



## Management of Acute Bleeding in Patients with Hemophilia in Health Systems

### Educational activities can serve as the stimulus for pharmacists to make practice changes.

After participating in an educational activity, intentions may be good to bring new ideas back to your practice site. But does that really happen? According to the results of a survey of participants in a live symposium and simultaneous webcast about challenges in managing acute bleeding in patients with hemophilia held during the 47th ASHP Midyear Clinical Meeting and Exhibition in December 2012, the answer is yes. Conducted three months after the symposium, the survey indicated that each of the following practice changes were implemented, improved, or planned by at least 64% of the 45 respondents (range 64-78%):

- Be more confident in decision-making skills regarding which product would be best choice for different situations,
- Lead discussions with colleagues about key differences among available products,
- Review formulary and make recommendations as necessary,
- Initiate hemostatic agent in patients with hemophilia with acute bleeding, and
- Identify laboratory tests to be ordered and monitored.

Several respondents offered tips about how they overcame barriers when changing their practice to

address the challenges in managing acute bleeding in patients with hemophilia:

- Develop a deep understanding of the clinical and economic situations before beginning discussions related to the practice change.
- Tie the implementation back to a comparison of cost savings, patient safety, and efficacy.
- Delegate responsibility for different aspects of the implementation plan.
- Provide education for those questioning the practice.

If you missed the Midyear symposium and these practice changes pique your interest, a free



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 **ACUTE BLEEDING IN HEMOPHILIA**

on-demand version of the activity is available. It is approved for 2 hours of continuing pharmacy education. Eighty-three percent of the survey respondents indicated that they would recommend the activity for other pharmacists who are interested in learning more about this topic. As one respondent described, "It was really interesting to see the detrimental effects that hemophilia has on the entire body." Another noted, "I still refer to notes from the presentation in my daily work."

In addition to the on-demand activity, you can take advantage of other learning activities. Included are podcasts of a faculty roundtable discussion and e-newsletters, such as this one that provides an overview of system issues related to the management of acute bleeding in patients with hemophilia. The [March e-newsletter](#) focused on considerations related to bleeding management and patient assessment. All of the learning opportunities are designed to build on each other, focusing on interventions and practical strategies for preventing and treating acute bleeding associated with trauma or surgery in patients with hemophilia.

**ABOUT HEMOPHILIA**

Hemophilia is a hereditary bleeding disorder caused by a genetic mutation on the X chromosome that results in a deficiency or absence of clotting factor VIII (hemophilia A) or less commonly, clotting factor IX (hemophilia B).<sup>1</sup>

The disorder affects approximately 20,000 American males.<sup>2</sup> It is a major cause of disability because of repeated bleeding into the joints followed by cartilage and bone destruction and bone remodeling, usually involving the ankles, knees, and elbows.<sup>2</sup>

Clotting factor VIII or IX concentrate derived from donated plasma or recombinant DNA technology is used to treat clotting factor deficiencies, prevent and control bleeding, and prevent joint damage in patients with hemophilia.<sup>3</sup> The dosing of these agents is guided in part by measurement of clotting factor levels in blood and bedside bleeding assessments.

The development of inhibitors that neutralize clotting factor VIII or IX is a complication occasionally observed in this patient population. As many as one

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in three patients with hemophilia develop these inhibitors, which are antibodies to exogenously administered clotting factors.<sup>4</sup> In patients with low titers of inhibitors (<5 BU/mL), the effectiveness of clotting factor concentrates is reduced, increasing dosing requirements and cost. In patients with high titers (≥5 BU/mL or higher), inhibitors render clotting factor concentrates ineffective, and a different bypassing agent may be required to promote coagulation in these patients. Recombinant factor VIIa and activated prothrombin complex concentrate (which contains clotting factor VII in an activated form and clotting factors II, IX, and X mainly in a non-activated form) are the two bypassing agents currently available in the United States.

 ACUTE BLEEDING IN HEMOPHILIA**SYSTEM ISSUES RELATED TO MANAGING ACUTE BLEEDING**

Hemophilia, a common congenital bleeding disorder, is managed primarily in hemophilia treatment centers, where a multidisciplinary team of experienced hematologists, orthopedic surgeons, physical therapists, nurses, social workers, and other health professionals provide comprehensive care.<sup>3</sup>

Although treatment for hemophilia usually is provided on an outpatient basis or at hemophilia treatment centers (HTCs), patients with hemophilia and traumatic bleeding or who are planning surgeries with a high risk for bleeding may be admitted to hospitals or other health systems. Each health system should consider convening a hemophilia management team to develop a plan for meeting the needs of these patients, with input from the departments of medicine (e.g., surgeons, hematologists, emergency physicians), nursing, pharmacy, coagulation laboratory, social work, physical therapy, and genetics.

The closest HTC should be identified, and contact should be made with HTC staff or local hemophilia experts to facilitate coordination of care, especially transitions of care when patients are transferred directly between institutions. A searchable [database of hemophilia treatment centers](#) is available online from the Centers for Disease Control and Prevention.

Communication among hemophilia management team members is vital for developing and implementing an effective management plan. The plan should outline staff member responsibilities for various aspects of patient care. For example, health-system pharmacists should ensure that clotting factor concentrates and bypassing agents are ordered, dispensed, used safely and appropriately, and billed for in a timely manner.

