.16) before and during tacrolimus use with H2RA, PPI, SB or MO therapy.

CONCLUSION: Patients did not experience a reduction in tacrolimus serum level when tacrolimus and H2-receptor antagonists, proton-pump inhibitors, sodium bicarbonate, or magnesium oxide were co-administered.

300. Superior acute rejection prophylaxis of thymoglobulin compared to OKT3 in cadaveric and living-unrelated renal transplants. Lonnie D. Smith, Pharm.D., K. Troy Somerville, Pharm.D., Aimee Sundberg, Pharm.D., Jason Crompton, Pharm.D., John M. Holman, M.D., Ph.D., Edward W. Nelson, M.D., Fuad Shihab, M.D.; University of Utah, Salt Lake City, UT.

BACKGROUND: The purpose of this study is to compare the use of thymoglobulin (THG) to anti-CD3 monoclonal antibody (OKT3) for induction therapy.

METHODS: A retrospective review of consecutive cadaveric (CAD) and living-unrelated (LURD) renal transplants from 5/30/99-5/30/01. Immunosuppression consisted of cyclosporine or tacrolimus and corticosteroids. Induction was with thymoglobulin (THG) to anti-CD3 monoclonal antibody (OKT3) for induction therapy.

RESULTS: OKT3 5 mg for 10 days or THG 3 doses of 1.5 mg/kg/dose. Scr after transplant, early readmissions, infection, incidence of rejection at 3 and 6 months, and graft loss at 6 months were evaluated.

RESULTS: The OKT3 group included 38 pts (24 male, 33 CAD, 5 LURD and 5 re-transplants) the THG group included 37 pts (26 male, 34 CAD, 3 LURD, and 9 re-transplants). Four deaths occurred in the OKT3 group, none of the THG group. Three died from infectious causes one cardiac related. Two lost their grafts in the THG group one to B cell lymphoma, and one stopped his medications. Mean follow-up was 21.8 ± 5.7 months for the OKT3 group and 10.1 ± 3.4 months for the THG group. At 6 months 29% vs. 5% p=0.017 had a rejection and 5% vs. 2% lost their graft in the OKT3 and THG groups, respectively. There were 6 CMV related admissions in the OKT3 group vs. 3 in the THG group.

CONCLUSIONS: THG induction resulted in a statistically significant decrease in acute rejection episodes at six months. In the three dose THG protocol resulted in a significant cost savings compared to OKT3. Longer follow-up is needed to assess the impact of THG induction on pharmacokinetics and chronic allograft nephropathy.


PURPOSE: The high cost of transplantation impacts all transplant recipients. The relationship between the cost of post-transplant medications and medication compliance has not been fully investigated.

METHODS: We sent a mail-survey to all transplant recipients with a
functioning allograft identified by clinic and UNOS records excluding pediatric recipients (<18 years). Responses were collected anonymously.

RESULTS: A total of 589 surveys were mailed and 292 (50%) were returned, of those, 290 (49%) could be analyzed. Respondents included kidney (72%), heart (21%), and lung (7%) recipients. At the time of the survey, 30% of respondents reported that they were currently having trouble paying for medications. A large number (40%) reported having trouble paying for medications at some point after transplantation. Interestingly over 50% of patients having trouble paying for medications did have insurance coverage. Medication noncompliance due to cost issues alone was reported by 18% of respondents. The most commonly missed medications were immunosuppressants (53%), antihypertensives (46%), and lipid-lowering medications (33%). Medical complications were reported by 54% of the noncompliant recipients. Complications noted on the surveys included rising blood pressure (50%), worsening diabetes (29%), and elevated serum creatinine (24%). Regardless of noncompliance, an alarming 21% of recipients reported missing “basic necessities” to pay for medications, and 26% decided against taking a job or receiving a job training for fear of losing Medicare/Medicaid funding.

CONCLUSION: The high cost of medications following solid organ transplantation definitely impacts transplant recipients. Financial issues can lead to medication noncompliance and medical complications after transplantation.

302. Pharmacokinetic study of mycophenolic acid in Korean kidney transplant patients. Eun Young Cho, M.S., Jung M. Oh, Pharm.D., Ok S. Park, M.S., Duck J. Han, M.D., Ph.D.; Sookmyung Women's University; Asian Medical Center; Seoul, Korea.

PURPOSE: The purpose of this study was to characterize the pharmacokinetic parameters of mycophenolic acid in Korean kidney transplant patients.

METHODS: Plasma MPA concentrations of ten Korean patients administered with suboptimal dose of MMF (750 mg BID) were measured 2 weeks after the therapy by HPLC method.

RESULTS: Plasma MPA concentration-time curve showed an early sharp peak within one hour and small second peak in some patients at 4-12 hours post-dose. Mean Cmax was 8734.65 µg/ml, and mean MPA AUC was calculated as 18454.25 µg*h/mL. This AUC level was lower than the reported target range and also lower than the AUC of the Caucasians who were administered with 1000 mg twice a day. The mean fraction of free MPA which is pharmacologically active was 1600%. Patients’ age, weight, body surface area, and renal function did not influence the MPA AUC. However, difference in AUC according to sex was statistically significant (p=0.0227). MPA free fraction seemed not to be affected by serum albumin and renal function (serum creatinine or creatinine clearance). Correlation analysis for the limited strategy of MFM therapeutic drug monitoring resulted that concentrations of pre-dose, 1 hour post-dose, and 8 hour post-dose were positively related with AUC value, and their coefficient of correlation were 0.74545 (p=0.0133), 0.68485 (p=0.0289), 0.63636 (p=0.0479), respectively. It means that peak and trough concentration can be used to estimate MPA AUC.

CONCLUSION: It can be recommended that full dose (1000 mg BID) of MMF should be administered in Korean kidney transplantation, particularly during the early post-transplant period. Patients demonstrated wide variability in MPA pharmacokinetics, thus emphasizing the need to individualize dosing of MMF and to further evaluate important pharmacokinetic/pharmacodynamic parameters and endpoints that impact on clinical outcomes. Further studies involving more patients and pharmacodynamic outcomes are underway to help identify optimal MMF dosing strategies.

Urology

304. Cardiovascular safety of vardenafil, a potent, highly selective PDE-5 inhibitor in patients with erectile dysfunction; an analysis of five placebo-controlled clinical trials. Robert A. Kloer, M.D., Ph.D., Puneet Mohan, M.D., Ph.D., Christiane Norenberg, Kenneth Pomrants, Ph.D., Thomas Segersen, M.D., Stephen P. Glaeser, M.D.; Good Samaritan Hospital, Los Angeles, CA; Bayer Corporation Pharmaceutical Division, West Haven, CT; Bayer AG, Wuppertal, Germany; University of Minnesota, Minneapolis, MN.

PURPOSE: The cardiovascular (CV) safety profile of vardenafil was assessed in men with erectile dysfunction (ED).

METHODS: Data were pooled from 5 randomized, double-blind Phase III trials in which 2718 men with ED for ≥6 months received vardenafil 5, 10, or 20 mg or placebo as needed for 12 weeks. CV-related adverse events (AEs), changes in vital signs (VS) and ECG were recorded; VS were also obtained in a subgroup receiving antihypertensive medications (HTM, data recorded 11 min. post-dose).

RESULTS: In 2605 patients valid-for-safety (vardenafil=1812, placebo=793), CV risk factors included hypertension (35%), hyperlipidemia (24%), smoking (62%), diabetes (30%), and CVD (7%). Vardenafil was associated with mild reduction in BP (-4.6±3.1 [SBP], 1.7±1.9 [DBP]), and small increase in HR (2.0 bpm). In patients receiving placebo ± HTM (n=183), no consistent changes in BP and HR were observed. In patients receiving vardenafil ± HTM (n=620), minimal additional reductions in SBP and DBP were observed, generally similar across HTM classes (ACEI, Ca2+ antagonist, or β-blockers, diuretic, and ARB). Dizziness and hypertension were equally reported by 1.0% and 2% of patients receiving placebo or vardenafil. The incidence of abnormal ECG, edema, syncope, anemia, hypotension, and myocardial ischemia was 0.0-0.6%, and was not dose-related. One patient receiving placebo had an MI, CVA, and CV surgery. One vardenafil patient experienced MI.

CONCLUSION: In this analysis of men with ED and CV comorbidities, vardenafil exhibited a favorable CV safety profile whose incidence of CV-related AEs was similar to that of placebo.

305E. Efficacy and safety of vardenafil, a selective and potent PDE-5 inhibitor in men with erectile dysfunction: the north American Pivotal Placebo-Controlled Trial. Wayne J.G. Hellstrom, M.D., Marc Gittelman, M.D., Gary Karlin, M.D., Marc Thibonnier, M.D., Thomas Segersen, M.D., Harin Padma-Nathan, M.D.; Tulane University Medical Center, New Orleans, LA; South Florida Medical Research, Aventura, FL; Lawrenceville Urology, Lawrenceville, NJ; Bayer Corporation, West Haven, CT; The Male Clinic, Beverly Hills, CA.

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Women's Health

306. Double-blind, randomized, placebo-controlled, crossover study of estradiol in premenstrual asthma. Mary H.H. Ensom, Pharm.D., FASHP, FCCP, Puneet Mohan, M.D., Marc Thibonnier, M.D., Thomas Segersen, M.D., Gary Karlin, M.D., Marc Thibonnier, M.D., Thomas Segersen, M.D., Harin Padma-Nathan, M.D.; Tulane University Medical Center, New Orleans, LA; South Florida Medical Research, Aventura, FL; Lawrenceville Urology, Lawrenceville, NJ; Bayer Corporation, West Haven, CT; The Male Clinic, Beverly Hills, CA.

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ACCP 2002 ANNUAL MEETING ABSTRACTS
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Gina Chong, Bev Beaudin, RRT, Stephen Shalansky, Pharm.D., Tony R. Bai, M.D.; University of British Columbia; St. Paul’s Hospital, Vancouver, BC, Canada.

PURPOSE: In females with premenstrual asthma (PMA): 1) to characterize asthma symptoms and pulmonary function throughout two menstrual cycles, with and without exogenous estradiol administration; 2) to determine the effect of estradiol administration on asthma symptoms, pulmonary function, quality of life, and biomarkers of airway inflammation. METHODS: Following informed consent, 12 women with documented PMA (20% premenstrual worsening of asthma symptoms and/or of peak expiratory flow rate [PEFR]) during a one-month screening phase were randomized to follow for two complete menstrual cycles in a double-blind, randomized, placebo-controlled, crossover fashion. Subjects received either estradiol 2 mg or placebo orally between cycle days 23 and 28 (i.e., “premenstrually”). Throughout both cycles, subjects recorded daily morning and evening PEFR readings and asthma symptoms. They reported to our clinic on Days 8 (follicular phase), 22 (luteal phase), and 28 (premenstrually) of both the estradiol and placebo cycles (denoted as visits 1 and 4, respectively) for spirometry testing and measurement of serum estradiol and biomarkers of airway inflammation. During the two premenstrual visits (Day 28), the Asthma Quality of Life Questionnaire also was administered. RESULTS: Patient demographics (mean ± SD) upon enrollment consisted of the following: age, 38.8 ± 7.1 year; weight, 76.7 ± 11.8 kg; height, 163.2 ± 7.0 cm; and forced expiratory volume in one second (FEV1), 2.60 ± 0.78 L. No significant differences were found in FEV1 (2.53 ± 0.62 vs. 2.51 ± 0.67 L), serum creatinine (1.08 ± 0.42 vs. 1.16 ± 0.40 mg/dL), or quality of life scores [all domains (170 ± 26 vs. 174 ± 27)] for the estradiol vs. placebo cycle, respectively. CONCLUSIONS: When examined in a double-blind, randomized, placebo-controlled, crossover fashion, exogenously-administered estradiol did not have a significant effect on PMA. As in the case of premenstrual syndrome (PMS), with up to 60% of patients reporting improvement on placebo alone, the placebo effect appears to be prominent in PMA as well. Further studies are warranted to discern underlying mechanisms for the worsening of asthma in relation to menstruation.


PURPOSE: To characterize intravenous immunoglobulin (IVIG) pharmacokinetics in females with the antiphospholipid antibody syndrome (APS), who are contemplating pregnancy. To date, no pharmacokinetic data for IVIG exist for this patient population, despite its usage in obstetrics, expense, and worldwide shortage.

METHODS: Thirty non-pregnant females with APS, based on a history of recurrent miscarriage, participated in this pilot; 7 were part of a larger observational pharmacokinetic study and 6 were part of a larger randomized placebo-controlled clinical trial. Of these subjects, 10 received IVIG (Gammunune N 5%) and 3 received placebo (in an equivalent volume of normal saline). Following informed consent, subjects received IVIG 500-1000 mg/kg (or placebo) over a 3- to 6-hour period and underwent serial blood sampling pre- and post-infusion and at 0.5h and 1.25, and 4 weeks following the dose. Serum concentrations of IgG were measured by rate nephelometry and traditional non-compartmental pharmacokinetic analysis was performed.

RESULTS: Mean (± SD) age was 35 ± 5 year (IVIG group, n=10) and 32 ± 6 year (placebo, n=3); weight was 64.4 ± 16.3 kg (IVIG) and 77.6 ± 2.4 kg (placebo). Patients in the IVIG and placebo groups had a history of 6 ± 2 and 3 ± 1 spontaneous abortions, respectively. Mean (± SD) IVIG dose was 43.1 ± 12.1 g. Pharmacokinetic parameters (mean ± SD) were as follows:

- IVIG (n=10)
  - Cmax (g/L) 26.6 ± 5.0 12.1 ± 2.2 12.1 ± 2.2
  - AUC0-1 (g•h/L) 12130 ± 1477
- Placebo (n=3)
  - Cmax (g/L) 10.4 ± 3.0 9.5 ± 2.9 6220 ± 1957

The roughly-estimated contribution of exogenously-administered IVIG to the total AUC0-1 [calculated as mean AUC0-1 (IVIG group) minus mean AUC0-1 (placebo group)] was 5910 ± 1370 g•h/L. This suggests that every gram of IVIG administered yields an estimated 137 g•h/L increase in AUC0-1 (determined by dividing the difference in AUC0-1, values by the mean dose) or approximately 2.17 g/h per kg body weight.

CONCLUSIONS: In our patient population of non-pregnant females with APS, the estimated contribution of exogenously-administered IVIG (i.e., 5910 ± 1370 g•h/L) to the total AUC0-1, was relatively low compared to endogenous IgG (i.e., 6220 ± 1957 g•h/L). These pre-pregnancy data also will be useful as baseline values to track pharmacokinetic changes that may occur with IVIG throughout pregnancy.


PURPOSE: The purpose of this study was to determine whether differences exist in the pharmacokinetics of low molecular weight heparin (LMWH) and unfractionated heparin (UFH) before pregnancy and during the first, second, and third trimesters of pregnancy in women with the antiphospholipid antibody syndrome (APS). To date, no systematic data exist on the effect of pregnancy on LMWH or UFH pharmacokinetics in women with APS.

METHODS: Following informed consent, women who were contemplating pregnancy, were randomized to one of two treatment groups [LMWH (dalteparin) or UFH] and taught how to self-inject their heparin subcutaneously following an empiric dosing schedule. All patients received aspirin 81 mg per day concurrently. They underwent 4 serial blood sampling days (pre-pregnancy, first trimester, second trimester, and third trimester). Blood samples were collected at 0, 0.5, 1, 2, 3, 4, 6, 8, 12, and 24 hours following a steady-state dose of LMWH and at 0, 0.5, 1, 1.5, 2, 2.5, 3, 4, 8, and 12 hours following a morning dose of UFH. Plasma concentrations of heparin were measured by determining anti-factor Xa activity using an automated method with chromogenic substrate. Pharmacokinetic parameters were calculated by non-compartmental methods. One-way repeated measures analysis of variance (followed by Student-Newman-Keuls test, if appropriate) was used to determine statistical significance, defined as p<0.05.

RESULTS: We report preliminary results of 13 women (n=8 on LMWH and n=6 on UFH) who have completed the study and had a successful pregnancy. Mean (± SD) age at study enrollment was 33 ± 2 year (LMWH) and 34 ± 6 year (UFH). Patients had a history of 4 ± 1 (LMWH) and 3 ± 1 (UFH) spontaneous abortions. Pharmacokinetic parameters (mean ± SD) were as follows:

<table>
<thead>
<tr>
<th>Time Period</th>
<th>LMWH (U/L)</th>
<th>UFH (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First trimester</td>
<td>2.85 ± 2.14</td>
<td>0.05 ± 0.03</td>
</tr>
<tr>
<td>Second trimester</td>
<td>2.75 ± 2.14</td>
<td>0.05 ± 0.03</td>
</tr>
<tr>
<td>Third trimester</td>
<td>2.55 ± 2.14</td>
<td>0.05 ± 0.03</td>
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</tbody>
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The t1/2 of UFH was not calculated.

