Late Breakers in Pharmacotherapy, II

Activity Number: 0217-0000-15-148-L01-P, 1.50 hours of CPE credit; Activity Type: A Knowledge-Based Activity

Wednesday, October 21, 2015
8:00 a.m. to 9:30 a.m.
Continental Ballroom 5

Moderator: Robert B. Parker, II, Pharm.D., FCCP
Professor, University of Tennessee College of Pharmacy, Memphis, Tennessee

Agenda

8:00 a.m.	Women's Health *Nicole E. Cieri, Pharm.D.* Clinical Assistant Professor, Department of Pharmacy Practice, D'Youville College School of Pharmacy, Buffalo, New York
8:15 a.m.	Psychiatry *Stephanie Phan, Pharm.D., BCPP* Clinical Assistant Professor, Associate Department Head, Southwest Georgia Clinical Campus, University of Georgia College of Pharmacy, Albany, Georgia
8:30 a.m.	Vaccines/Immunizations *Scott J. Bergman, Pharm.D., BCPS* Southern Illinois University Edwardsville School of Pharmacy, Edwardsville, Illinois
8:45 a.m.	Geriatrics *Stephanie M. Crist, Pharm.D.* Assistant Professor of Pharmacy Practice, Division of Ambulatory Care, St. Louis College of Pharmacy, St. Louis, Missouri
9:00 a.m.	Nephrology *Mary Vilay, Pharm.D.* Associate Professor, University of New Mexico College of Pharmacy, Albuquerque, New Mexico
9:15 a.m.	Neurology *Melody Ryan, Pharm.D., MPH, FCCP, BCPS, CGP* Professor, University of Kentucky College of Pharmacy, Lexington, Kentucky

Conflict of Interest Disclosures
Scott J. Bergman: Speaker's bureau for Sanofi-Pasteur.

Stephanie M. Crist: no conflicts to disclose.
Nicole E. Cieri: no conflicts to disclose.
Robert B. Parker: no conflicts to disclose.
Stephanie Phan: no conflicts to disclose.
Melody Ryan: no conflicts to disclose.
Mary Vilay: no conflicts to disclose.

Learning Objectives

1. Identify/discuss new and emerging clinical data or patient care trends affecting pharmacotherapy and/or health outcomes in pharmacogenomics.
2. Identify the limitations/controversies associated with these late-breaking trials.
3. Discuss approaches to apply and implement the new findings into practice.

Self-Assessment Questions

Self-assessment questions are available online at www.accp.com/gc15.

2015 ACCP Global Conference on Clinical Pharmacy

Flibanserin: The 'Female Viagra'
Nicole Cieri, Pharm.D., BCPS
October 21st, 2015

Conflict of Interests

- None

Learning Objectives

- Analyze and interpret the results of the most recent trials of flibanserin, the first drug approved for hypoactive sexual desire disorder (HSDD) in women this past June.
- Identify the limitations/controversies associated with these trials
- Choose an appropriate patient for use of flibanserin in practice

Background

- Hypoactive sexual desire disorder (HSDD):
  - American Psychiatric Association Definition (DSM-IV-TR):
    - Persistent or recurrent deficiency in, or absence of, sexual fantasies and desire for sexual activity that causes marked distress or interpersonal difficulty
  - Multifactorial Disorder
    - Dysregulation of excitatory/inhibitory signals in the CNS that regulate sexual response
    - Dopamine, Norepinephrine, Testosterone: stimulation of sexual desire
    - Serotonin: inhibition of sexual desire

Simon JA, Kingsberg SA, Shumel B, et al. Efficacy and safety of flibanserin in postmenopausal women with hypoactive sexual desire disorder: results of the SNOWDROP trial. Menopause. 2014;21(6)633-640.

Background

- DSM-IV-TR: HSDD and female Sexual Arousal Disorder (FSAD) were diagnosed separately
  - DSM-5 diagnostic criteria combine HSDD and FSAD into female sexual interest/arousal disorder
- Consideration for future studies and selecting patients as candidates
  - Approval of flibanserin to treat these disorders has been studied based on now obsolete criteria

Nappi RE. Why are there no FDA-approved treatments for female sexual dysfunction? *Exper Opin Pharmacother.* 2015;16(12):1735-38
American Psychiatric Association. Highlights of changes from DSM-IV-TR to DSM-5. *American Psychiatric Press.* Washington D; 2013

Background

- Prior to flibanserin, no approved pharmacologic treatment for HSDD.
- 2004: Testosterone patch (Intrinsa) was reviewed by the FDA for HSDD but was not approved
  - Patch was available in Europe but was recently withdrawn due to low usage

Simon JA, Kingsberg SA, Shumel B, et al. Efficacy and safety of flibanserin in postmenopausal women with hypoactive sexual desire disorder: results of the SNOWDROP trial. Menopause. 2014;21(6)633-640.