Pharmacists should ensure that at least one clotting factor VIII concentrate, one clotting factor IX concentrate, and one bypassing agent (activated prothrombin complex concentrate [aPCC] or recombinant factor VIIa [rFVIIa]) is included in the formulary (or readily available from a source outside the health system) and spearhead the formulary evaluation process for these products. Switching from one factor VIII or IX concentrate to another usually is not effective in cases of refractory bleeding. By contrast,

**Key Pharmacy Considerations in Use of Clotting Factor Concentrates**

- Are sufficient amounts of clotting factor concentrates available?
- Is the right clotting factor agent dispensed?
- Is the dose correct?
- Who determined the dose, and how was it chosen?
- Is the dose safe?
- Is the dose effective?
- Is a change in therapy under consideration?
  - » Will the dose be adjusted?
  - » Will the mode of administration (i.e., bolus versus continuous infusion) be modified?
  - » Will therapy be discontinued or temporarily withheld?
- How can waste and costs be minimized?
- Was the correct preauthorization obtained, and was billing promptly performed?

both of the bypassing agents currently available in the United States (aPCC and rFVIIa) should be included in the formulary because if one agent is ineffective, the other agent should be tried. Moreover, sequential therapy (i.e., alternating aPCC and rFVIIa) may be considered for life-threatening bleeding in hemophilia patients with inhibitors.

 ACUTE BLEEDING IN HEMOPHILIA

Pharmacists with the assistance of pharmacy technicians can provide a valuable service to the institution and the patients it serves by assuming responsibility for optimizing the use of these costly clotting factor concentrates. Specific responsibilities include

- Answering questions that arise among staff members about proper dosing and administration of the agents,
- Ensuring that supplies are adequate but not excessive to avoid waste of expired inventory, and
- Coordinating the timing of blood draws for accurate measurement of clotting factor levels and dispensing of clotting factor doses to minimize waste due to discontinuation of therapy after a dose has been prepared for a specific patient.

Awareness of departmental responsibilities and communication among members of various disciplines within the health system are critical for ensuring that management of bleeding in patients with hemophilia is cost-efficient. Policies and procedures should be established to promote effective communication by outlining these responsibilities and the steps in the delivery of patient care. Algorithms or guidelines might be developed to streamline patient assessment (e.g., urgency of situation, type of hemophilia, presence and titer of inhibitors, clotting factor levels) and initial management. Patients with active bleeding require more prompt intervention than patients planning surgery. Laboratory capabilities to perform factor level assays and the time required to obtain test results should be ascertained because sending blood samples to a laboratory outside the institution may result in unacceptable delays in obtaining test results.

The storage location for clotting factor products (e.g., pharmacy department, blood bank) and contact information for key clinicians in the institution and local HTC should be readily retrievable in an urgent situation. A mechanism should be established to quickly obtain additional supplies of clotting factor concentrates and bypassing agents from a local wholesaler, HTC, or other institution if needed. Arrangements should be made for transporting

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products (e.g., contracts with courier services) before they are urgently needed or stabilization and transfer of patients to a facility where treatment can be provided.

A compendium with current, easy-to-follow information about usual dosing of and preparation procedures for clotting factor concentrates and bypassing agents might be compiled and made available in electronic form to facilitate prompt initiation of therapy and avoid delays in emergent situations. Computerized alerts could be developed to ensure that patient assessment is comprehensive and important steps in the delivery of patient care are not inadvertently overlooked.

A mechanism for providing feedback to key decision makers is needed as part of the hemophilia management plan. The feedback should include selected laboratory assay results with the timing of the blood draw. Notification should be provided to pharmacy personnel about decisions to change the dose or mode of administration (i.e., use of continuous instead of bolus infusion) of clotting factor concentrates or bypassing agents or plans to discontinue or temporarily withhold therapy.

 **ACUTE BLEEDING IN HEMOPHILIA****EVALUATING ORDERS FOR CLOTTING FACTORS**

New patient orders for clotting factor concentrates should be evaluated by health-system pharmacists for appropriateness.

The evaluation should be based on the patient medical history, including the type of hemophilia, dose, frequency or rate of administration, clotting factor level, and if applicable, inhibitor titer. The dosing information in the manufacturer's prescribing information for these products may be used as a starting point. However, frequent reassessment of factor levels and coagulation assays and frequent discussion among members of the hemophilia management

team are needed because of the dynamic nature of bleeding status and changes in the target factor level in patients with hemophilia. Clotting factor dosage adjustments may be warranted, especially if the measured factor level exceeds the target because excessive dosing is costly, wasteful, and associated with a risk for thrombosis.

**OPPORTUNITY FOR PHARMACISTS**

Knowledge of the management of acute bleeding in patients with hemophilia may be limited among staff in health systems because admission of such patients is infrequent.

The health-system pharmacist may be among the clinicians with the greatest knowledge about this therapeutic area at the institution. Pharmacists should stay up to date on the latest developments in the management of bleeding in patients with

hemophilia and seize the opportunity to share their knowledge of therapeutic interventions (particularly clotting factor concentrates and bypassing agents) with members of other departments. The need for this insight is not limited to academic medical centers.

**REFERENCES**

1. Berntorp E, Shapiro AD. Modern haemophilia care. *Lancet*. 2012; 379:1447-56.
2. Centers for Disease Control and Prevention. Hemophilia: facts. July 5, 2011. <http://1.usa.gov/Yu8lvP> (accessed 2013 Apr 15).
3. Centers for Disease Control and Prevention. Hemophilia: treatment. June 21, 2011. <http://1.usa.gov/15Bcr5a> (accessed 2013 Apr 15).
4. Centers for Disease Control and Prevention. Hemophilia: inhibitors. July 18, 2012. <http://1.usa.gov/WJVYep> (accessed 2013 Apr 15).

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