CONCLUSIONS: In females with APS, our current empiric dosing regimen of LMWH yielded the least and greatest drug exposure (i.e., AUCmax during the first and third trimesters of pregnancy, respectively) with UFH yielding the least and greatest drug exposure (i.e., AUCmax during the first and third trimesters of pregnancy, respectively). No notable differences were observed before and during pregnancy in women with the antiphospholipid antibody syndrome (APS) who were on low molecular weight heparin (LMWH) or unfractionated heparin (UFH) throughout pregnancy.
1.07 ± 0.08 g/cm² and 1.03 ± 0.08 g/cm², respectively (hip; p<0.05).

CONCLUSIONS: The results confirmed that the degree of obesity has a strong predictive value of the need for insulin in the treatment of GDM. One unexpected finding was that 15 patients with a BMI > 30 were able to control their glycaemia with diet modification while fifty-four patients required insulin. The strong predictive value of the need for insulin in the treatment of GDM. One unexpected finding was that 15 patients with a BMI > 30 were able to control their glycaemia with diet modification while fifty-four patients required insulin. The mean BMI of patients requiring insulin was 36 (range: 20-75). Based on the p value of the logistic regression model (p = 0.0131), there appears to be a significant relationship between pre-pregnancy BMI and insulin requirement.

RESULTS: Thirty-seven patients were able to maintain acceptable levels of glycemia with medical nutrition therapy alone while others require insulin. This study analyzed the relationship between pre-pregnancy body mass index (BMI) and the need for insulin in GDM. METHODS: Data was analyzed in 91 newly diagnosed GDM patients seen in the Community Women's Clinic between June 1, 2000 and May 31, 2002. Collected demographics included patient age, race, gravity, parity, and prepregnancy BMI. Insulin was initiated if fasting blood glucose was > 105 mg/dL. A logistic regression model was used to examine the relationship between pre-pregnancy BMI and the need for insulin in GDM. RESULTS: Thirty-seven patients were able to maintain acceptable levels of glycemia with diet modification while fifty-four patients required insulin. The mean BMI of patients requiring insulin was 36 (range: 20-75). Based on the p value of the logistic regression model (p = 0.0131), there appears to be a significant relationship between pre-pregnancy BMI and insulin requirement.

CONCLUSIONS: The results confirmed that the degree of obesity has a strong predictive value of the need for insulin in the treatment of GDM. One unexpected finding was that 15 patients with a BMI > 30 were able to control their glycaemia with diet modification while fifty-four patients required insulin. The mean BMI of patients requiring insulin was 36 (range: 20-75). Based on the p value of the logistic regression model (p = 0.0131), there appears to be a significant relationship between pre-pregnancy BMI and insulin requirement.

Clinical Pharmacy Forum

These abstracts describe the delivery, development, justification, or documentation of innovative clinical pharmacy services; they may be descriptive only and need not contain an evaluative component.

312. Clinical community pharmacists overcome turf barriers to advance pharmaceutical care in a health system, Julia A. Borghmann, Pharm.D., Terry A. Pence, R.Ph.; Cardinal Health System, Muncie, IN.

The provision of health care can be fragmented between the inpatient and outpatient setting with multiple health care professionals contributing to patients' care. Our Health Care System is comprised of a tertiary care hospital, primary care physician practices with outpatient pharmacies, home care, and wellness. The clinical community pharmacist (CCP) is the most accessible member of the health care team and can serve as a valuable tool to facilitate this care. We utilize our CCPs to promote adverse drug reaction reporting in our physician practices, control sample medications, and provide medication assistance programs. A pediatric CCP is a breast feeding consultant who teams with the lactation consultants to serve as an information and product resource. In our disease management programs pharmacists team with dietitians and respiratory therapists to provide asthma and lipid services. CCPs partner with wellness specialists to provide cholesterol screenings. Our CCPs are members of our Diabetes Care Center, teaching classes at our outpatient locations, providing a wide array of products, and meeting individually with patients unable to attend the classes. The pharmacist serves the outpatient HIV population also participates in our multidisciplinary HIV clinic located at the hospital. Intervention programs by the community pharmacist to monitor the use of digoxin in the elderly, methotrexate, steroid induction, compliance, and liver function testing, can help to avoid unnecessary hospitalizations. The novel integration of CCPs with other health care professionals within a health care system can enhance the continuity of care and advance of pharmaceutical care.

313. Evaluation of an acute pain initiative in a community teaching hospital, Dianne Brundage, Pharm.D., Kristine J. Peterson, R.N., MSN, Juli Jordon, R.N.; Methodist Hospital/Park Nicollet Health Services, Minneapolis, MN.

PURPOSE: During the last 4 years, our institution assessed changes made in the management of acute pain.

METHODS: A baseline survey of 69 hospitalized patients provided information on the problems in acute pain management. An interdisciplinary committee decided on goals, strategies, and methods for improvement of pain management. The Quality Resources department provided measurement of goals. Physicians, nurses and pharmacists attended education programs. Administration sent out system-wide notices of congratulations when goals were met.

RESULTS: Baseline data showed: 81% of patients had a pain score > 4 (on a 0 to 10 scale), minimal documentation of a pain assessment, prolonged waiting times for pain medication, and fears and misconceptions regarding narcotic use. Meperidine use decreased in the post anesthesia care unit from 76% to 11%, while the number of patients with pain scores < 4 increased from 43% to 89% over 3 quarters. The use of meperidine in total hip and knee replacement patients went from 69% to 0%, while the number of patients with pain scores ≤ 4 increased from 44% to 75% during the same time period. Hospital-wide meperidine use declined from 47% to ≤ 14% of all injectable opioid doses, and has remained at this level for almost two years. Ninety-one percent of patients have pain documented as the 5th vital sign.

CONCLUSIONS: Improvements in acute pain management can be made through an interdisciplinary effort. Keys to success included: support of organizational leadership, participation by all disciplines, and education supported by leaders in each discipline.

314. Drug use evaluation: intravenous amiodarone, Jodie M. Fink, Pharm.D., Michael A. Miliotello, Pharm.D., BCPS; Cleveland Clinic Foundation, Cleveland, OH.

PURPOSE: Increasing expenditures of intravenous (IV) amiodarone at our institution resulted in a pharmacist-driven drug use evaluation meeting its determination. The goal was to identify patients on IV amiodarone suitable for oral administration or IV dose reduction. Secondary, direct cost savings associated with pharmacy interventions were assessed.

METHODS: A prospective, chart review was performed on all adult patients initiated on IV amiodarone from October to December 2001. Pharmacy interventions were made to either change IV to oral amiodarone, or to reduce the infusion rate, when appropriate.

RESULTS: Of the 173 patients analyzed, most patients were elderly men (69% men, mean age 69.5 years), on IV amiodarone for atrial fibrillation (84%). Days of IV amiodarone use totaled 560, with an average of 3.2 days (SD: ± 3.3) per patient. Most common doses were 1 mg/min (302 days) and 0.5 mg/min (210 days). Two patient groups were identified for further pharmacy intervention: patients receiving IV amiodarone, and b) patients on higher than recommended rates of IV amiodarone administration. These interventions have an estimated potential cost savings of $900,000/year (average wholesale price). Seventy-seven pharmacy interventions for 63 patients were documented. 42 (55%) were accepted, with a direct pharmacy cost savings of about $41,000.

CONCLUSION: The interventions have been identified as having direct cost savings, and have the potential for even greater cost minimization. Through the Pharmacy & Therapeutics Committee, pharmacy will develop a program supporting cost containment of IV amiodarone.


Amiodarone has been associated with multiple toxicities, some of which can be potentially fatal. At present, this medication is a mainstay of therapy for many patients with both atrial and ventricular arrhythmias. A pharmacist-
PURPOSE: Aggressive control of blood glucose has been shown to decrease mortality in cardiac and critical care patients. The goal of this process improvement (PI) project and descriptive study is to evaluate the efficacy of an intensive insulin protocol in controlling blood glucose in critically ill patients. The protocol was recently approved for use in MICU patients.

METHODS: We initiated a comprehensive program to control blood glucose levels in the MICU by development of an intensive insulin protocol. A physician order sheet was developed with the collaborative efforts of key physicians, critical care nurses, and pharmacist. The main aims of this study were: 1) to implement an algorithm of stress ulcer prophylaxis to guide the medical staff on their decision. The agents chosen for the algorithm of treatment were omeprazole and misoprostol; 2) to review the availability of a PO or per tube route.

RESULTS: The incidence of bleeding was similar for both pre and post groups. A comprehensive educational program to medical house staff and nursing personnel will be conducted after pilot data proves the efficacy of this approach to glycemic care.

CONCLUSIONS: This PI initiative should provide for enhanced blood glucose control which will be first piloted in a MICU. Access to the physician order sheet will be via the hospital intranet Web site. Intended future projects include: expansion of this initiative to other ICUs and a transitional study to evaluate alternatives to insulin infusions once the patients no longer meet inclusion criteria. A comprehensive educational program to medical house staff and nursing personnel will be conducted after pilot data proves the efficacy of this approach to glycemic care.
CONCLUSION: Guidelines for use of DAA in conjunction with prospective review by a pharmacist resulted in the appropriate use of this agent with significant cost savings.

321. Incorporation of a cardiovascular risk factor awareness program in the core curriculum of a rural Mississippi high school. T. Kristopher Harrell, Pharm.D., Deborah S. King, Pharm.D., Howard T. Crenshaw, Pharm.D., Marq age R. Woolf, M.D., MPH, Daniel W. Jones, M.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: The purpose of this study was to incorporate a CVD educational program in the curriculum of health classes at a rural Mississippi high school. The objectives were to assess CVD risk factor awareness and to utilize pharmacy students to emphasize the importance of routine risk factor screenings.

METHODS: Initially, a questionnaire was given to assess baseline knowledge. Throughout a one-week period sixth-year pharmacy students led classroom discussions on “knowing risk factor numbers.” Those students for whom parental permission was given were also screened for blood pressure, blood glucose, cholesterol, and body mass index. Students were given a one-on-one encounter with a pharmacy student who explained risk factor numbers. To evaluate the educational effectiveness, students repeated the questionnaire four weeks later. Outcome measures included awareness rates of risk factor numbers.

RESULTS: A total of 80 students participated in the screenings. Of these, 67 students completed questionnaires before and after the program. At baseline, 39% of students answered blood pressure goals correctly and at follow-up 44% answered correctly. Likewise, for blood glucose goals, at baseline 12% of students answered correctly and 76% at follow-up. For cholesterol, 10% answered correctly at baseline and 84% at follow-up. For BMI 6% answered correctly at baseline and 75% at follow-up.

CONCLUSION: Utilizing pharmacy students was an effective way of teaching high school students the importance of understanding CVD risk factors. The pharmacy students were also given the opportunity to be involved at the community level to promote CVD risk factor awareness and routine screenings.

322. Medication safety program for minority, refugee, and low-income older adults. Thomas L. Lentz, Pharm.D., Michael S. Monaghan, Pharm.D., Janet L. Ekeler, BSN, Allison M. Jorgensen, Pharm.D., James D. Bramble, Ph.D.; Creighton University, Omaha, NE.

A program which offers a medication safety screening survey with two levels of follow-up care, as well as culturally appropriate medication education, was started in a medium size mid-western city in an attempt to identify and assist an ever-growing minority, refugee and low-income older adult population who are at risk of illness or injury due to medication noncompliance, drug interactions, poly-pharmacy or other medication related issues. The survey was completed in English, Vietnamese, Spanish, Russian, Arabic and Bosnian languages and distributed to health and social service agencies, community health and resource fairs, cultural, community, senior and recreation centers, and church and civic groups. Follow-up phone calls were conducted to those considered “at risk” by a nurse and then by a pharmacist to resolve medication related issues. Four pharmacist-led, conducted educational videos on diabetes, hypertension, depression and medication safety were produced in English, Vietnamese and Spanish and distributed to the same locations as the safety screening survey. 653 total surveys from 47 sites were completed with a mean age of 76.6 years (63.5% female). Respectively, 64% did not know the purpose of all their medications, 10% took over-the-counter medications unknown to their pharmacist or physician, 12% used more than 1 pharmacy, and 7% reported having medication related problems. 100 persons answering the survey reported having diabetes mellitus. Of these surveys, 25% did not check blood sugar daily, 22% reported self-adjusting their medications, and 10% had blood sugar levels out of range. 256 total follow-up calls were completed.

323E. Development of a managed care pharmacy practice residency. Ragucci, Pharm.D., Joli D. Cerveny, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate pharmacy student and resident perceptions of an innovative Web site utilized during ambulatory care rotations.

METHODS: A Web site was developed to standardize the core education and evaluation experience among four ambulatory care rotation sites. Within the Web site, an on-line anonymous survey using a 5-point ordinal scale (1=strongly disagree-strongly agree) was designed to evaluate navigation and content, as well as to assess overall perceptions. Over a 12-month time frame, each student and resident was instructed to complete the survey at the end of their ambulatory care rotation. Survey results were compiled and analyzed.

RESULTS: Surveys were completed by 80% of residents (12/15) and 90% of students (28/31). Overall, learners found the Web site easy to navigate without distraction (median=4). Additionally, learners found the content useful (median=4). There was a discrepancy between student and resident learners regarding specific content areas. Students found the directed reading questions and self-assessment quizzes more useful than the residents (93% vs. 75% and 79% vs. 56%, respectively). In addition, students felt more comfortable evaluating preceptors on-line (89% vs. 67%). Residents believed they would use the Web site on future rotations more frequently than students (83% vs. 57%). Both students and residents appreciated the ease of accessibility and the links to other resources. The major weakness identified was inoperative links.

CONCLUSIONS: Perceptions of a Web site utilized during ambulatory care rotations were positive. The survey results reinforce the continued use of this teaching method and will enable preceptors to make appropriate adjustments for future rotations.

326. Teaching about death and dying in the pharmacy curriculum: a student-focused approach. Ragucci, Pharm.D., Joli D. Cerveny, Pharm.D., BCPS, Western University of Health Sciences, Pomona, CA.

BACKGROUND: Death and dying has been a component of our pharmacy curriculum since its inception. During the early years, an instructor from the physician's assistant program taught the dynamic lecture which incorporated slides and a video describing his wife's life and death. Becoming emotionally exhausting, he declined to continue the lecture, and the topic was almost dropped from the curriculum. When this was determined, the lecture was taken over by a pharmacy practice faculty and incorporated into a homeostasis block using a student-focused approach.

METHODS: Students wrote an essay about an experience they have had with death and submitted it before the lecture. Students could choose to anonymously share their essay with the class. The lecture consisted of stages of grief, and a number of personal accounts of the faculty's experiences with death and dying. Essays were incorporated into a single document and distributed to the class after the lecture.

RESULTS: A majority of students agreed to share their essay with the class. Topics included included death of a family member or friend, helping someone else in coping with death, dealing with a dying patient, personal and spiritual beliefs about death and dying, or dealing with mass tragedies. Students commented that participating in this assignment helped them to deal with the death of a loved one. Others commented that it helped them put another perspective on how a pharmacist can help others face the experience of death. All comments from the course evaluations about this topic were positive.

CONCLUSION: Having students reflect upon their own experiences with death and dying was a positive experience for this class, and students suggested maintaining this educational format.

327. Development and implementation of a transitional orientation experience for Pharm.D. students prior to longitudinal clerkship

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experiences. John A. Dougherty, M.B.A., Pharm.D., Justine S. Gortney, Pharm.D., P.D., Wayne State University, Detroit, MI.

PURPOSE: To describe the development, implementation and evaluation of the orientation clerkship at the Detroit Medical Center (DMC) for Wayne State University (WSU) Pharm.D. longitudinal students.

METHODS: Pharm.D. students at WSU have the opportunity to complete all experiential clerkships for the year at same institution. This is known as a longitudinal advanced practice program (LAPP). Students who are enrolled in LAPP at the DMC complete a 6 week orientation clerkship to prepare the student for their clinical clerkships. We sought to develop an orientation that achieves the following: familiarity with drug distribution system, application of clinical skills and knowledge, and development of communication skills. Discussions and hands on experience occurred in the following areas: drug distribution (multiple components), antimicrobial, infectious disease principles, pharmacokinetics, interpersonal skills, nutrition, pain management, pharmacokinetics, and special populations. Students rated the orientation experience.