Background

- Flibanserin
  - Post synaptic agonist of the serotonin (5-HT) receptor-1A and antagonist of 5HT-2A
    - Induction of transient decreases in serotonin and increases in dopamine and norepinephrine
  - Approved on June 4, 2015 as the first drug for boosting female sexual desire
    - 3rd time before the FDA

Simon JA, Kingsberg SA, Shumel B, et al. Efficacy and safety of flibanserin in postmenopausal women with hypoactive sexual desire disorder: results of the SNOWDROP trial. Menopause. 2014;21(6)633-640.

Trial Timeline

- 2014 SNOWDROP
- 2013 BEGONIA
- 2012 SUNFLOWER
- 2012 VIOLET
- 2012 DAISY
- 2011 ROSE

Review

- SNOWDROP
  - Flibanserin 100mg PO qHS vs placebo x24 weeks for naturally postmenopausal women of any age diagnosed with HSDD according to the DSM IV criteria lasting ≥6 months
  - Co-primary endpoints
    - Satisfying Sexual Events (SSE) in 28 days
    - Female Sexual Functional Index (FSFI) score
  - Secondary endpoint
    - Female Sexual Distress Scale-Revised (FSDS-R)

Simon JA, Kingsberg SA, Shumel B, et al. Efficacy and safety of flibanserin in postmenopausal women with hypoactive sexual desire disorder: results of the SNOWDROP trial. Menopause. 2014;21(6)633-640.

SNOWDROP

- Results
  - Significant improvement in SSE compared to placebo
    - 1.0 vs. 0.6 (p=0.004)
  - Significant improvement in FSFI
    - 0.7 vs 0.4 (p<0.001)
  - Significant decrease in FSDS-R
    - -8.3 vs -6.3 (p=0.006)
  - Most frequent adverse events:
    - Dizziness, somnolence, nausea, headache
    - 12 serious AE but none deemed related to treatment
    - No evidence of suicidal ideation

Simon JA, Kingsberg SA, Shumel B, et al. Efficacy and safety of flibanserin in postmenopausal women with hypoactive sexual desire disorder: results of the SNOWDROP trial. Menopause. 2014;21(6)633-640.

Interpretation/Analysis

- SNOWDROP had slightly smaller increase in SSEs compared to previous trials of flibanserin in premenopausal women
  - 1.0 vs 1.6-2.5
- Potentially high placebo effect
- List of prohibited medication greatly reduced compared to previous trials
- Limited to patient in heterosexual relationship and naturally induced menopause

Simon JA, Kingsberg SA, Shumel B, et al. Efficacy and safety of flibanserin in postmenopausal women with hypoactive sexual desire disorder: results of the SNOWDROP trial. Menopause. 2014;21(6)633-640.

Review

- BEGONIA
  - Flibanserin 100mg PO qHS vs placebo x24 weeks for naturally postmenopausal women of any age diagnosed with HSDD Primary endpoints
  - Co-primary endpoints
    - Satisfying Sexual Events (SSE) in 28 days
    - Female Sexual Functional Index (FSFI) score
  - Secondary endpoint
    - Female Sexual Distress Scale-Revised (FSDS-R)

Katz M, DeRogatis LR, Ackerman R, et al. Efficacy of flibanserin in women with hypoactive sexual desire disorder: results from the BEGONIA trial. *J Sex Med.* 2013;10:1807-1815.

BEGONIA

- Results
  - Significant improvement in SSE compared to placebo
    - 2.5 vs. 1.5 (p<0.001)
  - Significant improvement in FSFI
    - 1.0 vs. 0.7 (p<0.001)
  - Significant decrease in FSDS-R
    - -9.4 vs -6.1 (p<0.001)
  - Most frequent adverse events:
    - Dizziness, somnolence, nausea
    - 6 serious AE but none deemed related to treatment
    - No evidence of suicidal ideation

Katz M, DeRogatis LR, Ackerman R, et al. Efficacy of flibanserin in women with hypoactive sexual desire disorder: results from the BEGONIA trial. *J Sex Med.* 2013;10:1807-1815.

Choosing a Patient

- Postmenopausal
  - Women with naturally induced menopause, at least one ovary and diagnosed with HSDD of ≥ 6 months' duration
    - Excluded women with other sexual dysfunction, certain psychiatric d/o's, several gynecologic and pelvic pathology d/o's and concomitantly taking certain medications that may affect sexual function
    - Relationship criteria

Choosing a Patient

- Premenopausal (Approved Indication)
  - Women ≥18yo diagnosed with HSDD of ≥ 6 months' duration
    - Excluded women with other sexual dysfunction, certain psychiatric d/o's, several gynecologic and pelvic pathology d/o's and concomitantly taking a more extensive list of medications that may affect sexual function (compared to postmenopausal)
    - Relationship criteria
    - eDiary criteria
  - Previous extension trial: safety up to 52 weeks
  - Previous withdrawal trial: safety demonstrated

Jayne C, Simon JA, Taylor LV, et al (SUNFLOWER study investigators). Open-label extension study of flibanserin in women with hypoactive sexual desire disorder. *J Sex Med.* 2012;9:3180-3188.
Goldfisher E, Breaux J, Katz M, et al. Continued efficacy and safety of flibanserin in premenopausal women with hypoactive sexual desire disorder (HSDD): results from a randomized withdrawal trial. J Sex Med. 2011;8:3160–72.

