A Pharmacist-Staffed Inpatient Antithrombosis Service

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**Background**

Pharmacists and physicians within the University of California at Davis Medical Center (UCDMC) have been interested in optimizing the management of thromboembolic diseases since the early 1980s.\(^1,2\) One of the earliest improvements in managing patients requiring anticoagulation was the establishment of an outpatient anticoagulation clinic in 1985 to monitor warfarin therapy. A pharmacist was added to the staff in 1993. In 1992, clinicians managing inpatients became increasingly concerned about measured dose responses when using warfarin or unfractionated heparin (UFH) and about occurrences of bleeding or thrombotic complications. At the request of the medical staff, the pharmacy department began to assist in the day-to-day management of inpatients requiring anticoagulation therapy.

**Description**

A formal pharmacist-managed anticoagulation service was one of two programs developed in 1991 as an expansion of pharmacy services to address drug use concerns identified by the institution’s Pharmacy and Therapeutics (P & T) Committee. The other program was a formal Clinical Pharmacy Consult Service to review requests for medication therapies that were identified as high risk or high cost; all such reviews were to be done before any drugs were dispensed. A small group of pharmacists, which included the anticoagulation specialist, was identified to fulfill these tasks, enabling cross-coverage between services for continuity of care. The initial charge for the pharmacist assigned to the anticoagulation service was to explore ways of improving patient care and approaches to resolving issues in the management of thrombosis. At this time, the two primary anticoagulants in use were UFH and warfarin.
Outcomes Assessment/Impacts

Before formally advising physicians on the management of anticoagulation, an audit of patients receiving warfarin and later heparin was undertaken concurrently with a review of current literature and incorporation of the American College of Chest Physicians (ACCP) guidelines on the management of anticoagulation therapy (second ACCP Consensus Conference). During the completion of the audit phase, the identified anticoagulation specialty pharmacist began making patient rounds and assisting with anticoagulation management together with selected medical services, starting with cardiothoracic surgery. Consultations expanded during a 1-year period to include all patients receiving warfarin and selected patients requiring UFH. Because the UCDMC is a teaching hospital, it was preferred that the anticoagulation service follow and provide consultations for each patient receiving warfarin to optimize patient care while educating the medical staff about any related pharmacotherapy observations. Such observations might include dosing adjustments, timing of follow-up assessments, and even modification of other medication classes such as concurrent antimicrobials. Upon achieving this, a cohort of 60 patients was randomly matched to a similar set of 60 patients for indication of anticoagulation therapy. Analysis of the two cohorts revealed a significant reduction in reported international normalized ratio values above either the target range or critical value (> 6.0). The length of patient stay within the hospital was also reduced after adjusting for overall shortened length of stay of inpatients. On exploring outcomes for recurrent thrombosis and bleeding in the two cohorts within 3 months of discharge, outcomes for both were lower when the pharmacist was involved in inpatient anticoagulation care. The conclusion of the analysis was that a pharmacist providing inpatient warfarin management could improve patient care in addition to creating a notable cost savings to the institution.
Shortly after completion of the analysis, the low-molecular-weight heparins (LMWHs) came onto the market. The anticoagulation service was charged with evaluating each LMWH request for safety and correct dose prescribing, especially when treatment of venous thromboembolism (VTE) expanded the area of LMWH use. During this time, some preliminary information became available regarding the management of VTE in the outpatient setting using an LMWH at home while transitioning to warfarin. A safety analysis was undertaken using the LMWH enoxaparin as an outpatient transition to warfarin for acute deep venous thrombosis/pulmonary embolism, with good results obtained in 100 patients. This same approach was taken later with tinzaparin. The unique part of this practice was its inclusion of stable patients with pulmonary embolism. Our experiences suggest that a pharmacist can provide a vital role in facilitating the transition from the inpatient setting to the outpatient management of a VTE before warfarin becomes therapeutic. The success of the program was based on the anticoagulation pharmacist providing patient education, verifying insurance coverage, and ensuring prompt follow-up postdischarge with either the primary care physician or, when possible, an established anticoagulation clinic. Working closely with the outpatient anticoagulation clinic, the institution saw a notable cost savings at the same time as improved patient care was observed.