RESULTS: A 6-week, multi-site, team-taught orientation rotation was created. The rotation included all the topics we had intended. All students completed the rotation. The clerkship experience was well received. Students felt confident in pharmacokinetic dosing, pain management, and increased understanding of both distributive and clinical services. Some students felt this experience had little value in their training as future pharmacists.

CONCLUSION: A 6-week orientation clerkship that introduces distributive, clinical, and patient care skills was successfully developed. Most students find this experience beneficial, however, some do not see the relevance of such a clerkship. We will re-evaluate students’ assessment of their orientation rotation after the completion of clinical rotations.

328. Inhaler technique in hospitalized patients: effect of patient education by a pharmacist. Athakrar Nakham, B.Sc, Pharm.D., Pavena Soonthosombat, Pharm.D., BCPS, Nanuesuan University, Phuket Thailand.

PURPOSE: to determine if hospitalized patient could use inhaler correctly after pharmacist intervention.

METHODS: Patients using inhaler(s) admitted with exacerbation of asthma or chronic obstructive lung disease between January 7th and February 7th, 2002 at 800-bed hospital were evaluated. Patients were asked to use inhaler and step-by-step technique intervention comprises of discussion and correct demonstration of the device. Patients were then asked to use the device again and again after the first demonstration until they could do it correctly on that day. Pharmacist asked patients to repeat all steps again although they did correctly the day before and made correction everyday until they could do it perfectly.

RESULTS: None of twenty-one patients showed all steps correctly before intervention. Exhaling slowly via mouth (step 6) and waiting 1 minutes between puffs (step 7) were ones that patients did correctly most (71.73 %) and least (23.81 %), respectively. Exhaling slowly (step 2), inhale slowly (3-5 seconds (step 4), hold breath for 5-10 seconds (step 5), step 6, and step 7 were shown to have significant improvement (p < 0.05) after intervention. Some steps had to be educated twice for patients to do it correctly. About 60% of patients did correctly the day before, they still did some steps wrong the day after. Pharmacist had to intervene patients for three consecutive days to have all patients did all steps correctly. After intervention.

CONCLUSIONS: A pharmacist could improve patients’ inhaler technique by intervention repeated and continuously.


PURPOSE: Clinical pharmacy services have recently expanded to include extensive Diabetes Self-management Education (DSME). The following project was conducted to evaluate the effect of pharmacist-administered DSME on glycemic control and to ascertain the economic impact on improved glycemic control.

METHODS: A literature search was conducted to establish the potential health-care costs associated with improvements in glycemic control and examples of pharmacist-administered DSME. Glycemic control, measured by Hemoglobin A1c (HbA1c), and the number of patients achieving a goal HbA1c of <7% were measured prior to and after 6 months of the initiation of pharmacist-administered DSME. Cost avoidance, based on comparisons from the literature, were calculated for patients with a 1% reduction in HbA1c.

RESULTS: Twenty-six months of pharmacist administered DSME, a 50% increase (N = 61) in the number of patients with a HbA1c of <7% were measured prior to and after 6 months of the initiation of pharmacist-administered DSME. Cost avoidance, based on comparisons from the literature, were calculated for patients with a 1% reduction in HbA1c.

CONCLUSIONS: A community pharmacy-based program to detect risk factors for complications of diabetes.
following pharmacy intervention (p=0.071). The goal HbA1c was attained in
pharmacy call center in a group model health maintenance organization.

Implementation of allergic rhinitis treatment guidelines by a clinical
pharmacy-based diabetes management program. resulted in improvement in the provision of diabetes care in a rural family
decreased from 122 mg/dL to 98 mg/dL following pharmacy intervention
with 43 patients in the post-intervention period. The mean LDL cholesterol
nine patients received lipid profile testing prior to the intervention compared
achieving the ADA blood pressure goal increased from three to eight. T wenty-
modest decline in mean systolic and diastolic blood pressures was noted

Is there consistency in warfarin monitoring at different ambulatory
care settings within the Veterans health system? Christine M. Miller,

334E. Effect of a length of therapy guarantee contract on appropriate antibiotic use: placing a pharmaceutical manufacturer at risk. Donna M. Chieffari, Centrus (NMHC Rx), Latham, NY.

335. Is there consistency in warfarin monitoring at different ambulatory care settings within the Veterans health system? Christine M. Miller, Pharm.D., Denise Waddell, Pharm.D.; North Florida/South Georgia Veterans Health System, Gainesville, FL.

PURPOSE: This study was undertaken to evaluate the management of warfarin therapy in patients at three different ambulatory care settings within VISN8 of the Veterans Health System.

METHODS: Patients were randomly selected for review according to the location of the provider that wrote the warfarin prescription. Twelve months of warfarin monitoring were evaluated starting with the most recent INR. Time to follow-up after initiation of warfarin, a change in warfarin dose and during stable maintenance of warfarin therapy was calculated. Average Time in Therapeutic Range (TTR), total number of INRs per patient in twelve months, and number of hemorrhagic and thromboembolic events were calculated.

RESULTS: The average TTR of patients on warfarin for more than one year, with 2 or more INR values ranged from 35% to 64%. For patients followed by MD, ARNP, PA, or PHRM the average TTR was 35%, 53%, and 64%; the average number of INRs in the previous twelve months was 8.9, 9.8, and 13.5 for patients followed at medical centers (MC), community based outpatient clinics (CBOC), and outpatient clinics the average (OPC) the number of INRs was 13, 9, 6; the average TTR was 63%, 49%, 27%, respectively.

CONCLUSION: The data suggest that (1) TTR is greatest for patients followed in the medical centers, followed by the outpatient clinics, and then by the CBOCs; (2) TTR is highest for those patients monitored by a pharmacist, followed by nurse practitioner/physician assistant, and then by physicians; (3) a) 1 in 10 and b) the number of follow-up is greatest in pharmacist managed clinics in the medical centers than in the CBOCs or OPCs that do not have pharmacist managed anticoagulation services. 

336. Pharmacist-managed anticoagulation service reduces adverse events. Christy Locke, Pharm.D., Susan L. Ravnan, Pharm.D., Patricia A. Carlton, Pharm.D.; St. Joseph's Medical Center; University of the Pacific, Stockton, CA.

Optimal management of anticoagulated patients reduces adverse events improving quality of life and decreasing overall health care costs. St. Joseph's Medical Center (SJMC) shared in managed care affiliations with a local Independent Physician Association and shared in financial risk for that patient population. In October 1997 SJMC financed and implemented a pharmacist managed anticoagulation clinic (AC) to provide cost effective anticoagulation management and augment the health status of their managed care patients. In December 2000, adjustments in the program were made to further reduce the frequency of provider visits and improve patient outcomes. We will illustrate that pharmacist managed clinics enhanced patient outcomes and reduced hospital costs as compared to routine medical care.

METHODS: 420 patients were managed in the AC. Data was analyzed 6 months prior to and after clinic closure. The clinical endpoints were number of hospitalizations for any hemorrhagic or thromboembolic event and total hospital days accrued due to an adverse event.

RESULTS: Six months prior to clinic closure, 3 hemorrhagic events occurred amounting to 8 total hospital days. Six months after clinic closure, 14 hospitalized adverse events (7 hemorrhagic and 7 thromboembolic) occurred for a total of 74 hospital days. Given an average insurance contract price of $1,500/hospital day, under pharmacist management, the patient population incurred $12,000 in hospital costs as compared to $111,000 under physician management.

CONCLUSION: A pharmacist managed AC improved patients quality of life and decreased health care costs by substantially reducing total hospital days.


PURPOSE: From July to November 2001, our institution realized a 10-fold increase in purchase costs for erythropoietin (EPO) over the prior year. A therapeutic review for EPO was conducted to accomplish the following objectives: 1) create evidence based practice guidelines for EPO 2) evaluate current prescribing practices to define variant prescribing and 3) identify future initiatives to optimize EPO utilization.

METHODS: A MEDLINE search was conducted to identify all clinical trials investigating the benefit of EPO. Disease states for which results demonstrated a statistically and clinically significant improvement in outcomes were included as appropriate use in the guidelines. A point prevalence study was completed between 12/17/01 and 1/08/02 to evaluate guideline compliance and identify variant practice, by clinical indication and physician speciality.

RESULTS: Evidence was identified supporting EPO use for anaemia associated with: chronic kidney disease, myelodysplastic syndromes, myelosuppressive chemotherapy, radiation therapy, autologous blood donation, elective nonvascular noncardiac surgery, critical illness, congestive heart failure, rheumatoid arthritis, zidovudine therapy, Jehovah's Witness surgical patients and prematurity. Investigation of EPO utilization revealed an 82% (60/73) rate of compliance with the guidelines. Of the patients not meeting the guidelines, six (1%) of those monitored by a pharmacist, five (11%) were classified as moderate deviations and did not meet the inclusion criteria of the published clinical trials. These non-evidence-based indications contributed to in excess of $200,000 of annual EPO expense.

CONCLUSIONS: This analysis suggests the majority of EPO utilization is evidence based. Target areas for improved compliance include EPO discontinuation after critical illness resolution and anemia of chronic disease.


PURPOSE: Evaluate the outcomes associated with providing an anticoagulation monitoring service.

METHODS: Patients from three ambulatory care sites who were being followed for anticoagulation monitoring from April 1, 2001 through March 31, 2002 were identified. These patients were evaluated for hospitalizations, emergency room visits, thromboembolic events, and major/minor bleeding episodes during this time frame. Data were compiled, evaluated, and compared to an established control group.

RESULTS: A total of 259 patients were followed for one year, compared to 21 patients in the control group. The total number of hospitalizations for the monitored service was 7 (3%) compared to 7 (33%) in the control group. The total number of emergency room visits in the monitored group was 4 (1.5%). There were 3 (1.2%) reported episodes of major bleeds ending results in hospitalization, compared to 1 (4.8%) in the control group, and 13 (5%) recorded episodes of minor bleeding in the monitored group, compared to 1 (4.8%) episode in the control group. The total number of thromboembolic events in the monitored group was 4 (1.5%), compared to 7 (33%) in the

PURPOSE: Our purpose was twofold: 1) to perform an enoxaparin drug use evaluation (DUE) and 2) to determine which population of patients were at risk for an adverse drug event (ADE).

METHODS: The DUE was a retrospective chart review from Jan 1, 2001-Mar 15, 2001. All patients who received a 1 mg/kg dose of enoxaparin were included. Variables collected included gender, age, weight, creatinine clearance, dose, indication, comorbid medications, and ADEs.

RESULTS: 119 patients were identified as having received enoxaparin 1 mg/kg Q12H. Six of the 61 males and 10 of the 58 females had an ADE during treatment, within 12 hours of discontinuation of enoxaparin. There was no difference between the males who had an ADE and the males who didn’t. But, there were statistically significant differences among the females. Those who had an ADE were older, had lower body weights, and lower creatinine clearances (p<0.05 in all cases).

CONCLUSION: Based on this, a physician order form was implemented (August 2001) to identify patients with renal impairment who may not be candidates for the 1 mg/kg dose of enoxaparin. Dosing for patients with extraneous renal impairment was also addressed. Until an alternative is recommended as an alternative due to ease of monitoring. During the last quarter of 2001 there were 12 pharmacist interventions changing the 1 mg/kg enoxaparin dose to 0.5 mg/kg or UFH due to the order form. And there was only 1 ADE with enoxaparin. We feel the new form has helped to prevent ADEs with enoxaparin.

340. A novel approach to implement a pharmacist-based anticoagulation service. Christopher C. Lamer, Pharm.D.; Cherokee Indian Hospital, Cherokee, NC.

PURPOSE: The purpose of the Anticoagulation Service is to enable pharmacists who are practicing in a busy outpatient pharmacy to clinically assess and manage patients who have been prescribed warfarin. It incorporates clinical services that can be performed in a timely manner within the normal outpatient pharmacy workflow.

METHODS: Policy and procedures were developed to nationally credential pharmacists through the Indian Health Service and the local governing board, empowering them with prescriptive authority to assess warfarin therapy. There was no adjust warfarin dosages according to protocol. Due to the busy nature of the hospital pharmacy, the establishment of a clinic was not feasible. A service was created that could be incorporated into the standard outpatient workflow.

A specialized medical record form has been developed to assist the pharmacist in collecting and assessing pertinent patient data in a quick and reliable manner.

RESULTS: After 4 years of data collection, the pharmacy based anti-coagulation service has resulted in increased provider, patient, and pharmacist satisfaction. INR values have remained within goal ranges as well as or better than previous care.

CONCLUSIONS: The implementation of the anticoagulation service has been a highly successful method of increasing clinical pharmacy services within a busy outpatient pharmacy.


PURPOSE: The decision to centralize dispensing of epoetin alpha and filgrastim, in conjunction with continued clinical monitoring, was made after repeated unsuccessful attempts to match expenditure with usage.

METHODS: Epoetin alpha and filgrastim were removed from all pharmacy satellites except for minimum par levels to facilitate dispensing of “stat” doses. Using a “target drug study list”, the designated clinical pharmacist dispenses and monitors the growth factors by nursing units on a daily basis. Weekend orders are prepared on Friday evening for individual patients and left in the satellite pharmacy. All requests for missing doses are referred to the pharmacist assigned to this project. Clinical monitoring of the appropriate use of epoetin alpha includes: hemoglobin, hematocrit, weight, indication, dose, administration frequency, and use of supplemental iron. Filgrastim orders are screened for indication, dose, administration frequency. WBC, and Absolute Neutrophil Count (ANC).

RESULTS: As a result, a success rate of over 95% was achieved in challenging missing dose requests from patient care areas. An immediate impact on the budget was realized, and the Pharmacy Department achieved a savings of approximately $100,000 within the first year. This dispensing procedure for the growth factors continues to date, and the Pharmacy Department continues to realize tremendous cost savings from being able to accurately match expenditure with usage.

CONCLUSION: Epoetin alpha and filgrastim are costly items and consequently, do have a high propensity for diversion in addition to their potential for inappropriate use. This method has proved effective in drastically reducing unnecessary costs associated with procuring and dispensing growth factors.

342. Implementation of pharmaceutical care services in an HIV high-risk pregnancy clinic. Patty Fan-Havard, Pharm.D., Eric J. Knudtson, M.D., Sheila K. Kang, Lakshmi Vasist, Jennifer W. Jende, Michael Para, M.D., Michael Brady; Ohio State University, Columbus, OH.

Women constitute the fastest growing population at risk for HIV infection in the United States. Combination antiretroviral therapy (ART) is now routinely recommended in pregnant HIV-1 infected women to improve maternal health and reduce HIV-1 perinatal transmission by massively suppressing maternal viral load. Antiretroviral therapy is associated with numerous complexities including pill burden, drug-food and drug-drug interactions, and adverse events. Adherence to ART is critical to achieve optimal virologic suppression and immune preservation, prevent vertical transmission of enoxaparin. There was no difference between the males who had an ADE and the males who didn’t. But, there were statistically significant differences among the females. Those who had an ADE were older, had lower body weights, and lower creatinine clearances (p<0.05 in all cases).

CONCLUSION: Epoetin alpha and filgrastim are costly items and consequently, do have a high propensity for diversion in addition to their potential for inappropriate use. This method has proved effective in drastically reducing unnecessary costs associated with procuring and dispensing growth factors.

343. Development of an HIV antiretroviral order form in a tertiary care teaching hospital. John J. Faragon, Pharm.D., Douglas G. Fish, M.D., Peter J. Piliero, M.D., Timothy S. Lesar, Pharm.D., Elle Cioppa, M.S.; Albany College of Pharmacy; Albany Medical College; Albany Medical Center Hospital, Albany, NY.

PURPOSE: Published data from our institution revealed that prescribing errors related to antiretroviral therapy increased from 2% of HIV admissions in January 1996 to 12% of HIV admissions in October 1998. The most common errors were related to incorrect dosage (25.5%) and dosing frequency (30.3%). A standardized HIV antiretroviral order form was developed to simplify ordering and to reduce the frequency of prescribing errors. This order form was developed to simplify ordering and to reduce the frequency of prescribing errors associated with antiretroviral therapy (HAART).

METHODS: The study hospital is a 631-bed tertiary care teaching hospital located in upstate New York. The standardized HIV antiretroviral order form was developed by an HIV clinical pharmacy specialist and reviewed by HIV attending physicians, pharmacists, and nurses familiar with HAART prescribing.

RESULTS: Development of the HIV antiretroviral order form was completed and approved for use in June 2002. The order form is available on the Antiretroviral Pregnancy Registry. The pharmaceutical services have been successfully implemented and the patient demographics and outcome data will be presented at the poster.


A collaborative practice between a pharmacy practice faculty member and a community-based infectious disease specialist for the management of patients...
345. Implementation and evaluation of a pharmacist-managed service for the treatment of anemia of chronic kidney disease. Greg S. Bradford, Pharm.D., Carin T. Rutland, Pharm.D., Christi T. Hightower, Pharm.D. candidate, Alison C. Irwin, Pharm.D., Daniel H. Gillis, III, Pharm.D., Shannon M. Lee, Pharm.D., BCPP, Catherine C. Herndon, Pharm.D., BCPP, Princeton Baptist Medical Center; Samford University; Pfizer Inc., Birmingham, AL. PURPOSE: This project is designed to 1) describe the implementation of a novel pharmacist managed anemia service in a large community hospital, and 2) evaluate clinical and pharmacoeconomic outcomes over six months before and after implementation of this service. METHODS: A medical record review was conducted in erythropoietin-treated patients with primary or secondary diagnosis of chronic kidney disease who were admitted to the hospital between July 1 and December 31, 2000 (n = 165). An anemia management protocol based on current National Kidney Foundation Disease Outcomes Quality Initiative guidelines was implemented by the clinical pharmacy service in September 2001. Data collection was continued in chronic kidney disease patients who were managed by the pharmacy service from October 1, 2001 to March 31, 2002 (n = 152). RESULTS: The pre-protocol evaluation revealed significant variation in erythropoietin and intravenous iron prescribing patterns. Mean erythropoietin doses declined following implementation of a management protocol (150 units/kg pre-protocol vs. 112 units/kg post protocol). Intravenous iron replacement therapy was prescribed in 6.7% of the pre-protocol patients and 56.6% of the post-protocol patients. A mean hemoglobin value ≥ 11 g/dL was attained in 12.1% of pre-protocol patients and 20.4% of post-protocol patients (p=0.045). Mean drug costs per patient were $722 in the pre-protocol period and $667 following protocol implementation. CONCLUSION: Implementation of the anemia management service resulted in lower doses of erythropoietin, increased utilization of intravenous iron, and an increase in mean hemoglobin values. Additionally, mean drug costs per patient decreased following protocol implementation.

346. Use of oral ondansetron versus intravenous ondansetron as initial antiemetic therapy in oncology patients receiving moderate to highly emetogenic regimens. R. Ph., Steven DiCrescento, R. Ph., Dalia Abdelmackssoud, B.S., Pharm.D., New York University Medical Center, New York, N.Y. PURPOSE: Several studies demonstrate the cost efficacy and therapeutic equivalency of oral formulations of 5HT3 antagonists versus the intravenous form in moderate to highly emetogenic chemotherapy regimens. The oral form provides convenient dosing, decreased administration time and supplies, and improved quality of life. The purpose of the study is to maximize the use of oral ondansetron versus the intravenous form. METHOD: Extensive efforts were undertaken to educate the medical community and Oncology Nurse Specialists on the advantages of oral ondansetron in moderate or highly emetogenic chemotherapy. Anti-emetic guidelines were developed by the Departments of Oncology/Hematology, Medicine and Pharmacy. A list of patients receiving ondansetron was reviewed daily. The Oncology Clinical Pharmacist assessed response to oral ondansetron 24-48 hours after chemotherapy. Parameters evaluated included emetogenic potential of chemotherapy based on the Hesketh algorithm, ondansetron dose, steroid therapy, tolerance of oral ondansetron, previous compliance and cost savings. Outcome measures include: incidence of nausea and vomiting at weeks 1, 3, and 4 of treatment and patient ability to ambulate and eat meals. RESULTS: Twenty-seven patients were assessed prior to a chemotherapy cycle with moderate to highly emetogenic chemotherapy. Eighty-one percent of the patients were chemotherapy naïve and 19% were non-chemotherapy naïve. Eighty-five percent of the patients received moderately emetogenic chemotherapy. One patient received steroid therapy. Seventy-seven percent of the patients demonstrated complete response and 23% demonstrated major response (mild nausea occurred). All patients were able to eat and ambulate. CONCLUSION: Oral ondansetron provides control of nausea and vomiting comparable to intravenous ondansetron with an associated substantial cost savings.

347. Multidisciplinary quality improvement initiative for cardiovascular disease and stroke in the family medicine center. Andrea M. Wessell, Pharm.D., Elizabeth W. Blake, Pharm.D., Steve M. Ornstein, M.D.; Medical University of South Carolina, Charleston, SC. PURPOSE: This project evaluated an intervention to improve adherence with clinical practice guidelines for cholesterol screening, diabetes, and hypertension in an academic Family Medicine Clinic. The project was modeled after ‘Practice Partner Research Network-Translating Research into Practice (PPRN-TRIP)’, an AHRQ-funded study designed to improve adherence with process indicators for the prevention of the cardiovascular disease and stroke in primary care practices. METHODS: Adherence with guidelines was determined from data in the electronic medical record (EMR). Interventions were selected to include management of diabetes, hypertension, and cholesterol screening in adult patients. Identified patients were then seen in clinic by the pharmacist and the physician. Point-of-care and letter templates were used to guide care during visits and provide patient-specific results and treatment goals. Patient outreach was performed via letters and/or telephone calls. Statistical analyses were performed using paired t-test and McNemar’s test as appropriate. RESULTS: In patients with hypertension (n=64), systolic BP (SBP) decreased throughout the intervention (142 to 136 mm Hg, p=0.0042) without a change in diastolic BP. Measurement of HDL (n=101) increased during the study (29% to 35%, p=0.0001). Measurement of BP, measurement and control of HbA1c, BP, and LDL in patients with diabetes (n=63), and measurement of total cholesterol did not change significantly. Response to outreach varied. CONCLUSIONS: By applying practice guidelines, this intervention produced a decrease in SBP in HDL measurement, but did not significantly alter other parameters evaluated. Study results were limited by short duration of intervention (9 months) and small sample size.

348. Implementation of a telephone-based, tablet-splitting education program in a Veterans Affairs medical center. Ellen M. Schellhase, Pharm.D., Russell E. Mathis, R.Ph.; Purdue University; West Lafayette, IN; Roudebush Veterans Affairs Medical Center, Indianapolis, IN. PURPOSE: The purpose of this program was to implement and monitor a program educating tablet splitting to enable the patients to receive appropriate dosing and improve short-term adherence with the VA’s Administration cost-savings initiative. METHODS: The initial target medications were atorvastatin and simvastatin due to potential cost-savings. A computer-generated list was used to determine initial patient eligibility. Medical records were reviewed to assess qualification for enrollment. Educational encounters were conducted via telephone by a registered nurse. An algorithm designed by pharmacy guided the process. During the initial telephone call, an assessment was made to ensure patient capability of utilizing a tablet splitter, and then a 14-day trial was initiated. Medication supply, tablet splitter, and educational handouts were mailed to the patient. Patients were contacted at the end of the trial to determine if they were capable of continuing tablet splitting based on their responses to interview questions. All encounters were documented in the electronic medical record. RESULTS: After 12 weeks, 613 patients entered into the trial phase. There were 472 patients unavailable by phone, not eligible after screening, or that declined to participate in the tablet splitting program. At this time, 483 patients successfully completed the trial phase and continued tablet splitting. Implementation of tablet splitting in these patients resulted in an estimated $75,000.00 cost savings annually. CONCLUSION: This program is an acceptable way to provide patient education on tablet splitting. This program will continue in order to provide patient education while improving cost-effective therapy for patients at this facility.

349. Documentation of clinical pharmacy interventions for pediatric patients. Mark R. Haase, Pharm.D., BCPS, Michelle E. Corden, Pharm.D., Sherry A. Luedtke, Pharm.D., Allyson S. Gaylor, Pharm.D., Nicholas R. Blanchard, Pharm.D., M.Ed., James C. Grier, Pharm.D.; Texas Tech University Health Sciences Center, Amarillo, TX. PURPOSE: Documentation and characterization of clinical interventions is now essential for the justification of clinical positions in pharmacy. This project is an ongoing study of the Pediatric Practice Team’s (PPT) documentation of clinical activities using a standardized documentation system, and will serve to educate hospital faculty, residents, and students at TTUHSC School of Pharmacy. 2 Characterize types of interventions performed, and 3) Document the impact of our pediatric pharmacy practices. METHODS: All interventions made from January - June 2002 by the PPT will be included. Interventions are documented in an Access™ driven database at each TTUHSC School of Pharmacy campus. Types of data collected include: date, location, diagnosis, time involved, significance, drug involved, type of intervention. Faculty members review all interventions for accuracy of
RESULTS: In the first three months of 2002, 12 clinicians accounted for a total of 1154 documented interventions. Of the interventions, residents, faculty, and students made 41%, 39%, and 20%, respectively. Forty-nine adverse drug events were prevented or detected and corrected. Drug allergy change, drug monitoring, drug information, and patient counseling were the most common activities, accounting for 75% of all interventions. Additional data, at least through June 2002 will be added to current results.

CONCLUSION: The Pediatric Practice Team at TUTHSC School of Pharmacy is an effective document clinical interventions using a standardized documentation system. Further analysis may help us to identify patients who are likely to require significant intervention and document the impact of pharmacist care.

350. Translation of an asthma patient education program from English to Arabic: A Pilot Study using a Focus Group Method
Dan Moellentin, Pharm.D., Michael Warmuth, R.Ph., Jeanette Towns, R.Ph., David Crabtree, C.Ph.T., M.S., James J. Pitcock, Pharm.D., Elizabeth H. Hood, Pharm.D.; University of Mississippi, Jackson, MS.

PURPOSE: This project provided educational materials in Arabic for use in children with asthma when the patient, parent or caregiver cannot read or speak English.

METHODS: The Peter Puffer(C) asthma materials were translated from English to Arabic by the Arab Community Center for Economic and Social Services. Two physicians with Arabic as their first language independently back translated the Arabic version into English. A focus group of 5 with Arabic as their first language reviewed the translated version for readability and understanding. A survey regarding the final Arabic version was completed by selected members of the Arab community. Survey responders consisted of 6 adults and 6 children or their caregivers with asthma, and 6 adults without asthma.

RESULTS: Elements of Peter Puffer successfully translated include information regarding: asthma pathophysiology, triggers, pets, house dust mites, cockroaches, molds, cigarette and tobacco smoke, attack warning signs, symptoms and course of action, asthma medications in general and an action plan. The focus group concluded the documents in Arabic were easily understood and readable. They recommended no further changes. All 18 survey responders indicated the Arabic documents 1) would be of benefit to patients and caregivers, 2) helped increase understanding of asthma, and 3) should be used within the Arab community for the prevention and treatment of asthma. Seventeen of 18 responders found the documents easy to understand.

CONCLUSION: Peter Puffer was successfully translated into Arabic and provides useful written information for patients with asthma or their caregivers.

351. Comparison of pharmacy cost reduction analysis of computer-based, single event interventions versus automated problem list interventions.
Dan Moellentin, Pharm.D., Michael Warmuth, R.Ph., Shewan Aziz, R.Ph., Ph.D., David Crabtree, C.Ph.T., M.S., James J. Pitcock, Pharm.D., Eastern Maine Medical Center, Bangor, ME.

PURPOSE: The Cerner® software available in Pharmacy computers at Eastern Maine Medical Center (EMMC) has the capability to alert pharmacists to potential adverse drug events (ADEs) due to inappropriate drug dosage, renal dysfunction, culture and sensitivity reports, or drug-electrolyte imbalance. Two basic types of alerts are available, such as alerts which prompt the pharmacists during order entry and review when the abnormal laboratory values are available (synchronous) and alerts that activate when the laboratory values become abnormal during inpatient stay due to changes in patient condition or status (asynchronous). More specifically, the asynchronous alerts are programmed to fire with abnormal drug lab values (event-driven) or when a patient with a high utilization of medications (automated list) is identified. The purpose of this study was to determine the relative pharmacy drug cost reduction and the relative potential cost savings generated by ADEs prevention from the two types of asynchronous alerts.

METHODS: A database of interventions by EMMC pharmacists was retrospectively reviewed to determine the relative economic return of interventions initiated by either single event alert or automated list. Preventative single event alerts fire when abnormal drug serum concentrations are found, renal dosing adjustments are required after initial exposure, cultures and sensitivities are confirmed, or serum electrolytes are abnormal with possible drug implication. However, automated problem list fires are the basis of presence of multiple broad negative indicators of health, such as abnormal serum albumin, platelet levels, changes in serum creatinine, and multi-system organ involvement. Single event firing prompt the clinical pharmacist to fully review and explore patient clinical status to make appropriate recommendations on that particular issue. When automated list alert fires, the clinical pharmacist performs a complete pharmacotherapy review. The event-driven and automated list interventions were reviewed for cost saving outcomes for a period of 120 days from December 1, 2001 to March 30, 2002. Total cost saving outcomes were calculated as cost reduction and cost avoidance. Cost reduction is measured largely as the avoidance of drug expenses. Cost avoidance is measured as predicted total drug expense (indirect saving) and reduced hospital expenses not incurred due to intervention. Methods for calculating cost-avoidance were modifications of previously reported techniques. The personnel costs to provide the clinical pharmacy services were standardized over a year.

RESULTS: Interventions resulted in either cost reduction or avoidance of both. Between December 1, 2002 and March 30, 2002, there were a total of 126 interventions resulting from event-driven rule firings. The pharmacy cost reduction associated with these interventions was $11,556 with an average of $91.50 per intervention. These same interventions resulted in a cost avoidance of $25,658 or an average of $206 per intervention. During the same period, 420 interventions resulted from automated lists requiring a comprehensive review by a clinical pharmacist. These interventions resulted in a cost reduction of $26,375 with an average of $63 per intervention. The cost avoidance with the later interventions was $121,380 with an average of $289.00 per intervention.

CONCLUSION: Our data suggests that a higher medication cost reduction is associated with focused single event interventions as compared to an automated document-based pharmacological review induced by automated list intervention ($91.50 versus $63.00). In contrast, the in-depth pharmacological review resulted in a higher cost avoidance ($280.00 versus $206.00). Although event alerts prompted specific actions and have a relatively higher cost-reduction return, they fail to replace pharmacotherapeutic reviews. Both types of asynchronous rules are useful in reducing costs of potential ADEs.

352. Economic outcomes of asthma disease management: the University of Mississippi pharmaceutical care clinic experience.

PURPOSE: To determine whether Pharmaceutical Care Clinic (PCC) management of adult asthma patients will lower direct patient care costs.

METHODS: Prospective cohort study. Enrollment open to referred patients followed for at least 12 months. The enrolled cohort acted as its own historical control. The outcome of interest was direct costs of care associated with Emergency Department (ED) and hospital utilization; data were recovered from University Medical Center (UMC) billing records. The study interval constituted one year prior to PCC referral compared to one year after.

RESULTS: Seventy-five consecutive patients were enrolled: mean age 36.3 years, 60% male, 75% African American. The number of ED visits fell by 66% (from 170 to 104) following PCC management, accruing a cost saving of $13,960.00; and the number of hospitalizations fell by 16% (from 34 to 18), accruing a cost saving of $85,325.00. The annualized rate of cost saving per study participant was $1,324.00. All statistical comparisons were significant.

CONCLUSION: In 1998, the Health Care Financing Administration (HCFA), through the Division of Mississippi Medicaid, approved reimbursement of pharmacists for their participation in disease management. This outcome analysis reveals that cost savings accrue to the care of asthma patients enrolled in a PCC. Study limitations include a prospective design of the program and hospital utilization at non-UMC facilities prior to PCC referral, and an underestimate of actual cost savings after referral due to unrecovered and unanalyzed costs associated with non-UMC care. Although analysis was limited to direct costs, quality of life (QOL) data ratify the benefit of PCC asthma management.

353. Antipsychotic cost savings: utilization of medication assistance programs in a county mental health system.
Douglas Del Paggio, Pharm.D., M.P.A., Richard P. Singer, M.D., Bernie Mullen; Alameda County Behavioral Health Care Services, Oakland, CA.

PURPOSE: To determine the effectiveness of antipsychotic patient assistance programs (PAPs) by analyzing the application process, eligibility criteria, acceptance percentage, approval period and ultimate cost savings for a network of community mental health service providers.

METHOD: A total of 320 indigent patients receiving atypical antipsychotics (olanzapine, quetiapine, risperidone) from 12 different sites were prospectively enrolled during the period 07/01/2000-06/30/2001. Data collected included the PAP identified, approval period and ultimate cost savings. 

RESULTS: Each PAP was unique in regards to overall process, eligibility requirements, medication quantity supplied, and re-application. Olanzapine (n=61): 65% approval, 614 prescriptions, cost savings $157,798. Quetiapine (n=46): 61% approval, 61 prescriptions, cost savings $13,237. Risperidone (n=118): 54% approval, 176 prescriptions, and total cost savings $30,096. Sixty-five percent of the patients achieved third-party eligibility at 1 year.

CONCLUSIONS: Although none of the PAPs were ideal, favorable characteristics included provider eligibility determination, bulk medication shipment and streamlined communication. Each PAP was assessed as cost reducing and patient cost avoidance. The olanzapine PAP had the highest approval rate and associated cost savings.
Impact of a pharmacy-driven antibiotic renal dosing program in a large teaching institution. Lillian I. M., R.P.H., Steven DiCrescento, R.Ph., Dhania Abdelmacksoud, B.S., Pharm.D., New York University Medical Center, New York, NY.

PURPOSE: The purpose of the program is to assess the appropriateness of antibiotic doses in patients with compromised renal function and make resultant interventions to improve the effect of such a program on patient safety and to determine the cost savings associated with dose adjustments.

METHOD: The following “focus” intravenous antibiotics are assessed: imipenem/cilastatin, cefazolin, meropenem, piperacillin/tazobactam, levofloxacin, and ampicillin/subtactum. These agents were chosen for their noted renal dosing profile and potential adverse effects for non-adjusted doses. Daily data collection includes: prescribed dose, start and end date of therapy, age, gender, height, weight and serum creatinine. Creatinine clearance is calculated using the Cockcroft-Gault equation. The prescribed doses were compared to the antibiotic renal dosing guidelines established at our institution. If variances existed, a recommendation is made to the prescriber to change to the appropriate dose or frequency.

RESULTS: From January 1, 2002 to July 31, 2002, a total of 360 patients received one of the five focus antibiotics and was assessed for appropriate dose/frequency by the designated clinical pharmacist. The following is a summary of these dosing assessments: 170 patients received ampicillin/subtactum requiring 5 interventions; 34 patients received levofloxacin requiring 3 interventions; 40 patients received piperacillin/tazobactum requiring 2 interventions; 74 patients received imipenem/cilastatin requiring no interventions; 14 patients received meropenem requiring no interventions. The interventions generally consisted of a change in frequency interval or a decrease in the prescribed dose. Cost savings was minimal.

CONCLUSION: Preliminary interventions demonstrate adverse drug reaction avoidance and enhanced patient care despite minimal cost savings in drug expenditure.


In 1997 we established a pharmacist-managed heart failure (HF) clinic. The pharmacist-practitioner is responsible for all clinic activities and our goals are to maximize medication regimen of proven efficacy, reduce morbidity and mortality, and improve quality of life. Ultimately, our objectives were to prolong life, improve quality of life, and decrease the cost of HF management. After 3 years of practice we selected a random sample of patients for outcome evaluation. We evaluated number of ER (Emergency Room) visits and hospitalizations, number of patients at ACE-inhibitor goal, and relative cost of treatment for six months prior to and six months after clinic enrollment. Compared to historical controls, the HF clinic patients experienced significantly fewer HF-related ER visits and hospitalizations over a six-month period. All clinic patients achieved ACE-inhibitor goal compared to 80% of the historical controls. Number needed to treat analysis demonstrated each patient treated in clinic for six months avoided one HF-related ER visit or hospitalization. All interventions generally consisted of a change in frequency interval or a decrease in the prescribed dose.

356. Personal digital assistant technology to facilitate appropriate prescribing and assessment of the use of activated protein C (drotrecogin alfa). Linda M. Hoyle, Pharm.D., BCPS, Edward Liu, M.D., Kathleen K. Casey, M.D., Michael L. Kohute, Pharm.D., Jersey Shore Medical Center, Neptune, NJ; Rutgers University, Piscatway, NJ.

The use of activated protein C (drotrecogin alfa) in a patient with severe sepsis requires a thorough evaluation of the patient in order to assess medication appropriateness, consider benefits and risks, and determine optimal management. In order to aid physicians in the appropriate use of activated protein C, a multidisciplinary team in our institution developed a protocol and order sheet for the prescribing of this medication. We then integrated the items on the order sheet into a handheld personal digital assistant (PDA) by creating an application in a commercially available database program (HandBase®). We provided this program, along with applications for calculating APACHE II scores, to attending and resident physicians and clinical pharmacists involved in caring for critically ill patients. Within the database, each patient’s information is organized by name and medical record number, and the data can be transferred to the PDAs of other individual’s responsible for the care of the patient. Following this bedside assessment, the data is then transferred from the PDA to a desktop computer to allow for further prospective and retrospective analysis by a multidisciplinary team. Each case of severe sepsis can then be evaluated on an individual basis to determine the appropriateness of the drug and outcomes of its use on survival, length of stay in the intensive care unit, and overall length of hospital stay. By continually evaluating the use of activated protein C, the team will be able to identify potential areas for improvement with the utilization of this drug.

357. Is a doctor's visit just a doctor's visit? The role of a clinical pharmacist in a collaborative care clinic. Tracy Bahr, Pharm.D., Austin Bailey, M.D., Carol Paffly, Ph.D., Kathleen Jones, M.A., Kathy Machin, L.P.N., Jennifer Anderson, M.Ed.; Family Medicine Residency Program, Fort Collins, CO.

PURPOSE: Initiate an integrative, collaborative care clinic in a family medicine resident training program in order to 1) enhance resident training, and 2) meet a variety of patients’ comprehensive needs.

METHODS: The team (physician, clinical pharmacist, behaviorist, wellness counselor, and project coordinator) conducted 301 consultations in 6 weeks with faculty in presence for resident training. The team presented weekly and after clinic to review the patients. Patients were screened to identify needs and the team recommended specialists for each patient. The patients selected one or several team members. Patient and provider satisfaction was assessed.

RESULTS: All patients (26) were seen by the physician and nurse. Of the total, 23% (6/26), 19% (5/26), and 15% (4/26) were seen by the clinical pharmacist, wellness counselor, and behaviorist, respectively. One or more pharmacy intervention-disease/medication education, medication initiation/discontinuation, and dose increase—occurred in 23% (6/26) of the patients. Medication change occurred in 19% (5/26) of patients. A clinical pharmacy follow-up occurred for two patients. All of 46% (12/26) responded to the patient satisfaction survey. A total of 17% of the surveyed patients and providers responded favorably to the collaborative clinic.

CONCLUSION: Collaborative clinic was proven to be an efficient and comprehensive method to see patients. This method allows patients’ needs to be considered by different specialists in an interdisciplinary, collaborative manner. Patients perceived this care to be very beneficial. This is a promising method to demonstrate the multidisciplinary approach to patient care as well as teaching integrative pharmacotherapy to medical residents.

358. A model for providing cardiovascular risk assessment to community health center patients. Laura Shane-McWhorter, Pharm.D., BCPS, FASCP, CDE, BC-ADM, Richard H. Ensign, Pharm.D., BCPS, Mark A. Balk, M.D., R.P.H.; University of Utah; Pfizer, Salt Lake City, UT.

PURPOSE: Community Health Centers (CHCs) provide medical services to underserved, culturally diverse patients. The CHC patients have a high prevalence of diabetes, hypertension, and hyperlipidemia. To provide outreach education and information about cardiovascular disease to CHC patients, health fairs were conducted on a quarterly basis. At the health fairs, 
patients' 10-year cardiovascular risk was calculated using a specialized software program.

METHODS: Patient demographics, health history, and the following parameters were obtained at the health fairs: blood pressure, blood glucose, and cholesterol. The information was entered into the software program, Coronary Heart Disease (CHD) Risk Factor Calculator. The program calculates 10-year risk for cardiovascular events, based on the Framingham Heart Study. Modifiable risk factors were identified and used to educate patients.

RESULTS: Cardiovascular risk assessment results were printed and given to patients, to serve as an education tool, and to convey the information to their primary care provider. Results were provided in a graph format so patients could readily understand their individualized risk. Summary reports and recommendations were given to clinic providers to increase awareness of patients' risk profiles. Recommendations included more aggressive treatment of elevated blood pressure, hyperlipidemia, and smoking cessation. Thus far, 50 patients have been evaluated and 32 (64%) are at high risk for cardiovascular disease. Patients reported an increased understanding of the factors that may contribute to a cardiac event.

CONCLUSION: A model for providing cardiovascular information to underserved CHC patients is to use a specialized software program at health fairs. Similar services may be initiated in other patient settings.

360. The impact of anticoagulation guidelines and low molecular weight heparin therapeutic intervention on resource utilization in a community hospital.

John A Novicky, Pharm.D., Brian J Gaffney, M.D., Ather Iqbal, M.D., Jon Bushnell, R.P.H.; Mohawk Valley Heart Institute; St. Elizabeth Medical Center, Utica, NY.

PURPOSE: To describe the development and implementation of anticoagulation guidelines in a community hospital. The purpose of these actions were to examine the impact of the financial outcome of this facility without affecting quality of patient care.

METHODS: A low molecular weight heparin (LMWH) and unfractionated heparin (UFH) Drug Utilization Review (DUR) was completed which addressed dosing issues, Length of Stay (LOS) and bleeding comparisons. Results from this review and extensive literature search were used to develop "Anticoagulation Guidelines" in conjunction with Cardiology, Hematology, Critical Care, Family Practice and other members of the medical staff. Guidelines developed prefer Unfractionated Heparin (UFH) for all indications and use of dalteparin (rather than enoxaparin) when a LMWH is necessary.

RESULTS: The DUR (performed prior to Guideline implementation) revealed that while all UFH patients achieved therapeutic range within 24 hours using Heparin protocol, 14 patients (15%) received improper doses of enoxaparin. The Length of Stay was similar for UFH and LMWH at 6.1 ± 4.0 and 5.9 ± 4.8 (p=0.87) days respectively and 4 UFH patients (12.5%) vs. 11 LMWH patients (16.9%) had some evidence of bleed. Six months after Guideline implementation, there was no increased LOS nor pattern change in average daily census or patient discharges for this institution. The year before implementation of Anticoagulation Guidelines, this hospital spent $550k on Heparin protocol, 14 patients (15%) received improper doses of enoxaparin.

CONCLUSION: Implementation of Anticoagulation Guidelines has positively impacted resource utilization in this medical center without apparent effect on gross measures of outcome.

361. Diabetes management quality improvement in a family practice residency program.

James D. Hoehns, Pharm.D., BCPS, E. Diabetes management quality improvement in a family practice residency program. John E. Sutherland, Pharm.D., BCPS, Mark Drews, M.D., Northeastern University, Boston, MA; Whitlät Street Health Center, Roxbury, MA.

PURPOSE: To assess the effectiveness of providing pharmaceutical care in a community health center serving a multicultural population in which Spanish is the primary spoken language.

METHODS: After 20 months of establishing the service, a retrospective analysis of a physician referral, pharmacist-managed diabetes clinic was conducted. Eligible patients were those whom HgbA1C values were available 6 months prior to and 6 months after pharmaceutical intervention. Patients served as their own controls. Data on lipid levels, aspirin usage, vaccination months prior to and 6 months after pharmaceutical intervention. Patients reported an increased understanding of the factors that may contribute to a cardiac event.

RESULTS: 1) 55 occurrences of 2 of 6 target medications were found, 196 profiles contained at least one potentially interacting medication. 2) 97% compliance rate. The total cost for the medications including pharmacist time and dispensing materials amounted to $445.50. Both resident and attending physicians have found the program helpful in prompting more appropriate medication choices.

CONCLUSIONS: We were able to efficiently provide low-cost, vital medications to our underserved patients. With this baseline data, we secured permanent funding to sustain the program and add additional medications including albuterol inhalers and antidiabetic agents. We hope to further explore clinical outcomes.

364. Integration of an academic pharmacy initiative and pharmacy professional experience program with a progressive community pharmacy clinical practice program.

Angela M. Wisniewski, Pharm.D., Cori A. Mikieje, R.P.H., Pamela A. Eppolito, R.P.H., Gene D. Morse, Pharm.D., Michael Rossi, R.P.H.; SUNY, University at Buffalo; Eckerd PatientCARE™ Centers, Buffalo, NY.

PURPOSE: To implement clinical activities within the framework of traditional community pharmacy with the goal of transitioning from dispensing-focused towards pharmaceutical care based practice by integrating a university-based clinical practice and Pharmacy Professional Experience Program.

METHODS: The University at Buffalo and Eckerd established a joint faculty position. The faculty member, two PatientCARE™, and 9 dispensing pharmacists participated. A clinically oriented clerkship experience integrated into pharmacy activities and contributed to data collection.

Clinical programs included criteria-based, medication profile reviews to identify patients receiving ≥1 narrow therapeutic index target medication, 2) implementation of the Eckerd PatientCARE program, including two PatientCARE pharmacists, 3) fourth professional year pharmacy clerkship experiences with objective assignments, and 4) community-based health screening events in multi-resident housing complexes.

RESULTS: 1) Overall, 375 occurrences of ≥1 of six target medications were found, 196 profiles contained at least one potentially interacting medication. 2) 97% compliance rate. The total cost for the medications including pharmacist time and dispensing materials amounted to $445.50. Both resident and attending physicians have found the program helpful in prompting more appropriate medication choices.

CONCLUSIONS: We were able to efficiently provide low-cost, vital medications to our underserved patients. With this baseline data, we secured permanent funding to sustain the program and add additional medications including albuterol inhalers and antidiabetic agents. We hope to further explore clinical outcomes.
molecular-weight heparin for VTE prophylaxis. This report documents the success of a program implemented to convert medical patients from enoxaparin to LDUH for VTE prophylaxis.

METHODS: Hospitalized patients receiving enoxaparin for VTE prophylaxis during the period from November 2001 through March 2002 were considered for potential conversion to LDUH. Patients excluded from conversion were those in the post-operative period, patients with a history of heparin-induced thrombocytopenia, or with evidence of minor bleeding. Data was collected for intervention acceptance rate, days of enoxaparin avoided, and the occurrence of documented cases of significant bleeding.

RESULTS: Throughout this five-month period, 256 patients were reviewed for potential conversion to LDUH. Of these, 58 were considered to be candidates for conversion. Ten patients were discharged prior to any intervention. Of the remaining 46 patients (77%) were successfully converted resulting in an avoidance of 150 days of enoxaparin prophylaxis and an associated medication cost savings of $3123. The remaining 11 (23%) patients utilized 76 days of enoxaparin at a medication cost of $1774. No patients in the LDUH conversion group or the enoxaparin group experienced a documented VTE or significant bleed during their admission.

CONCLUSION: Patients that meet criteria can be converted from enoxaparin to LDUH for VTE prevention. This economically attractive conversion can significantly reduce drug expenditure for hospital pharmacies while following national guidelines.

366. Performing statewide medication usage evaluations utilizing handheld technology. Dean M. Najarian, Pharm.D., BCPS; Tewksbury State Hospital, Tewksbury, MA.

PURPOSE: To utilize handheld technology in order to provide standardized medication usage evaluation (MUE) data collection in a closed statewide health system and to identify patients at risk for adverse drug reactions and to document existing gaps in benchmarking standards between State facilities. This information is utilized to improve patient outcomes and assess disease state management in a time efficient manner.

METHODS: The clinical pharmacy team of twelve clinical specialists develops a medication usage evaluation calendar that is presented once a year to the State Pharmacy and Therapeutics (P&T) Advisory Board. The data assessment tool is developed for individual medications, groups of medications, or specific disease states that reflect current consensus guidelines or prescribing information. This tool is converted and programmed for handheld use that is accessible to each clinical pharmacist through a handheld device.

RESULTS: The handheld program collects the data into an easy to manage spreadsheet. The clinical team will present individual site findings and recommendations to their respective P&T Committee for discussion. The clinical director compiles a summary document, which is presented to the State P&T Advisory Board for discussion, recommendations and follow-up.

CONCLUSIONS: The use of handheld technology provides a consistent data collection tool when utilized by multiple users when compared to the traditional handwritten paper tool. Standardized reports contain important benchmarking data such as proper diagnosis, proper monitoring parameters, adverse drug reaction detection, and patient education assessment as well as document clinical interventions to improve patient outcomes. Time efficient data collection also allows the clinical pharmacist to be more available for other clinical activities.

367. The effects of pharmaceutical care on quality of care and cost on patients in a family practice residency program. Ila Mehra Harris, Pharm.D., BCPS; Tewksbury State Hospital, Tewksbury, MA.

PURPOSE: The primary purpose of this study was to evaluate the effect of pharmaceutical care on quality of care and cost on patients in a family practice clinic/residency program.