Summary and Further Considerations

- Flibanserin is the first pharmacotherapy option approved for the treatment of HSDD (in premenopausal women)
- Balance the safety of a chronic treatment for a non life threatening condition
- Obsolete diagnostic criteria
- Root cause
- Therapeutic lifestyle changes

Additional References

- DeRogatis LR, Komer L, Katz M, et al. Treatment of hypoactive sexual desire disorder in postmenopausal women: efficacy of flibanserin in the VIOLET study. *J Sex Med.* 2012;9:1074-1085.
- Thorp J, Simon J, Dattani D, et al. Treatment of hypoactive sexual desire disorder in postmenopausal women: efficacy of flibanserin in the DAISY study. *J Sex Med.* 2012;9:793-804.
- Troconiz IF, Boland K, Staab A. Population pharmacokinetic/pharmacodynamic model for the sedative effects of flibanserin in healthy volunteers. *Pharm Res.* 2012;29:1518-1529

Additional References

- Kennedy S. Filbanserin: initial evidence of efficacy on sexual dysfunction on patients with major depressive disorder. *J Sex Med.* 2010;7:3449–3459.
- Thorp J, Palacios S, Symons J, Simon J, Barbour K. Improving prospects for treating hyperactive sexual desire disorder (HSDD): development status of flibanserin. *BJOG*. 2014;121:1328-32.
- Meixel A, Yanchar E, Fugh-Berman A. Hypoactive sexual desire disorder: inventing a disease to sell low libido. *J Med Ethics.* 2015;0:1-4.
- Lodise NM. Hypoactive sexual desire disorder in women: treatment options beyond testosterone and approaches to communicating with patients on sexual health. *Pharmacotherapy.* 2013;33(4):411-421.

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Late Breaker: Psychiatry
Stephanie V. Phan, Pharm.D., BCPP
October 21, 2015

Conflict of Interests

- Nothing to disclose

Learning Objectives

- Identify concerns with reportedly increasing antipsychotic use in young people
- Describe antipsychotic use among younger and older children, adolescents, and young adults in the United States

Background

- Antipsychotic risks and benefits appear to be different in young people compared to adults
  - Higher risk of metabolic adverse effects
  - Unclear impact of hyperprolactinemia on growth
  - Greater incidence of extrapyramidal symptoms
  - Unknown effects on central nervous system development, brain maturation
- Efficacy of antipsychotics is best evaluated in schizophrenia, autism spectrum disorders, and bipolar disorder

Schneider et al. J Psychopharm 2014;28:615-23.

Antipsychotics in Youth

Antipsychotic	Age group, y	FDA-Approved Indication(s)
Aripiprazole	13-17 10-17 6-18 6-17	Schizophrenia Bipolar I, manic/mixed Tourette's disorder Irritability/aggression with autistic disorder
Asenapine	10-17	Bipolar I, manic/mixed episode
Olanzapine	13-17 13-17 10-17	Schizophrenia Bipolar I, manic/mixed episode Bipolar I, depressed episode (with fluoxetine)
Quetiapine	13-17 10-17	Schizophrenia Bipolar I, manic/mixed episode
Paliperidone	12-17	Schizophrenia
Risperidone	13-17 10-17 5-17	Schizophrenia Bipolar I Irritability/aggression with autistic disorder
Ziprasidone	10-17	Bipolar I, manic/mixed episode

Worldwide Data

- Despite study heterogeneity, the general trend is increased antipsychotic use in youth
  - European countries, Canada, United States, Australia, others
  - May include increased frequency of new use and longer duration of use
  - Conditions being addressed: ADHD, conduct and behavioral disturbances, mood disorders

Patten SB, et al. Can J Psychiatry 2012;57:717-21.; Karanges EA, et al. Aust N Z J Psychiatry 2014;48:917-31.

Late Breaker: Psychiatry

- Treatment of Young People With Antipsychotic Medications in the United States
  - Olfson M, King M, Shoenbaum M.
  - JAMA Psychiatry 2015;72(9):867-74.
    - September 2015
- Population-level, retrospective, observational study of young people aged 1 to 24

Study Design

- Objective: To describe the national prevalence of antipsychotic use in young people
- Data Sources
  - IMS LifeLink LRx Longitudinal Prescription databases
    - Data on filled prescriptions in 2006, 2008, and 2010
    - National representation by age, sex, insurance
    - Captured 63% of all retail prescriptions in the U.S.
  - Medical Expenditure Panel Survey
    - Percentage who did not fill prescriptions
  - 2009 IMS Medical Claims Database
    - Merged with pharmacy claims from 2009 LRx database

Results

- Percentage of young people with any antipsychotic prescription by age category

Year	Population with Prescription by Age, %			
	1-6 y	7-12 y	13-18 y	19-24 y
2006	0.14	0.85	1.10	0.69
2008	0.16	0.87	1.18	0.75
2010	0.11	0.80	1.19	0.84

Results

- Percentage of young people, by sex, with any antipsychotic prescription by age category

Year, by sex	1-6 y (%)	7-12 y (%)	13-18 y (%)	19-24 y (%)
Males				
2006	0.20	1.28	1.35	0.70
2008	0.24	1.33	1.43	0.76
2010	0.16	1.20	1.42	0.88
Females				
2006	0.08	0.45	0.87	0.68
2008	0.09	0.47	0.95	0.75
2010	0.06	0.44	0.95	0.81

Results

- Percentage of antipsychotic users with any antipsychotic by prescription source

Age category, y	Population with Prescription by Year, %					
	2006	2008	2010	2006	2008	2010
	Psychiatrist			Child/adolescent psychiatrist		
1-6	61.0	51.2	57.9	32.1	31.0	29.3
7-12	74.7	71.9	71.9	41.9	39.8	39.2
13-18	79.7	81.0	77.9	40.2	39.0	39.2
19-24	71.1	73.4	70.4	13.2	13.7	14.2

Results

- Other classes of psychotropic among young people with antipsychotics in 2008

Prescription Medication	Population with Prescription by Age, %			
	1-6 y (n=50,725)	7-12 y (n=247,111)	13-18 y (n=332,051)	19-24 y (n=228,329)
Stimulants	58.7	68.7	44.5	17.1
Antidepressants	20.3	34.0	50.8	59.1
Mood stabilizers	16.5	24.6	34.9	41.4
Benzodiazepines	6.4	6.0	11.7	33.5
Antipsychotics only	27.8	15.0	16.2	18.1

Results

- Use of any psychotherapy in 2009 among young people with antipsychotic prescriptions, by age:
  - 1-6 years (n=925): 13.5%
  - 7-12 years (n=5,939): 20.4%
  - 13-18 years (n=8,198): 24.8%
  - 19-24 years (n=5,353): 18.8%
- Diagnoses in 2009 among young people with antipsychotic prescriptions, following slide

Results – By Diagnoses

Diagnosis (2009)	Population with Diagnosis by Age, %			
	1-6 y	7-12 y	13-18 y	19-24 y
ADHD	52.5	60.1	34.9	11.3
Autism or mental retardation	23.1	13.8	8.4	5.7
Disruptive behavioral disorders	20.6	15.7	13.0	2.2
Bipolar disorder	8.1	12.7	20.5	26.6
Anxiety	6.9	10.4	13.0	22.9
Depression	1.8	2.6	24.4	34.5
Adjustment-related disorders	0.8	0.3	2.7	2.2
Substance use	0.3	0.2	0.2	0.8
Schizophrenia	23.5	21.0	1.4	7.5
Other mental disorder	13.5	20.4	22.6	18.1

Limitations

- Prescription database captures purchased medications
- Data not available on antipsychotic safety and/or efficacy
- Population denominator was a possibly imprecise estimate
- Service claims data were not available for all patients
- Diagnostic data were not validated by an expert
- Current practices may be different

Conclusions

- Antipsychotic use in younger and older children decreased, but increased in young adults between 2008 and 2010
- Peak antipsychotic use is in adolescents; higher for males
- Antipsychotic prescriptions are more likely to come from a psychiatrist than a child and adolescent psychiatrist
- Stimulants are most often co-prescribed in younger and older children; more likely to have ADHD diagnosis
- Psychotherapy use may be underutilized

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Late Breaker: Psychiatry
Stephanie V. Phan, Pharm.D., BCPP
October 21, 2015

2015 ACCP Global Conference on Clinical Pharmacy

Vaccine/Immunization Late Breaker
Scott Bergman, PharmD, BCPS (AQ ID)
Oct 21st, 2015

Conflict of Interests

- Sanofi-Pasteur
  - Speaker's Bureau

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Learning Objectives

1. Identify/discuss new and emerging clinical data or patient care trends affecting pharmacotherapy and/or health outcomes in vaccines/immunizations.
2. Identify the limitations/controversies associated with these late-breaking trials.
3. Discuss approaches to apply and implement the new findings into practice.

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The Impact of Age on the Efficacy of 13-valent Pneumococcal Conjugate Vaccine in Elderly

van Werkhoven CH, Huijts SM, Bolkenbaas M, Grobbee DE and Bonten MJM.
Clinical Infectious Diseases. Advanced Access Ahead of Print Sept 2, 2015

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Pneumococcal conjugate polysaccharide vaccine

- PCV - Prevnar 13
  - Produces memory B-cells
  - Subsequent exposure boosts response
  - FDA-approved: 50 years and up, 2011
  - CDC-recommended:
    - All infants & children, 2010
    - Immunocompromised adults, 2012
    - Everyone 65 years and up, 2014

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Pneumococcal polysaccharide vaccine

- PPSV – Pneumovax 23 (1983)
  - Still recommended for adults $\geq$ 65 years old
    - 1 year after PCV13
  - Ages 2-64 years with risk factors
  - T-cell dependent response
  - Decreases invasive pneumococcal disease (IPD)
    - Reduction in pneumonia and mortality not compelling

Paradiso PR. Clin Infect Dis. 2012;55(2):259-64

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Community-acquired Pneumonia Immunization Trial in Adults (CAPITA)

- Randomized, double-blind, placebo-controlled efficacy trial of PCV13
  - Adults ≥65 years old
  - The Netherlands
    - Limited use of PPSV
- Primary endpoint: community-acquired pneumonia (CAP) from vaccine serotypes
- N=84,492 subjects

Bonten MJ, et al. New Eng J Med. 2015(Mar 19);372:1114-15

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CAPITA results

Primary endpoint:

- 45.6% efficacy for confirmed CAP
  - CI: 21.8 to 62.5%

Secondary endpoints:

- 75% efficacy for IPD due to vaccine serotype
  - CI: 41.4-90.8%
- 5% overall reduction in pneumonia (NS)

CI = 95% Confidence Interval, NS=Not significant

Bonten MJ, et al. New Eng J Med. 2015(Mar 19);372:1114-15

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CAPITA population

Age range (years)	Subjects (n)	% of study participants
65-69	32,933	39.0
70-74	25,145	29.8
75-79	15,758	18.7
80-84	7,715	9.1
≥85	2,941	3.5

van Werkhoven CH, et al. Clin Infect Dis. 2015

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CAPITA results by age

Vaccine efficacy against first episode of VT-CAP or VT-IPD in mITT population

	Total number of episodes	Number of episodes in PCV13 group	Number of episodes with Placebo	Vaccine Efficacy (95% CI)	P-value
All subjects	184	68	116	41.4% (21.4;57.4)	<0.001
Age <75	113	38	75	49.3% (26.2;67.1)	<0.001
Age ≥75	71	30	41	26.8% (-15.2;55.1)	0.094

Abbreviations: VT: vaccine-type, CAP: community-acquired pneumonia, IPD: invasive pneumococcal disease, mITT: modified intention-to-treat.

van Werkhoven CH, et al. Clin Infect Dis. 2015

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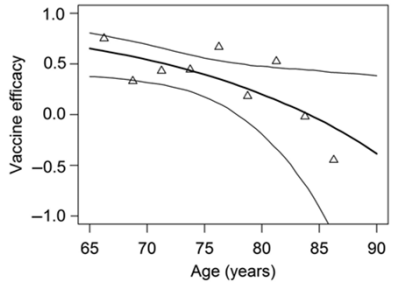
Model derived vaccine efficacy (VT-CAP-IPD in mITT population)



Vaccine efficacy by age for first episode of vaccine-type community-acquired pneumonia (VT-CAP) or invasive pneumococcal disease (VT-IPD) in modified intention-to-treat (mITT) population using a Cox proportional hazards model.

van Werkhoven CH, et al. Clin Infect Dis. 2015
Used with permission

Clinical Infectious Diseases

Discussion

- Overall results indicate benefit of PCV13 in those 65 years and older
- No difference detected in preventing pneumonia and IPD if ≥75 years
- Antibody response did not differ by age
- Phagocyte function may decline over time
- Booster could have some benefit

van Deursen, et al. IDweek (#1104) 2014.

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Limitations

- Post-hoc analysis combining CAP and IPD
- Small number of patients enrolled ≥85 years
- Population had not received previous PPSV
- PCV only recently recommended for children in The Netherlands
- 13% of CAP caused by vaccine serotypes

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Conclusion

- Efficacy of PCV13 declines with age
- May not be worth giving PCV after 75 or 80 years of age
- Cost-effectiveness to be determined
- Future studies needed with PPSV as "booster"

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Vaccine/Immunization Late Breaker

Scott Bergman, PharmD, BCPS (AQ ID)
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2015 ACCP Global Conference on Clinical Pharmacy

Late Breakers in Pharmacotherapy II: Geriatrics

Stephanie M. (Seaton) Crist, Pharm.D., BCACP, CGP

October 21, 2015

Conflict of Interests

- None to disclose

Learning Objectives

- Identify patient care trends affecting pharmacotherapy and health outcomes in geriatrics
- Identify risks associated with opioid use in patients with dementia
- Discuss approaches to applying these new data into evidence-based practice

Article Citation

Dublin S, Walker RL, Gray SL, Hubbard RA, Anderson ML, Yu O, Crane PK, Larson EB. Prescription opioids and risk of dementia or cognitive decline: a prospective cohort study. *JAGS* 2015;63(8):1519-1526.

Background

- Opioid use among older adults continues to rise
- Neuropathologic findings in young drug abusers similar to those seen in Alzheimer's disease (AD)
- Unanswered question: do opioids have long-term effects on cognition?

Volkow ND. America's Addiction to Opioids: Heroin and Prescription Drug Abuse. Available at: http://www.drugabuse.gov/about-nida/legislative-activities/testimony-to-congress/2015/americas-addiction-to-opioids-heroin-prescription-drug-abuse Accessed 9/5/2015.

Study Objective

To determine whether prescription opioid use is associated with higher dementia risk or greater cognitive decline

Methods

- Population-based, prospective cohort study within Group Health (Seattle area)
  - Data from Adult Changes in Thought (ACT) Study
- Opioid use identified from computerized pharmacy claims data
- Patient visits every two years
- Opioid exposure converted to morphine equivalent doses → total standard doses (TSD)
  - 1 TSD = morphine 30 mg

Methods

Inclusion Criteria

- Age ≥ 65 years
- Community-dwelling
- No baseline dementia
- At least 10 years of membership within Group Health

Exclusion Criteria

- < 1 follow-up visit
- Invalid cognitive score (CASI) at baseline
- Consent withdrawn

Cognitive Abilities Screening Instrument (CASI)

- Potential uses:
  - Screening tool for identifying dementia
  - Monitoring parameter for disease progression
  - Providing a profile of impairment among various cognitive domains
- Nine cognitive domains
- Total score range 0-100 (lower is worse)

Teng EL, et al. International Psychogeriatrics 1994;6(1):45-58.

Outcomes

- Primary
  - CASI (cut-point for cognitive analysis: ≤86)
- Secondary
  - CASI-IRT (Item Response Theory)
  - Nonsteroidal anti-inflammatory drug (NSAID) use

Study Participation

4,724 participants in original ACT study

- After exclusions:
  - 3,434 in the dementia analyses
  - 3,993 in CASI analyses

Results

- Baseline characteristics, n = 3,434:
  - Mean age: 74 years
  - 40% male
  - 72% regular exercise
  - 48% treated for HTN
  - 25% obese
  - 18% CAD
  - 10% depression
  - <5% current smoker
- 92% had a least one opioid fill:
  - 39%: codeine
  - 26%: oxycodone
  - 23%: hydrocodone

Results, continued

- Mean follow-up: 7.3 years
- 797 (23%) developed dementia
  - 637 with "possible" or "probable" dementia
- Slightly higher risk of all-cause dementia
  - Heaviest opioid use (≥ 91 TSDs), aHR 1.29 (1.02-1.62)
  - Heaviest NSAID use (≥ 541 TSDs), aHR 1.31 (1.07-1.62)
    - Cumulative heaviest NSAID use categorized as 1200 mg of ibuprofen daily for 1.5 years
- Recent opioid use was not associated with increased rate of cognitive decline

Critical Appraisal

- Overall younger population
- Insurance claims data does not account for medication adherence
- May under- or over-report NSAID use
- Higher opioid and/or NSAID use may represent poorer overall health compared to little or no opioid/NSAID use
- Conflicting results for risk of dementia with NSAID use
- Measures of pain lacking
- Relatively weak association, not causation

Application to Practice

- Caution use of opioids (and NSAIDs) in individuals who are:
  - Older
  - Female
  - Obese
  - Report fair or poor rate of health
  - Depression
  - Little exercise
- Opioid use (and/or NSAID use) does not equal long-term cognitive harm
- More studies necessary to further conclude risk

Self-Assessment Question 1

For the primary outcome, what does the HR = 1.29 represent?

a. There is a 1.29% chance of developing dementia when taking an opioid

b. A person is 1.29 times more likely to develop dementia with opioid use

c. Roughly 98% of patients who take an opioid will develop dementia

d. There is a 29% chance of developing dementia

Self-Assessment Question 2

Opioid use is associated with increased risk of all-cause dementia.

a. True

b. False

Thank you for attending.

QUESTIONS?

2015 ACCP Global Conference on Clinical Pharmacy

Late Breakers in Nephrology
Mary Vilay, PharmD
Wednesday, October 21, 2015

Conflict of Interests

- None to disclose

"The Association of Chronic Kidney Disease with the Use of Renin-Angiotensin System Inhibitors After Acute Myocardial Infarction"

Wetmore JB, Tang F, Sharma A, Jones PG, and Spertus JA

Am Heart J 2015 Oct; 170 (4): 735-743. (Epub 2015 Jul 26)

Background

- Renin-angiotensin system (RAS) inhibitors ↓ CV morbidity and mortality
- ACC/AHA recommend ACEI post MI/stable IHD (particularly if systolic HF present)
- ACEIs and ARBs used interchangeably
- RAS inhibitor use post AMI with EF <40% = quality performance measure
- Concerns of RAS inhibitor ADE
  - Renal effects
  - Hyperkalemia

Study Objective

- Determine current practice pattern of prescribing RAS inhibitors in patients with impaired renal function at time of AMI
  - Specifically interested in association of CKD, AKI and LV function on treatment patterns

TRIUMPH Study Patients from 24 US Hospitals

Inclusion

- ≥18 years old
- AMI, biomarker evidence myocardial necrosis and prolonged ischemia or ST-wave changes on ECG
- Admission SCr and subsequent in-hospital SCr
- Alive at discharge

Exclusion

- Documented RAS inhibitor contraindication

Data Collected & Definitions

- RAS inhibitor Rx at discharge recorded
- CKD-EPI equation used to calculate eGFR
- ESRD = chronic dialysis
- AKI = 0.3 mg/dL or 50% ↑ SCr during hospitalization vs admission value

Baseline Characteristics

1-way ANOVA (continuous); X^2 or Fisher's exact (categorical)

	ESRD (N=81)	eGFR <30 (N=146)	eGFR 30-59 (N=818)	eGFR 60-89 (N=1958)	eGFR ≥90 (n=1220)	Total (N=4223)	p-value
Age (y)	62	65	66	59	53	59	<0.001
Sex							<0.001
Male	54%	56%	56%	70%	72%	67%	
Female	46%	44%	44%	30%	28%	33%	
Race							<0.001
White	47%	62%	71%	71%	61%	67%	
Black	51%	32%	24%	22%	31%	26%	
Other	2%	6%	5%	7%	8%	7%	
Ethnicity							<0.001
Hispanic	6%	7%	4%	6%	9%	6%	
Non-Hisp	94%	93%	96%	94%	91%	94%	

Baseline Characteristics

1-way ANOVA (continuous); X^2 or Fisher's exact (categorical)

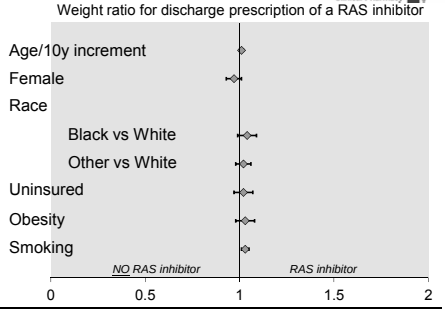
	ESRD (N=81)	eGFR <30 (N=146)	eGFR 30-59 (N=818)	eGFR 60-89 (N=1958)	eGFR ≥90 (n=1220)	Total (N=4223)	p-value
HTN	88%	91%	80%	64%	58%	67%	<0.001
DM	70%	64%	41%	26%	26%	31%	<0.001
Hx MI /PCI/CABG	52%	56%	57%	48%	45%	49%	<0.001
CHF	24%	30%	15%	7%	4%	9%	<0.001
MI dx							<0.001
STEMI	17%	16%	38%	46%	47%	43%	
NSTEMI	83%	84%	62%	54%	53%	57%	
AKI							<0.001
No AKI	0%	64%	79%	91%	89%	85%	
AKI	0%	36%	21%	9%	11%	13%	
Dialysis	100%	0%	0%	0%	0%	2%	

Use of RAS Inhibitors at Discharge

	ESRD (N=81)	eGFR <30 (N=146)	eGFR 30-59 (N=818)	eGFR 60-89 (N=1958)	eGFR ≥90 (N=1220)	p-value*
All	60.5%	50.0%	72.6%	76.9%	78.4%	<0.001
EF <40%	57.9%	52.4%	79.8%	83.0%	89.3%	<0.001
EF ≥40%	61.3%	49.0%	70.8%	75.6%	76.1%	<0.001
No AKI	---	54.8%	75.3%	77.9%	78.4%	<0.001
AKI	---	41.5%	62.4%	66.9%	77.9%	<0.001

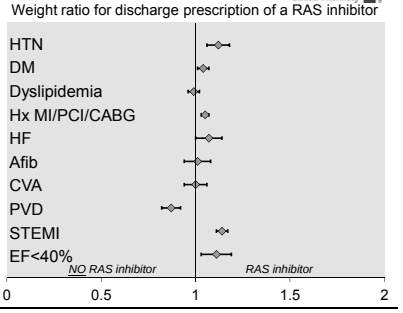
* Mantel-Haenszel trend test across eGFR categories, excludes ESRD

Interaction EF and eGFR p=0.4
Interaction AKI and eGFR p<0.01
Interaction AKI and EF p=0.25



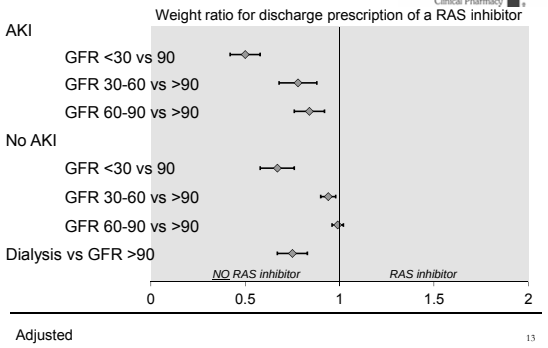
Adjusted

11



Adjusted

12



Limitations

- Use of admission SCr to estimate eGFR
- Information on hypotension missing
- Extensive collection of patient-level data
  - Risk of unmeasured confounding variable may still be present
- Few follow-up data available to better define adverse renal consequences for using/not using RAS inhibitors at discharge

Take Home Message

- ↓ RAS inhibitor use with ↓ eGFR
- RAS inhibitor prescribing may be influenced more by presence of CKD than ↓ EF
- AKI and CKD were barriers to RAS inhibitor prescribing post AMI
- Possibly patients who would benefit from RAS inhibitors are not receiving them
- More work is needed

2015 ACCP Global Conference on Clinical Pharmacy

Late Breakers in Neurology
Melody Ryan, PharmD, MPH
October 21, 2015

Conflicts of Interest

- Melody Ryan has no conflicts of interest

Learning Objectives

- Identify/discuss new and emerging clinical data or patient care trends affecting pharmacotherapy and/or health outcomes in the area of neurology.
- Identify the limitations/controversies associated with this late-breaking trial.
- Discuss approaches to apply and implement the new findings into practice.

FDA approves first 3-D printed medicine!

- Spritam® - rapidly disintegrating oral tablet of levetiracetam
- Approved 7/31/15
- 250 mg, 500 mg, 750 mg, and 1000 mg tablets
- Dissolves within 10 seconds with a sip of water; still must be swallowed
- Indicated for adjunctive therapy in the treatment of partial onset, myoclonic, and primary generalized tonic-clonic seizures

Spritam Product Information. Aprecia Pharmaceuticals Company. 1995:East Windsor, NJ.

3-D Printing

- First 3-D (additive manufacturing) performed in 1981 with plastics
- Computer-aided design is used to create a computerized model of a real object, it is converted into code, the printer head distributes layers of material (powder, liquid, metal, etc) until the item is printed
- Since that time, used for a wide variety of items from food to weapons

3-D Medical Printing

- Titanium jaw replacement March 2012
- Facial reconstruction with titanium replacements and 3-D modeling March 2014
- Printing skin directly into wounds July 2014
- Experiments with living cells on a cellulose matrix to produce cartilage and liver tissue August 2013
- FDA approves bone tether plate February 2015

http://www.bbc.com/news/technology-16907104
http://www.telegraph.co.uk/news/health/10691753/Man-makes-surgical-history-after-having-his-shattered-face-rebuilt-using-3D-printed-parts.html
http://3dprintingindustry.com/2014/07/21/us-armys-3d-printed-skin-near-ready-clinical-trials/
http://thediplomat.com/2013/08/chinese-scientists-are-3d-printing-ears-and-livers-with-living-tissue/
http://www.fda.gov/medicaldevices/productsandmedicalprocedures/deviceapprovalsandclearances/510kclearances/ucm429417.htm

3-D Printed Medicine

- First reported samples printed in 2000
- Able to make high-concentration tablets; up to 68% of tablet weight may be drug
- Controlled-release properties can be attained through mixtures or coatings
- No molding or compression needed
- Different tablet shapes are possible (sphere, pyramid, cube)

Katstra WE. J Controlled Release 2000;66:1-9.
Yu DG. J Pharm Sci 2007;96:2446-58.
Yu DG. J Pharm Pharmacol 2009;61:323-9.
Goyanes A. Int J Pharm 2015;

3-D Printed Medicines

- Zip-dose Technology
  - Layer of powder
  - Liquid in certain areas to hold tablet together
  - Layer of powder . . .

https://www.youtube.com/watch?v=FGpbiJxkkak
With permission of Mohamed Alhnan, PhD, MRPharmS
School of Pharmacy and Biomedical Sciences, University of Central Lancashire

Future Applications

- Individualized doses
- Multiple medicines in one dosage form
- Multiple release properties in one dosage form
  - Captopril, nifedipine, glipizide
- Distribution and access, especially in developing countries
  - Printers ~$150-300
- Imbed medicines into implants

Khaled SA. Int J Pharm 2015.
http://3dprint.com/87977/3d-printed-drugs-2/

Potential Problems

- Durability of tablets
- Degradation of medicine from printer heat
- Dose uniformity
- Different strengths could be many different weights; problems with automated dispensing
- Will pharmacies be needed?
- Patent protection
- Hacking, if software widely distributed
- Illicit drug printing