Because of the availability of additional antithrombotic therapies and the further recognition of hypercoagulable states, drug interactions, and unique dosing populations, there is an ongoing need to incorporate these advances into management plans. Yet situations still exist in which data are limited or multiple factors are present; in such instances, multidisciplinary approaches to management plans that include antithrombosis service are key to successfully managing patients. Examples of such circumstances include patients who are morbidly obese...
(i.e., in excess of 200 kg); patients with renal failure on various forms of hemodialysis with no intravenous access or mechanism for obtaining coagulation studies (and thereby determine any resistance to warfarin or heparin); postoperative patients with open surgical sites and heparin-induced thrombocytopenia (HIT); neonates and adults with severe antithrombin deficiency or other hypercoagulable disorders; patients with baseline coagulopathies from liver failure; patients with concurrent major bleeding and evolving thrombosis; and women with complicated pregnancies requiring continued anticoagulation. Other activities that require the expertise of anticoagulation pharmacists include risk stratification between bleeding and thrombosis for perioperative procedures, atrial fibrillation with requests for shifting to another anticoagulant, and short-term combination anticoagulant therapies. Another activity is to evaluate critical laboratory values or requests to reverse anticoagulation to meet immediate clinical needs and thus avoid the long-term challenges involved in reinitiating anticoagulation.

One notable challenge early in the establishment of the service was the emerging recognition of HIT. To facilitate the use of a new investigational agent (danaparoid) under compassionate care, the anticoagulation service was asked to become an investigator for treating patients with HIT. This placed the anticoagulation service in a position to expand its management beyond heparin or warfarin dosing to other potential thromboembolic states, where limited expertise existed. The scope continued to expand as the direct thrombin inhibitors became available and, given the high acuity of patients and the use of heparin in our institution, gave the service the opportunity to play a critical role in the recognition and management of HIT. One example is the ongoing process to validate and refine the proposed tools necessary to assess the probability of HIT and to identify patients who should receive alternative anticoagulant therapies. Numerous publications began to focus on experiences or observations gained during
the years of managing HIT when such insights or descriptions in the literature were limited.\textsuperscript{8–19} One critical component that emerged was a working relationship with the clinical laboratory to develop a clearer understanding of the connections between disease, anticoagulants, and related coagulation assays.\textsuperscript{11–15} One outgrowth of this cooperation has been the ability to facilitate the reach of details regarding the limitations of coagulation tests to bedside management. In selected cases, novel approaches have been developed to transition from heparin to a direct thrombin inhibitor when anticoagulation must be maintained during a concurrent procedure (ongoing surgery) or in the presence of a mechanical device (extra-membranous corporeal oxygenation) when there is a high risk for acute thrombotic or major bleeding complications.\textsuperscript{15} This has taken the anticoagulation pharmacist directly into the operating room at times.

Because it is part of an academic institution and regional referral center for high acuity cases, the anticoagulation service may be asked to handle many difficult cases or situations requiring unique approaches to anticoagulation. The process of exploring and improving the management of such challenging cases has resulted in a number of publications, from those dealing with infants and adults to those dealing with stable patients as well as dynamically changing patients in intensive care with multisystem organ failure.\textsuperscript{14–25} The service is also active in research involving thrombosis management.\textsuperscript{26}