METHODS: Data was collected over one year on patients enrolled in a Minnesota nonprofit Health Maintenance Organization (HMO). Charts of selected patients were reviewed by the pharmacist, and patients were then seen by the pharmacist for pharmacare. Each visit was fully documented into a computer software program.

RESULTS: Ninety-two patients were included in this study, with a total of 203 patient encounters. Drug therapy problems were identified in 90% of patients, for a total of 250 drug therapy problems found. Status improved in 45% of patients, 46% stayed the same, and 9% declined (p<0.001). A statistically significant improvement in status from baseline to end was found in hypertension (p=0.007), dyslipidemia (p=0.002), and asthma (p=0.011). A higher percentage of patients reached therapeutic goals for hypertension at the end for hypertension (38% vs. 62%) and dyslipidemia (21% vs. 50%), however these did not reach statistical significance. From baseline to end, significant improvement was seen for aspirin use in diabetes (57% vs. 81%, p=0.031), aspirin for prevention (50% vs. 0%, p=0.031). Polypharmacy was reduced from an average of 3.92 medications to 3.04 (p<0.001). The estimated total cost savings was $4,011.00.

CONCLUSIONS: Pharmaceutical care has a significantly positive impact on quality of care and cost on patients in this family practice clinic/residency program.

368. Measuring patient satisfaction with care in a neurology clinic: physician and pharmacist. Morli G. Majmudar, Pharm.D., Donna M. Givone, Pharm.D., Kiranpal S. Sangha, Pharm.D., Padmini Sekar, M.S.; University of Cincinnati, Cincinnati, OH; University of Illinois at Chicago, Chicago, IL; University of Alabama at Birmingham, Birmingham, AL.

PURPOSE: To use a patient satisfaction survey to measure patient’s perception of care provided by physicians and pharmacists in a neurology clinic.

METHODS: An 11-item questionnaire was developed to measure patient satisfaction. The questionnaire contained 10 closed-ended questions and one open-ended question. Patients following their visit with either the physician or the pharmacist at The University Hospital Neurology Clinic, filled out the questionnaire. Surveys were collected from January 2001 to July 2001 and September 2001 to April 2002. A five-point Likert scale ranging from 5 (strongly agreed) to 1 (strongly disagree) was used to grade the responses.

RESULTS: A total of 201 surveys were completed (N=110 physician group, N=91 pharmacist group). Three of the ten closed-ended questions showed statistically significant results for the pharmacist group when compared to the physician group. These three questions referred to the time spent by the practitioner with the patient (4.50 vs. 4.36; p=0.017), the choice of words used by the practitioner (4.37 vs. 3.94; p=0.011), and the overall satisfaction with the visit (4.57 vs. 4.29; p=0.023). Additionally, the composite total score of all the ten closed-ended questions was also significant for the pharmacist group (42.08 vs. 40.03; p=0.002). No statistical significance was found in the data between the two groups were analyzed based on age and gender. Patients frequently commented about the long wait in the open-ended question.

CONCLUSION: The mean scores were consistently high in the pharmacist group in comparison with the services provided. Patients were satisfied with the amount of time spent with the pharmacists, and the ability of the pharmacist’s to use words they could understand. This survey instrument should be used with caution until it is validated.

369. Cost analysis of a pharmacist-administered adult immunization service. James J. Sterrett, Pharm.D., Melissa M. Blair, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To conduct a cost-analysis of a pharmacist administered adult influenza immunization program in a pharmacy within a family medicine clinic.

METHODS: After administering over 300 immunizations, the product and personnel costs of delivering the immunization service and the reimbursement from patients and 9th parties were analyzed. Product costs included: medication, needles, syringes, and other supplies. Personnel costs included: appointment scheduling, shot provision and education, documentation, and billing. Personnel costs were calculated based on average time and type of personnel providing the service.

RESULTS: Average time spent providing services was as follows: 2 minutes to schedule an appointment, 5 minutes to prepare and provide the immunization, 5 minutes to document the encounter, and 5 minutes to bill, if required. These services were excluded for appointment scheduling which was shared with a technician. Based on an average yearly pharmacist’s salary of $70,000 and technician’s salary of $21,000, the per patient personnel cost of providing these services was $9.11. The product cost per patient was calculated to be $4.69. Reimbursements ranged from $8.06-$15.00 per immunization. The total cost to provide immunizations was $4208.44 and reimbursement was $3214.18. Therefore, the pharmacy lost $994.26, or $3.26 per immunization.

CONCLUSIONS: Based on the average product and personnel cost, a pharmacist administered adult influenza immunization service is not financially profitable at this pharmacy. Other benefits such as introduction of new business into the pharmacy, improving work flow to incorporate further disease state management, and changes in patient perception of pharmacists were not measured.


PURPOSE: Pharmaceutical manufacturer assistance programs (PMAPs) can provide medications to qualified patients who are unable to afford prescription drug therapy. Prior literature has reported success of pharmacist-coordinated assistance programs in decreasing hospital costs in hospital-based ambulatory care or specialty clinics. Our study assessed the effect of incorporating PMAPs into clinical pharmacy services in a private ambulatory care setting and reported cost savings for patients.

METHODS: Patients were prospectively evaluated for eligibility into PMAPs by the clinic pharmacist from March 2001 through March 2002. A universal intake form was created to simplify the enrollment and reappraisal process. The number of patients enrolled, patient demographics, medication dollar
value saved by the patient, the most commonly utilized programs by drug class, and time required by the pharmacists was recorded during the study period. RESULTS: A total of 44 patients were enrolled into 22 PMAPs most commonly providing antihypertensives, antidepressants, antilipemics, proton pump inhibitors, and antibiotic agents. The average age of patients was 65.7 ± 17.6 and 80% of patients were female. There were 115 medications processed and the annual cost savings to patients was $48,381. The time required by the clinic pharmacist to process each medication, including initial enrollment and reapplications, was estimated at 1 hour per patient. CONCLUSION: Incorporating pharmaceutical manufacturer assistance programs into clinical pharmacy services in a private practice setting can decrease patient expenses in a time efficient manner.

371. Processing fee justification for medication assistance programs. David M. Hachey, Pharm.D.; BCPS; Idaho State University, Pocatello, ID.

PURPOSE: Clinic and hospital-based patient assistance programs exist which support financially indigent patients in applying to pharmaceutical company sponsored medication assistance programs (MAP). Processing applications and dispensing medications to patients is time consuming and usually provided at no charge to patients. However, with the extensive time involved for managing these programs for many patients, clinics and hospitals are attempting to justify charging processing fees to patients to offset the cost of running a MAP. We set out to determine if practitioners who process applications for patients charge a fee and exactly how many applications they process monthly.

METHODS: A survey was administered electronically to the Ambulatory Care Pharmacy Research Network (AmCare PRN) asking practitioners who are involved with MAP if a dispensing fee was charged and if so, how much. They were also asked how many applications they processed monthly. The mean and median were calculated.

RESULTS: There were 32 responses. Six programs charged a processing/dispensing fee and 26 did not. For those that charged a fee, $5 was the average fee and the mean applications processed per month was 488 (range 100-1000; median 250). Those that did not charge a fee averaged an average of 42 applications per month (range 4-200; median 25).

CONCLUSIONS: The majority of survey respondents who run MAPs do not charge an application processing/dispensing fee. However, those that do charge a fee, process, on average, a larger number of applications per month.

372. Outcomes associated with diabetes management services provided by pharmacists in a family medicine center. Melissa M. Blair, Pharm.D., Andrea M. Wessell, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate the effect of pharmacist-provided diabetes management and education on glycemic control in patients at a Family Medicine Center.

METHODS: Patients were referred to pharmacists for diabetes management services. Patients attended clinic visits over the telephone. Glycemic control, as measured by glycosylated hemoglobin (HbA1c), was measured prior to, and at six months after the initiation of this service. Cost avoidance comparators, based on those found in the literature were calculated for those patients with a 1% increase in HbA1c. In patients with a > 1% increase in HbA1c, their charts were reviewed to determine reasons for worsened management.

RESULTS: A total of 44 patients were enrolled into 22 PMAPs most commonly providing antihypertensives, antidepressants, antilipemics, proton pump inhibitors, and antibiotic agents. The average age of patients was 65.7 ± 17.6 and 80% of patients were female. There were 115 medications processed and the annual cost savings to patients was $48,381. The time required by the clinic pharmacist to process each medication, including initial enrollment and reapplications, was estimated at 1 hour per patient. CONCLUSION: Incorporating pharmaceutical manufacturer assistance programs into clinical pharmacy services in a private practice setting can decrease patient expenses in a time efficient manner.

373. The effect of setting on patient perceptions of a pharmacist-administered immunization program. Elizabeth W. Blake, Pharm.D.; Melissa M. Blair, Pharm.D., Kenneth W. Kenyon, Pharm.D., Kirsri M. Hearn, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To compare patient perception of and satisfaction with an adult immunization program administered by pharmacists in a pharmacy versus clinic setting.

METHODS: Over the past two years, pharmacists have administered immunizations during influenza season in patient care rooms of the Family Medicine Center. In 2001, the service was moved into the pharmacy. Pharmacy employees performed all aspects of the immunization program including: patient registration, shot provision and education, documentation, and billing. After several months, immunized patients were contacted by telephone and asked to respond to a 10-item Likert scale survey. Two attempts were made to contact each patient. Survey results were then compared to results from a previous survey administered when the service was provided in the clinic setting and were analyzed using chi-square.

RESULTS: One hundred thirty-three patients (43%) completed the survey. More respondents (40% vs. 13%) recalled that a pharmacist had administered the immunization thus M. Wessell, Pharm.D.; Medical University of South Carolina, Charleston, SC.

increase in HbA1c, charts were reviewed to determine reasons for worsened management improved glycemic control with potential cost savings. Non-

including: patient registration, shot provision and education, documentation, immunizations during influenza season in patient care rooms of the Family

clinic setting.

Kenneth W. Kenyon, Pharm.D., Kirsi M. Hearon, Pharm.D., Maria A.L. Monteiro, Pharm.D., Maria L. Lemos, Pharm.D., Maria A. Martins, Pharm.D., Rufino Silva, M.D., Odete S. Isabel, Pharm.D.; Coimbrás University Hospital, Coimbra, Portugal.

PURPOSE: The pharmaceutical services of Coimbrás University Hospitals (HUC) started, in 1998 a clinical trial section. This section developed internal protocols related to prescription, distribution, preparation, administration, and information making the medication circuit safer, more rational and efficient. The objective is to analyze the contribution of the clinical trials section of the HUC to the rationalization of the verteporfin circuit.

METHODS: A protocol in which the clinical trials section participated was selected. The medication, verteporfin, concluded the study and once approved its introduction in the hospital formulary was tried with the protocol procedures.

RESULTS: The circuit of the medication established for the trial, which contemplated an active intervention of the pharmacist in all stages (including preparation), was maintained after the introduction of the verteporfin in the hospital. Between April and August of 2001, 28 patients were included (52 men), average age of 71.8 and 50 treatments were performed. The medication is prepared in the vertical flow chamber in the pharmaceutical services and monitored by pharmacists until administration. $46,977 U.S. dollars were spent, 21% less than expected.

CONCLUSIONS: The implanted circuit of verteporfin during the protocol was followed after the introduction in the hospital and proved to be safe, efficient and rational.

375. Impact of pharmacist-conducted patient education and counseling. Lynnette R. Klaus, R.Ph.; Pharm.D. candidate; Providence Portland Medical Center, Portland, OR.

PURPOSE: The Patient Safety Team at Providence Portland Medical Center (PPMC) identified the need for improved continuity of care as inpatients are discharged and transitioned to the outpatient setting. A pilot study was recommended to assess efficacy and impact of having a pharmacist involved in the discharge process.

METHODS: Patients on the respiratory care unit at PPMC between May 7 and June 14, 2001 were chosen for the pilot study. Patients selected for counseling were identified using predetermined criteria based on the population statistics of patients admitted to the respiratory care unit. The pharmacist initiated interventions to improve continuity of care, reduce potential adverse events and medication errors, and to provide patient education. The economic impact of the interventions provided by the pharmacist was evaluated along with patient, physician and nursing satisfaction.

RESULTS: Seventy-two patients were evaluated and counseled by the clinical pharmacist with 120 interventions performed. A total cost savings of $10,130 was calculated using ASTR (Compensation for interventions provided by the clinical pharmacist. Satisfaction surveys distributed had a response rate of 100%, 67% and 40% from the physicians, nurses and patients, respectively, with a response in favor of having a pharmacist involved in the discharge process. CONCLUSION: The clinical pharmacist provided a positive impact on the provision of care for inpatients being transitioned to the outpatient setting. The outcome measures of patient, nurse and physician satisfaction were found to positively advocate the benefit of a clinical pharmacist providing discharge counseling.

376. Development of a comprehensive primary care clinic pharmacy service. Cristina D. Gray, Pharm.D., BCPS; Dwight D. Eisenhower VA Medical Center, Leavenworth, KS.

PURPOSE: To develop a clinical pharmacy service within a multi-disciplinary specialty (primary care clinic in order to 1) provide comprehensive care to veterans, 2) increase opportunities for student training, 3) increase physician availability for more complex visits, and 4) reduce drug costs and enhance formulary compliance.
Impact of clinical pharmacy services on a Cuban pediatric hospital. A. Martínez Sanchez, Ph.D., De la Torre A. Rodríguez, B.S., Pharm., Alina de las Mercedes Martínez-Sanchez, University of Oriente South Pediatric Hospital, Santiago de Cuba, Cuba.

PURPOSE: To evaluate the impact of the activity of the clinical pharmacy in the identification, solution and prevention of drug-related harm.

RESULTS: A prospective review of pharmacy services on patients hospitalized during the year 2001 in the Pharmacy Services Southern Pediatric Hospital of Santiago de Cuba, Cuba, it is a pediatric hospital of 329 beds, a clinical pharmacist for the whole hospital.

The pharmacy report activities are analyzed taking into account the following markers:
1. Drug interactions: with regard to implication for the results of the pharmacotherapy of the patient
2. Drug adverse reaction: (demonstration through Naranjo’s Algorithm)
3. Pharmacy interventions.
4. Information to patients and health professionals about diseases and treatments.

RESULTS: A total of 29 pharmacy intervention profiles were reviewed, 15 medical interventions (adverse reaction of these 15% harmful, 33% not justified, 42 adverse drug reactions were detected 29% possible, 21% probable and 26% defined. 87 pharmacy interventions are carried out consisting in change of treatment. Eight seminars and three lectures are imparted to 18 health professionals of which three with B.A. in Nursing and 15 doctors, the topics being: treatment of the giardiasis, drug adverse reactions, drug interactions and uses of otomological drops. 13 patients received information about medications, the main pharmacological groups were: analgesic, antiinfectious and inhaled anti-asthmatic.

CONCLUSIONS: The results obtained show the importance of the existence of the clinical pharmaceutical services in Cuban pediatric hospital and its utility in the protections against drug-related harm that endanger the achievement of the optimal results of the pharmacotherapy. These ideas suggest the necessity that the clinical pharmaceutical services should be given in a continuous way to promote the safe and effective drug treatment for patients.


PURPOSE: Determine the feasibility of an asthma point of care program at a chain pharmacy.

METHODS: Patients receiving an asthma medication during the study period were instructed to see the pharmacist. Pharmacists obtained informed consent and use a standardized questionnaire and documentation form to record patient information. Pharmacists evaluated asthma control, medication use, inhaler technique, ability to identify rescue and controller medications, and existence of an action plan. Physicians were contacted with suggested interventions.

RESULTS: Seventy-five patients were program candidates, 62 provided informed consent. Fifty-three percent of patients had asthma, 75% noted bothersome asthma symptoms, 31.6% used a “quick-relief” inhaler more than 2/week, 17.1% woke up at night more than 2/month and 40.8% refilled the quick relief inhaler more than 2/year. Eighteen percent identified controllers as their “quick-relief” inhaler, 36% used the inhaler incorrectly, and 64.5% had an action plan. Pharmacists intervened in 89% of cases needing intervention. An average of 5.1 minutes was required to collect data and make interventions. Lack of time and incentive were barriers to the program. Pharmacists and patients were satisfied with the service.

CONCLUSIONS: An asthma point of care program is feasible in a chain pharmacy with some modifications. We found that a large number of patients did not identify their medications correctly, had adequate asthma control, use inhalers correctly or have an action plan. Modification of the service is in process to allow expansion of the service.

Health care provider survey of clinical pharmacy services in a family medicine clinic. Sara B. Jutte, Pharm.D., Melissa M. Blair, Pharm.D., Kely R. Ragucci, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To survey health care providers concerning the utilization and helpfulness of current clinical pharmacy services and to assess interest in expansion of pharmacy services in a Family Medicine Clinic.

METHODS: A one-page survey was designed and distributed through an internal mail system to nineteen health care providers: 17 physicians, 1 nurse practitioner, and 1 physician’s assistant. Providers were instructed to anonymously return surveys to a clinical pharmacist’s mailbox. If surveys were not returned, the provider was sent the survey again to increase response rate.

RESULTS: Fourteen of the nineteen (74%) health care providers returned surveys. Currently, the most utilized services were: anticoagulation (93%), diabetes (79%), asthma (57%), financial assistance (57%), and medication education (57%). Ninety-one percent of the providers found pharmacy services to be either helpful or very helpful. In addition to the above services, providers were interested in expanding pharmacist involvement in: medication discontinuation (57%), medication management (57%), congestive heart failure (50%), nutrition (50%), and pain management (50%). Increased pharmacist participation was also desired in the areas of research and herbal remedies. The only area of concern regarding pharmacy services was related to duplication of patient education with the clinic’s diabetes counselor.

CONCLUSIONS: A variety of clinical pharmacy services are currently utilized by health care providers and are perceived to be beneficial. In addition, several areas for expansion of services were identified. This information will enable clinical pharmacists to prioritize involvement in the Family Medicine Clinic.

Use of personal digital assistant to document primary care clinical pharmacy services. Elizabeth A. Chester, Pharm.D., BCPS, Rachana J. Patel, Pharm.D., Timothy J. Hartman, Pharm.D., BCPS; Kaiser Permanente, Aurora, CO; Kaiser Permanente, Denver, CO; Pfizer Pharmaceuticals Group, Parker, CO.

PURPOSE: Design and pilot a handheld computerized system for Primary Care Clinical Pharmacy Services (PCCPS) to facilitate on-the-spot documentation of daily activities and describe their value to the organization.

METHODS: A clinical pharmacy documentation tool (PharmDoc) was developed for personal digital assistants (PDA, Handspring VisorPro) using ThinkDB Software. From January to March 2002, seven primary care clinical pharmacists and clinical pharmacy specialists documented all daily activities (encounters including patient care activities, consultations, administrative activities, and cost avoidance).

RESULTS: During the 3-month pilot, the pilot group documented 3250 encounters. Eighty-four percent of encounters (n=2799) fell into the following categories: administrative time, hypertension, lipids, diabetes, headache, women’s health, mental health, adverse drug reactions, gastrointestinal disorders, and pain management.

CONCLUSION: Use of PharmDoc allowed the pilot group to document a higher than expected number of encounters and highlighted the diverse practice of PCCPS. If we consider these seven clinical pharmacy staff members a representative sample and extrapolate this data to 25 staff members, our service could potentially document over 46,000 encounters and $3 million in cost avoidance annually.

Assessment of a patient management information system to track and monitor use of baseline laboratory guidelines. Peter Massad, Pharm.D., MPH, BCPP, Cape Cod and the Islands Community Mental Health Center, Pocasset, MA.

PURPOSE: This study documented use of a facility designed patient management information system to track the monitoring, and appropriateness of baseline laboratory and electrocardiogram test results for initiating designated psychiatric modalities. These guidelines, termed “Best Practices Recommendations” were developed by the Pharmacy and Therapeutics Committee, and they were periodically updated as new knowledge became available.

METHODS: Laboratory records of 49 patients admitted between November 1 and May 31, 2002 to the Inpatient Unit were reviewed. Patients’ current medication regimen, in-hospital course, and specific laboratory tests ordered were assessed for consistency with the recommendations. Feedback from
purposes was then evaluated.

RESULTS: Laboratory tests were tracked in 49 patients and included clozapine (31%), divalproate (15%), lithium (9%), ziprasidone (10%), and carbamazepine (1%). A greater proportion of patients achieved clozapine in accordance with the guidelines more often than prescribed agent on the list, divalproate. Use of the guidelines provided a tool for ongoing assessment of prescribing practices, and it generated ongoing feedback as to the positive influence it placed on prescribing behaviors.

CONCLUSION: Clozapine was the predominant medication prescribed and the most intensely monitored in accordance with the guidelines for the period studied. Use of the patient management information system assisted the ongoing feedback reporting, and permitted the clinical pharmacist to recommend improvements in medication distribution rates in coordination with the initiation system. An unexpected outcome was the concurrent feedback by the medical staff toward creating enhancements to the Best Practices Recommendations as prescribing experience and the knowledge of the latest literature became available.

382. Assessment and reduction of antipsychotic polypharmacy in a psychiatric treatment and rehabilitation facility, Stephen M. Dolley, B.S., BCPP; Kathleen P. Whitley, M.D., Christopher C. Kennedy, M.D.; Worcester State Hospital, Worcester, MA.

PURPOSE: Antipsychotic polypharmacy has become common practice in many psychiatric settings despite little in the literature to support this practice. JCAHO ORYX data for Worcester State Hospital, a psychiatric treatment and rehabilitation facility, have indicated a higher rate of antipsychotic polypharmacy when compared to both state of Massachusetts and national averages.

METHODS: Members of the hospital Psychiatric Performance Improvement Committee, composed of representatives from the Departments of Psychiatry and Pharmacy, sought to understand this phenomenon with the goal of substantiating use of these combinations if clinically indicated and reducing their use where appropriate. The committee developed a physician survey that for each specific case of antipsychotic polypharmacy asked the prescriber to answer questions regarding the rationale for the current antipsychotic polypharmacy regimen and knowledge of single agent trials prior to the initiation of antipsychotic polypharmacy.

RESULTS: Survey results were reported to and discussed with all members of the psychiatry and pharmacy to understand this phenomenon with the goal of substantiating use of these combinations if clinically indicated and reducing their use where appropriate. The committee developed a physician survey that for each specific case of antipsychotic polypharmacy asked the prescriber to answer questions regarding the rationale for the current antipsychotic polypharmacy regimen and knowledge of single agent trials prior to the initiation of antipsychotic polypharmacy.

CONCLUSION: A multidisciplinary assessment of antipsychotic polypharmacy at a psychiatric treatment and rehabilitation hospital increased awareness of the proper use of these combinations among prescribers and impacted both the prescribing patterns and financial burden associated with these regimens.

383. A statewide program to increase medication access for indigent solid-organ transplant patients, Marie A. Chisholm, Pharm.D., FCCP, Bridgett D. Kendrick, C.P.H.T., Charlene J. Garrett, Herbert E. McGinty, B.S., Jeanie C. Turner, B.S., Joseph T. DiPiro, Pharm.D., FCCP; University of Georgia; Medical College of Georgia, Augusta, GA.

PURPOSE: Many solid-organ transplant (SOT) patients have inadequate prescription insurance and do not have the financial resources to pay for all of their medication needs. In recognition of this, many pharmaceutical manufacturers make their medications available for free, or at a reduced cost, through medication assistance programs. These programs are available to eligible patients who do not have access to essential medications by any other means. The Medication Access Program (MAP) assists patients in the enrollment process of these medication assistance programs and educates healthcare professionals about them.

METHODS: The MAP office has five employees, including two pharmacists. Georgia's SOT patients that are in need of medication assistance, or their physician, can contact the MAP office concerning the availability of medication assistance programs. MAP personnel instructs patients and healthcare personnel on the application process that is required by the pharmaceutical companies. MAP also serves as a liaison between the patient, physician, and the pharmaceutical companies. In a database, MAP personnel documents the number of patients served and the average wholesale price (AWP) of medications supplied through the program. Patients who used MAP's services, as of January 1999, were asked to complete a patient satisfaction survey.

RESULTS: From October 1999 to June 2002, MAP has assisted over 266 SOT patients in the enrollment into medication assistance programs, accounting for approximately $2.4 million (AWP cost) of medications. Approximately 51% of the $2.4 million represents immunsuppressive medications, the other 49% mostly represents that of cardiovascular, antimicrobial, and gastrointestinal medications. On the patient satisfaction survey, patients (n = 175) had a mean score of 95.2 ± 10.7 (highest achievable survey score was 100), indicating that MAP provided a valuable service to them.

CONCLUSION: The MAP program is successful in helping needy solid-organ transplant patients obtain medications, and patients are pleased with the services that the MAP program provides.

Student, Resident, Fellow Research in Progress

These papers describe original research by students, residents, and fellows in therapeutics, pharmacokinetics, pharmacodynamics, pharmacoeconomics, and pharmacoepidemiology in which the research effort is still on-going. The abstract title and authors are published in Pharmacotherapy; the full abstract will be published in the meeting program book.


385. Use of bivalirudin in patients undergoing percutaneous coronary interventions, Estela M. Trinino, Pharm.D., Peter G. Koval, Pharm.D., BCPP; Moses Cone Family Practice, Greensboro, NC.

386. Influence of polymorphism on the β1 and β2 adrenergic receptor genes in obesity, Cathy D. Cruwel, Pharm.D., Jianwei Wang, M.D., Hardge Garg, M.D., James Sylvester, Ph.D., John J. Lima, Pharm.D.; Nemours Children's Clinic, University of Florida, Jacksonville, FL.

387. Cytotoxicity of cisplatin bound to human serum albumin compared to free cisplatin, Susanne E. Liewer, Pharm.D., Robert J. Fountaine, Pharm.D., Jennie M. Berg, Pharm.D., BCPS; University of Kentucky, Lexington, KY.

388. A quality assessment study of adherence with health plan employer data information set criteria for blood pressure control in a managed care population, Tanya M. Moinian, Pharm.D., Andrea M. Haeflerin, Pharm.D., Rosalie P. Patel, Pharm.D., Barbara J. Zarowitz, Pharm.D., BCPS, FCCP, Henry Ford Health System, Detroit MI.

389. Inappropriate metformin use among hospitalized patients in an urban, tertiary care institution, Elizabeth Knapp, B.Sc., Peter Dumo, Pharm.D.; Wayne State University; Harper University Hospital, Detroit, MI.

390. Inhaled glucocorticoid effects on stiffness index and t-scores in female patients, Alicia B. Forinash, Pharm.D., Stephanie L. Evans, Pharm.D., Robert C. Baker, Pharm.D., John M. Burke, Pharm.D., FCCP; St. Louis College of Pharmacy; Family Medicine of St. Louis, St. Louis, MO.

391. Pharmacist intervention in prevention and treatment of glucocorticoid-induced osteoporosis at a family practice residency program, Sarah F. Hutton, Pharm.D., Peter G. Koval, Pharm.D., BCPP; Moses Cone Family Practice, Greensboro, NC.

392. Pharmacist intervention in lipid management at a family practice residency program, Sarah F. Hutton, Pharm.D., Peter G. Koval, Pharm.D., BCPP; Moses Cone Family Practice, Greensboro, NC.

393. Retrospective analysis of adverse events associated with long-term antibiotic therapy for serious Gram-positive infections, Bijal M. Shah, B.S., Steven J. Martin, M.D., Eric G. Sahloff, M.D.; St. Joseph Mercy Hospital, Toledo, OH.

394. Assessment of leukocyte function utilizing 18F-fluorodeoxyglucose, Kathleen M. Tornatore, Pharm.D., Robert J. Fountaine, Pharm.D., Jennie M. Berg, Pharm.D., BCPS; University of Kentucky, Lexington, KY.

395. Assessment of post-transplant osteoporosis in pre-menopausal and post-menopausal renal transplant recipients, Bharti Bhawardja, Pharm.D., Kathleen M. Tornatore, Pharm.D., Robert J. Fountaine, Pharm.D., Jennie Hom, M.D., Rocco Venuto, M.D.; State University of New York; University at Buffalo; Erie County Medical Center, Buffalo, NY.

396. Influence of polymorphism on the 5HT1A receptor gene in depression, Estela M. Trinino, Pharm.D., Peter G. Koval, Pharm.D., BCPP; Moses Cone Family Practice, Greensboro, NC.

397. Clinical pharmacokinetics of fentanyl citrate in the intensive care unit, Alvin R. Edmonston, Pharm.D., BCPS; University of Kentucky, Lexington, KY.

398. Amiodarone compliance with the 2000 advanced cardiac life support guidelines, Eric G. Sahloff, Steven J. Martin, Martin Ollinger, David Richards; University of Toledo; St. Vincent Mercy Medical Center, Toledo, OH.

399. Amiodarone compliance with the 2000 advanced cardiac life support guidelines, Jamie P. Reuter, Pharm.D., James Kirby, R.Ph., Steven E. Pass, Pharm.D., BCPP; Michelle L. Duising, Pharm.D., BCPP; University of Cincinnati, Cincinnati, OH.
RESULTS: Area under the curve (AUC) for percent decrease in forearm vascular resistance (FVR) from baseline was 727 ± 101 and 712 ± 133 during ACh (3,10,30 µg/min) following sildenafil and placebo, respectively. AUC for percent decrease in FVR from baseline was 888 ± 68 and 881 ± 72 during SNP (1.3, 10 µg/min) following sildenafil and placebo, respectively. Mean arterial pressure was unchanged following sildenafil administration. Heart rate increased slightly following sildenafil and was unchanged after placebo (p=0.02). Cardiac output and stroke volume were unchanged following sildenafil and placebo. Plasma catecholamines increased 58 ± 19% following sildenafil and 20 ± 19% following placebo (p=0.003).

CONCLUSIONS: Sildenafil did not improve forearm resistance vessel endothelium-dependent or -independent vasodilatation, nor did it significantly impact hemodynamics in healthy middle-aged men. Increases in sympathetic drive may result in changes in hemodynamics and forearm resistance vessel NO-mediated vasodilatation.


PURPOSE: The present study was designed to discern: (1) the relationship between exposure to an NSAID and first (incident) admission to hospital for congestive heart failure (CHF); (2) exposure to an NSAID among incident and prevalence cases of CHF; and (3) the relationship between NSAID half-life and admission for CHF.

METHODS: Prospective case-control study (n=343; ≥ 50 years). Cases (n=57; incident=100; prevalence=47) were patients admitted to hospital with a primary diagnosis of CHF. Controls (n=186) were patients admitted to hospital without CHF (or history of CHF). Exposure was defined as use of an NSAID for ≥ 1 week in the month prior to hospital admission. Data were collected via a structured interview. Multiple conditional logistic regression was used to generate odds-ratios and 95% confidence intervals (CIs), and to adjust for selected demographic and clinical factors. The a priori level of significance was set at p≤0.05.

RESULTS: Use of an NSAID for ≥ 1 week in the month prior to hospital admission was associated with a 21% increase (OR=1.21, CI=0.81-1.64; p=0.05) in the odds of admission for CHF (incident case). Prevalence CHF cases were 2.74 times less likely (OR=0.365, CI=0.149-0.895; p=0.05) to have used an NSAID for ≥ 1 week prior to hospital admission compared to incident cases. NSAID half-life was not found to influence hospital admission for CHF.

CONCLUSION: Use of an NSAID is associated with increased probability of first (incident) admission for CHF. Use of NSAIDs in persons ≥ 50 years warrants caution, and assessment of concomitant risk-factors for CHF.


PURPOSE: HIV infected persons who are highly experienced with combination antiretroviral therapies are common in the clinical setting. Suppression of viremia is often difficult to achieve and maintain. Failure to suppress viral replication may in part be due to suboptimal antiretroviral drug exposure in heavily pre-treated patients. To address this hypothesis, our primary objective is to determine the steady state pharmacokinetic parameters of amprenavir (APV) 600 mg PO q12h and lopinavir/ritonavir (LPV/RTV) 400/100 mg PO q12h when used in combination as part of a salvage antiretroviral treatment regimen.

METHODS: Subjects with 2 or more treatment regimen failures starting APV and LPV/RTV based salvage therapy will be recruited. Subjects will have no active opportunistic infections and plasma HIV-1 RNA ≥ 10,000 copies/mL on the two consecutive occasions. At week 0, blood will be drawn for viral genotype, viral phenotype, viral fitness test, and human DNA. At week 2, plasma will be collected over 12 hours for APV, LPV and RTV. Noncompartmental methods will be used to characterize APV, LPV and RTV plasma pharmacokinetics. Follow-up study visits for routine laboratory blood work, CD4 counts, HIV-1 RNA, and random APV, LPV, and RTV plasma samples will occur at weeks 4, 8, 12, 16, 20, and 24. Medication adherence will be monitored at each visit through subject interview and a self-administered questionnaire.

RESULTS: A total of 14 subjects will be recruited. The following plasma pharmacokinetic parameters will be determined for APV, LPV and RTV: Cmax, t1/2, Vp, CL/F, and AUC0-12. Descriptive statistics will be reported for all pharmacokinetic data. Exploratory analyses to look for relationships between metrics of drug exposure and changes in HIV-1 RNA and CD4 count are planned using linear regression.

CONCLUSIONS: By characterizing the steady state pharmacokinetic parameters of APV, LPV, and RTV as part of salvage therapy and exploring protease inhibitor exposure-response relationships in treatment experienced HIV-infected persons, we may begin to identify ways to optimize dosing and...
improve response and durability of future salvage antiretroviral treatment regimens.

407. Roche Transplantation Fellowship: CYP3A4*1B as a predictor for tacrolimus dosing in liver transplant patients. Kareem Albakarya, Christine Formea, Tuan LuuI, Heather Myers, Son Nguyen, Valerie Green, Shiro Fujita, Alan Hemmings, Willem Van der Werf, Alan Reed, Richard Howard, Janet L. Karlix; University of Florida, Gainesville, FL.

BACKGROUND: CYP3A4 is an important drug metabolism enzyme in the transplant population because it facilitates the metabolism of cyclosporine, tacrolimus, and sirolimus. Up to 40-fold inter-individual differences have been reported in the activity of CYP3A4. Recently, a transition mutation [A>G] in the 5'-promotor region in the CYP3A4 gene has been described. There are conflicting reports on the clinical relevance of this variant form of CYP3A4 [CYP3A4*1B]; however, it has been described as being associated with lower metabolism requirements. We hypothesized that the presence or absence of CYP3A4*1B would explain the large variability in CYP3A4 activity and thus impact tacrolimus dosing requirement in transplant patients.

PURPOSE: To determine the role of CYP3A4*1B on tacrolimus dosing in stable liver transplant recipients.

METHODS: Liver transplant recipients followed as outpatients at our center were stratified according to tacrolimus dose required to maintain target concentrations [5-15 ng/ml]. Genomic DNA was isolated from whole blood via Puregene DNA isolation kit [Gentra systems, Minneapolis, MN]. Genotype was determined via restriction fragment length polymorphism (RF) analysis.

RESULTS: This study included 45 liver transplant recipients whose tacrolimus dose was stable for at least 4 weeks, with a stable FK level [5-15 ng/ml] and who were on no drugs known to interact with tacrolimus. There were 31 wild type (A/A) patients and 14 variant (A/G and A/G homozygous and 11 heterozygous). The median tacrolimus dose was 0.94 mg/kg/dy in the variant group vs. 0.52 mg/kg/dy in the wild type group. In low FK dose grouping, [0.03 mg/kg/dy], 43% [43%] wild type were type vs. 614 [43%] variant. In high dose strata, [>0.1 mg/kg/dy] there were 0 variants. These data suggest that this SNP may be a predictor for low metabolizers.

CONCLUSION: The recently identified polymorphism [CYP3A4*1B] may be a predictor for low CYP3A4 activity and tacrolimus requirements in liver transplant recipients.


PURPOSE: Patients with end-stage lung disease awaiting lung transplantation are candidates for hepatitis B vaccination, but they have low rates of antibody response to the vaccine series. The objective of this study was to compare the hepatitis B vaccine-induced cell mediated immune response to hepatitis B surface antigen (HBsAg) in patients awaiting lung transplantation to healthy controls. We hypothesized that cell mediated immunity would be similar between the two groups.

METHODS: Four consecutively healthy controls and five patients awaiting lung transplantation were enrolled. Human peripheral blood mononuclear cells (PBMC) were isolated for use in the trans vivo delayed type hypersensitivity (DTH) assay. PBMC alone and with antigen are injected into the paw of an immunodeficient mouse causing a swelling that is a measure of T cell sensitization. We estimated that a difference of 15x10^6 inches would be a clinically significant difference and the power to detect this difference is greater than 90%.

RESULTS: The healthy control group is younger than the patients awaiting lung transplantation. However, we found no difference in DTH swelling elicited by HBsAg or with tetanus toxoid (TT) used as a positive control.

CONCLUSION: Patients awaiting lung transplantation do not have a DTH response to HBsAg that is similar to healthy controls in contrast to their markedly lower rate of antibody response. The role of cell mediated immunity in protection from infection requires further study.

409. Amgen Oncology Research Award: A novel antineoplastic agent with a unique mechanism of action. Shawan M. Aziz, R.Ph., Ph.D., BCOP; Vincent La Ross, M.D., Ph.D., BCOP; Francois Bertrand, M.D., Ph.D.; Eastern Cooperative Oncology Group, Washington University, Washington D.C.; University of Wisconsin, Madison, WI; Vanderbilt University, Nashville, TN.

Introduction: E3590 was a randomized, prospective trial of adjuvant radiation alone (Arm A) or radiation plus chemotherapy (Arm B) with etoposide and cisplatin in patients with resected II or IIIA NSCLC. NQO1 is a two-electron reductase, with a characteristic polymorphism (NQO1*2) that results in an inactive enzyme. Since NQO1 may be important in predicting chemosensitivity and toxicity, the influence of the NQO1*2 polymorphism on toxicity and overall survival in patients in E3590 was evaluated.

Methods: Genomic DNA isolated from primary lung tumors was evaluated for the NQO1*2 polymorphism by pyrosequencing, an automated sequencing method based on primer extension chemistry. Patients were designated as *1/*1, *1/*2, or *2/*2. Overall survival for these three groups was compared using Kaplan-Meier survival analysis with two-sided log rank tests. Results: There were 78 tumor samples available for analysis in Arm A, 54% of samples were *1/*1, 29% of samples were *1/*2, 16% of samples were *2/*2. There were 74 tumor samples available for analysis in Arm B, 55% of samples were *1/*1, 30% of samples were *1/*2, 15% of samples were *2/*2. In patients receiving radiation + chemotherapy (Arm B), NQO1 *2/*2 was a strong independent predictor of poor survival, with a median survival of 41.8 months for the *1/*1, 39.8 months for the *1/*2, and 16.2 months of the *2/*2. The median survival in patients receiving just radiation (Arm A) was 40.2 months for the *1/*1, 40.7 months for the *1/*2, and 34.0 of the *2/*2. The estimated hazard ratio comparing NQO1*2 in Arm B with NQO1*2 in Arm A was 3.6, with 95% confidence interval (1.4,9.2) p=0.028.

Conclusion: NQO1*2 predicts poor survival in NSCLC patients receiving radiation and chemotherapy. This genotype may help individualize cancer therapy, by predicting poor responders who may benefit from alternative therapies.

411. AstraZeneca Cardiovascular Research Award: Suppression of monocytie TNF-α/IL-10 balance in impaired in severe heart failure. Tien M. H. Ng, Pharm.D., Amy M. Vrana, B.S., Tom D. Sears, M.D.; University of Nebraska Medical Center, Omaha, NE.

BACKGROUND: The importance of the pro-inflammatory cytokine tumor necrosis factor (TNF-α) to the pathophysiology and progression of heart failure (CHF) has been recognized. Under normal physiologic conditions, TNF-α
production is counter-regulated by both interleukin-10 (IL-10) and sympathetic activation. A paradox exists in CHF as both norepinephrine (NE) and TNF-α are elevated, suggesting this negative feedback mechanism may be impaired, thus contributing to the pro-inflammatory state in CHF. The relationship between sympathetic activation and inflammatory cytokine balance in CHF has not been characterized. We hypothesized that attenuation of TNF-α production by NE in LPS-stimulated monocytes is diminished in CHF compared to healthy, age-matched volunteers.

METHODS: Monocytes were isolated via standard Nycoprep method, from 12 CHF patients (68 ± 12 y, NYHA FC III or IV, LV EF 20 ± 10%) and 14 healthy volunteers (66 ± 12 y). Isolated monocytes (1 x 10⁶/mL) were incubated with LPS 100 ng/mL, LPS+N = 10⁻⁶ M or neither (control) for 4 hours. TNF-α levels were determined by ELISA.

RESULTS: Basal TNF-α concentrations were higher in CHF patients than healthy subjects (6.3 ± 3.3 vs. 2.5 ± 2.6 pg/mL, p=0.004). Attenuation of TNF-α production by NE was diminished in CHF (-41 ± 17 CHF vs. -57 ± 9% healthy, p=0.01). Augmentation of IL-10 production by NE was also reduced in CHF (18 ± 18 CHF vs. 38 ± 23% healthy, p=0.01). Response of monocytes to NE was diminished to the greatest degree in NYHA FC IV patients compared to FC III and healthy controls for both TNF-α and IL-10 production (figure). There was a trend towards reduced IL-10 response in patients with LV EF < 20% when compared to those with LV EF > 20% (7 ± 12 vs. 25 ± 20%, p=0.07).

CONCLUSIONS: Sympathetic counter-regulation of inflammatory cytokine response in monocytes appears to be reduced in moderate to severe CHF. Impairment is greatest in NYHA FC IV This may be novel mechanism to explain increased expression of TNF-α in CHF. Future experiments to characterize the underlying mechanism are required.

412. Aventis Cardiovascular Research Award: Effect of grapefruit juice on digoxin pharmacokinetics in humans, Robert B. Parker, Pharm.D., C. Ryan Yates, Pharm.D., Ph.D., Judith E. Soberman, M.D., S. Casey Laizure, Pharm.D., University of Tennessee, Memphis, TN.

PURPOSE: Numerous studies demonstrate an interaction between grapefruit juice (GFJ) and drugs that are substrates for cytochrome P450 3A4 (CYP3A4). These investigations indicate that GFJ increases oral digoxin bioavailability via mechanism-based inhibition of intestinal CYP3A4. In addition, recent evidence suggests GFJ may also affect drug absorption via inhibition of the intestinal drug efflux transporter, P-glycoprotein (P-gp). To accurately characterize the interaction between GFJ and P-gp, it is necessary to use in vivo probes that interact with P-gp and not CYP3A4. Therefore, the purpose of this study is to determine the effects of GFJ on oral digoxin (a P-gp substrate that is not metabolized by CYP3A4) pharmacokinetics in normal healthy volunteers.

METHODS: Seven healthy non-smoking adult volunteers (4 male, 3 female) received 1.6 mg oral digoxin with or without GFJ in an unblinded, crossover design with at least a 2 week washout between treatments. Before digoxin treatment, GFJ was administered 3 times daily for 5 days to maximize any effect on P-gp. Blood and urine were collected at various times for 144 hours after digoxin administration. Digoxin plasma and urine concentrations were determined by RIA and pharmacokinetic parameters determined by WinNonlin®.

RESULTS: Pharmacokinetic parameters are summarized below:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Digoxin + Water (range)</th>
<th>Digoxin + GFJ (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC (0→∞) (µg.hour/mL)</td>
<td>8.4 ± 2.6 (5.3-11.9)</td>
<td>8.0 ± 5.9 (5.9-11.2)</td>
</tr>
<tr>
<td>AUC (0→48) (µg.hour/mL)</td>
<td>61.0 ± 33.4 (39.7-83.8)</td>
<td>8.4 ± 14.9 (40.2-87.2)</td>
</tr>
<tr>
<td>Cmax (ng/mL)</td>
<td>3.7 ± 1.9 (2.0-6.2)</td>
<td>3.1 ± 0.5 (2.0-3.8)</td>
</tr>
<tr>
<td>T1/2 (hour)</td>
<td>16.4 ± 7.2 (7.0-23.0)</td>
<td>20 ± 6.0 (12.0-40.4)</td>
</tr>
<tr>
<td>F (fraction)</td>
<td>3.0 ± 2.4 (0.5-6.6)</td>
<td>1.2 ± 0.5 (0.3-3.0)</td>
</tr>
<tr>
<td>Fcp (fraction)</td>
<td>0.32 ± 0.2 (0.16-0.47)</td>
<td>0.53 ± 0.34* (0.09-0.94)</td>
</tr>
<tr>
<td>Half-life (hour)</td>
<td>38.0 ± 6.1 (31.5-61.1)</td>
<td>36.9 ± 4.0 (32.0-48.0)</td>
</tr>
<tr>
<td>CL (0-144 hour) (l/hour)</td>
<td>4.9 ± 1.7 (3.2-7.5)</td>
<td>5.5 ± 1.3 (3.8-7.0)</td>
</tr>
</tbody>
</table>

*p<0.05 compared to water phase by paired t-test, data are mean ± SD.

CONCLUSIONS: 1) GFJ significantly reduced the rate of digoxin absorption which is consistent with the possibility of interaction with intestinal P-gp transport. 2) On average, GFJ did not affect the extent of digoxin absorption although there was large interindividual variability in the response to GFJ (e.g., the effect of GFJ on Cmax ranged from -45 to +41%); 3) GFJ did not affect systemic digoxin elimination; 4) Using digoxin as an in vivo probe, inhibition of intestinal P-gp does not appear to play an important role in drug interactions involving GFJ.

413. Aventis Cardiovascular Research Award: Effect of heart failure on myocardial P-glycoprotein expression, J. Jason Sims, Pharm.D., Brien L. Neudeck, Pharm.D., Jennifer M. Loeb, B.S., Nicholas A. Wiegert, B.S., University of Wisconsin, Madison, WI.

BACKGROUND: Heart failure is a complex of symptoms related to inadequate tissue perfusion that results in impaired quality of life, significant morbidity, and a shortened life expectancy. There are multiple "protective" proteins that are synthesized in response to the stressful physiologic stimuli produced by heart failure. These often include proteins that are thought to help stabilize and repair cell damage, P-glycoprotein (PgP), encoded by the MDR1 gene and most commonly linked to drug transport, contributes to cellular protection against potentially toxic substances by extrusion of these substances out of cells. Interestingly, PgP has been found to be present and functional in myocardium. Thus, we hypothesize that PgP expression is increased in heart failure.

METHODS: Twenty-nine dogs were randomized to rapid-pacing induced heart failure (n=13) or unpaced sham operated control (n=16). Dogs were euthanized after 4 weeks of pacing at 250 beats per minute or 4 weeks of un paced control. Left ventricular lateral wall myocardial samples were homogenized and prepared for protein analysis and RNA extraction. Total PgP protein was quantified using laser-induced fluorescence (Agilent 2100 Bioanalyzer). PgP and GAPDH mRNA expression was determined using semi-quantitative RT-PCR. RT-PCR data are presented as the normalized ratio of PgP/GAPDH.

RESULTS: RT-PCR revealed that heart failure increased mRNA expression of PgP (0.15 ± 0.02 control versus 0.34 ± 0.24 heart failure). However, heart failure did not alter the amount of PgP protein (0.14 ± 0.07 µg/ml control versus 0.12 ± 0.04 µg/ml heart failure).

CONCLUSIONS: Pacin induced heart failure increases p-glycoprotein mRNA expression. However, this increase did not alter the amount of total protein between control and heart failure. Thus, there appears to be a defect in the translation of p-glycoprotein during pacing induced heart failure. Therefore, an important cellular protection mechanism may be impaired during pacing induced heart failure.


The study purpose was to develop and validate an instrument to assess nausea intensity in children 4 to 18 years receiving chemotherapy.

A four-faced scale with a standard script for administration (pediatric nausea assessment tool [PeNAT]) was developed. Revisions were made following face validity testing with four pediatric oncology clinicians and four parents and pilot testing with 15 chemotherapy inpatients. Construct validity was evaluated by comparing PeNAT scores in 17 patients in each of 3 extreme groups: cancer chemotherapy recipients, cancer without chemotherapy, and no cancer. PeNAT scores were obtained 4 to 24 hours after chemotherapy; dietary intake (4-point scale) and emetic episodes were recorded for 4 hours prior. Criterion-related validity was evaluated by correlating PeNAT scores with emetic episodes and dietary intake in 36 chemotherapy recipients. Mean PeNAT scores were low in all groups: 1.24, 1.18, and 1.24, respectively (p<0.05). PeNAT scores correlated significantly with emetic episodes (Spearman's rho = 0.52, p<0.001) but not with dietary intake. Only 1 of 14 children ≤ 8 years reported any nausea compared to 9 of 22 children > 8 years. No, emetic episodes were reported in children ≤ 8 years. Dietary intake correlated positively with nausea in children > 8 years (rho = 0.32) but negatively in children ≤ 8 years (rho = 0.31).

In scores in PeNAT were observed among children who were expected to have variable nausea intensity. A more extreme group, children undergoing bone marrow transplant conditioning, will be tested. Criterion-related validity was supported for emesis only. Children ≤ 8 years may experience less chemotherapy-induced nausea and emesis than older children and they have a different dietary response. Further investigation of these potential effects of age is required.

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