**Applicability and Sustainability**

Because of the complexity of thrombosis and the relatively high incidence of morbidity and mortality, opportunities for increasing the understanding of related diseases and management are numerous. An example of a recent application of this concept was an exploration of the use of enoxaparin in younger pediatric patients at home by assessing, from a safety standpoint, the stability of a diluted solution that could be prefilled in a pharmacy.\textsuperscript{24} Another example was a
determination of the impact of activated recombinant factor VII (rFVIIa) on reversing warfarin- or trauma-related life-threatening bleeding situations in non-anticoagulated patients. Because of the high risk for thrombosis associated with rFVIIa, finding the safest optimal dose of rFVIIa to be given with fresh frozen plasma and vitamin K is an example of the recent frontiers explored by the service. Because of concerns about the notable costs associated with these agents, alternative management plans have resulted in significant financial savings for both the patient and health care provider. For example, prevention of excessive warfarin reversal can avoid prolonged use of a parenteral anticoagulant.

Recently, the oral direct thrombin inhibitor ximelagatran was evaluated for approval for many of the same indications as warfarin. There was concern that many anticoagulation services would have to reinvent themselves, with a reduced number of patients receiving warfarin. On the contrary, each time a new antithrombotic reaches the market or an expanded anticoagulant indication occurs, the role of the inpatient anticoagulation service broadens. Selection of an antithrombotic agent depends on the unique aspects of the patient’s clinical presentation and the multiple factors involved in establishing a successful management plan for the duration of therapy. In general, the selection of an anticoagulation regimen that can be continued for the desired duration of care must take into consideration the outpatient coverage and management resources available to the specific patient.

Because of the constantly changing landscape relative to anticoagulation therapy and the increasing costs of providing such care, there has been a constant adaptation process. Frequent evaluations of the literature and cost assessments with alternative therapies are done to avoid unnecessary financial expenditures, with the service acting to prompt the implementation of any identified changes. Continued observations of the purchasing costs of anticoagulants, rFVIIa, or
adverse events support maintaining the service from an economic and patient care basis. The service is staffed 7 days per week, with a pharmacist specialist in addition to the anticoagulation pharmacist specialist who is available on an on-call basis.

**Potential Problems and Possible Solutions**

One of the most notable challenges of the anticoagulation service is the development of a cooperative working relationship with all the medical disciplines. This is especially important because the service is in a position to alter a treatment plan on the basis of hospital policies and perceived patient safety but in opposition to the current understanding of the prescribing clinician. To allow the continued review of approaches to anticoagulation or hemostasis using a broader representation of specialties within the health care system, the Thrombosis Subcommittee of the P & T Committee was formed to work in conjunction with the anticoagulation service. The pharmacy department is responsible for all patients and, working under the guidelines of the P & T Committee, is not as prone to conflicts with the medical specialties. In general, the P & T Committee sets policy, whereas the inpatient and outpatient anticoagulation services work together prospectively to provide assistance to clinicians in managing antithrombotic therapy. Expansion of available agents, observation of indications, and recognition of variable patient characteristics constantly create new challenges for the service. The expertise gained throughout the years also contributes to the effective, safe management of the patient. By sharing these experiences with clinicians in training and other health care professionals, we have had an impact on the general public. Such positive effects of pharmacists on patient care are, in fact, common but often unrecognized. Sharing our expertise provides a means for improving the use of pharmacological agents.

**Future Perspectives**
Thromboembolic disease will continue to be a significant and common condition among patients and their health care providers. Newer assays, classes of anticoagulants, and diagnostic tests, in addition to established therapies, create the need to determine the optimal approach to the treatment or prevention of thromboembolic disease. The Joint Commission on Accreditation of Healthcare Organization currently has outlined, in draft form, the core measures and patient safety goals directly relating to anticoagulation therapy. Anticoagulation services in both the inpatient and outpatient setting have developed management plans to meet many of the proposed goals. Given the amount of information currently available, specialists with a background in pharmacotherapy can make an impact, as in the practice setting described above. Expanding the roles of pharmacists who have specialized skills in managing anticoagulants in both the inpatient and outpatient setting to optimize the management of antithrombotic therapies for the duration of their use continues to be an important goal for the clinical pharmacy discipline.

References:


