Perioperative Pharmacology: Blood Coagulation Modifiers

ABSTRACT

Blood coagulation is the process that results in the formation of a blood clot to stop bleeding from a damaged blood vessel. Various pharmacologic agents can affect the coagulation process. The American College of Chest Physicians’ evidence-based practice guidelines for perioperative management of antithrombotic therapy provide guidance for anticoagulant or antiplatelet therapy and bridge therapy. Perioperative nurses must understand the pharmacologic principles of the most common blood coagulation modifiers related to perioperative use. The perioperative nurse’s responsibilities regarding administration of blood coagulation modifiers include reviewing the patient’s pertinent laboratory results (eg, prothrombin time, partial thromboplastin time, international normalized ratio), recognizing the underlying conditions that require blood coagulation therapy, and documenting all pertinent information. Perioperative nurses also should participate in development of detailed storage and retrieval policies related to heparin. AORN J 93 (June 2011) 726-733. © AORN, Inc, 2011. doi: 10.1016/j.aorn.2011.01.012

Key words: thrombolytic, platelet aggregation inhibitor, heparin antagonist, anticoagulant, unfractionated heparin, UFH, low-molecular-weight heparin, LMWH.

Blood coagulation is an important process within the complex hematologic system by which a person’s host defense mechanism initiates action to stop blood loss from a damaged vessel. Blood coagulation disorders include excessive bleeding (ie, hemorrhage) or obstructive clotting (ie, thrombosis). Various pharmacologic agents can affect the coagulation process and are classified as blood products/modifiers/volume expanders (ie, blood coagulation modifiers) in the US Department of Veterans Affairs class index.¹ This class includes agents commonly known as anticoagulants, antiplatelet agents, thrombolytics, or antifibrinolytics (ie, hemostatic agents). Annually in the United States, more than 250,000 patients who are on some form of anticoagulant or antiplatelet therapy will undergo surgery or a less-invasive procedure.² Perioperative team members are likely to encounter blood coagulation modifiers in practice and,
therefore, should have a working knowledge of some of the most common agents within each class, as well as a thorough knowledge of perioperative guidelines for the management of antithrombotic therapy.

PERIOPERATIVE MANAGEMENT OF ANTITHROMBOTIC THERAPY
In June 2008, the American College of Chest Physicians (ACCP) published an update to its evidence-based clinical practice guidelines that provide direction for perioperative management of antithrombotic therapy. These guidelines are openly available to the health care community and carry the caveat that perioperative antithrombotic therapy is an emerging field. AORN’s “Guideline for prevention of venous stasis” summarizes risk factors for deep vein thrombosis, venous thromboembolism, and pulmonary embolism. According to a British guideline for the use and monitoring of heparin, risk originates from either the patient, the disorder (Table 1), or the therapy itself. An additional risk lies with the type of surgical procedure being performed (Table 2). Perioperative nurses can use this breadth of information when caring for the patient during the surgical experience.

The ACCP practice guidelines refer to anticoagulant or antiplatelet therapy as vitamin K antagonist (VKA) therapy. The ACCP guidelines provide direction regarding when to discontinue an agent before surgery, when to resume the agent after surgery, and how to identify which patients may require bridge therapy (ie, the transition from oral anticoagulant to parenteral anticoagulant therapy). The guidelines also describe how to assess the risk for a thromboembolic event against the risk for bleeding. To determine such risk, the authors of the guidelines encourage the use of patient-centered care principles to individualize patient care management.

For patients on VKA therapy who are considered to be at low risk for a thromboembolic event, the guidelines recommend stopping the

<table>
<thead>
<tr>
<th>TABLE 1. Patient and Disorder Risk Factors for Deep Vein Thrombosis, Venous Thromboembolism, or Pulmonary Embolism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Source</strong></td>
</tr>
<tr>
<td>Patient</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Disorder</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>


VKA agent five days before surgery. The surgeon, in collaboration with the primary care physician who ordered the initial therapy, should check the international normalized ratio (INR) before surgery, and, if it is elevated, the surgeon or primary care physician might order an oral dose of vitamin K. For practical purposes, this
means that the patient should arrive early enough on the day of surgery to have laboratory work completed, if it was not done the day before surgery. The surgeon, circulating nurse, and anesthesia professional should review the results of the most recent INR before the patient is transported to the OR. The ACCP guidelines recommend resuming the VKA agent between 12 and 24 hours after the surgical procedure when there is evidence that adequate hemostasis has been achieved (eg, the absence of frank bleeding, stable vital signs, dry dressings).

Categories of patients who have an elevated risk of a thromboembolic event are those with atrial fibrillation or those who have had a mechanical valve replacement. These patients may need bridge therapy from the time when the oral VKA agent is stopped until the time of the surgical procedure itself. The guidelines recommend changing these patients to either a low-molecular-weight heparin (LMWH) agent or beginning an IV infusion of unfractionated heparin (UFH). An LMWH agent can be administered in the outpatient setting; this avoids the need for hospitalization, which often is required for UFH administration. In addition, LMWH therapy does not necessitate close laboratory monitoring. The primary care physician should ensure that the patient administers his or her last dose of LMWH 24 hours before the surgical procedure. If the patient is receiving UFH, then the infusion should be stopped four hours before the surgical procedure. The guidelines recommend resuming therapy sometime between 48 and 72 hours after major surgery (ie, when the patient has achieved adequate hemostasis). The ACCP guidelines reinforce the value of preventing thromboembolic events in high-risk patients compared with accepting the risk of bleeding.

**UNFRACTIONATED HEPARIN**

Unfractionated heparin is a biologic substance derived most commonly from animal sources (eg, porcine, bovine). Heparin is a mixture of molecular chains that vary in molecular weight and length. Heparin works by activating antithrombin III, which controls activities of thrombin inhibition and activates clotting factors IX, X, XI, and the tissue factor (VIIa complex); therefore, heparin affects the intrinsic clotting cascade (Figure 1). After parenteral administration, heparin binds to a variety of cells (eg, macrophages, platelets) and plasma proteins (eg, fibrinogen, fibronecadin). Heparin, because of its high affinity for binding and the various interactions with cells and proteins, has high variation in plasma levels, which is compounded by heparin’s dose-dependent half-life. The peak effect of a single IV dose of
heparin can occur within two minutes after injection, and the agent has a half-life of approximately 60 minutes. After hepatic metabolism, heparin is excreted through the renal system in approximately six hours. These characteristics make it difficult to ascertain the optimal safe dose. Often, the dose is titrated with guidance from a weight-based nomogram and laboratory monitoring of activated partial thromboplastin time (PTT). The anticoagulant effect of UFH can be rapidly reversed by using protamine sulfate.

**Adverse Effects**

Heparin is considered a high-alert medication by the Institute for Safe Medication Practices, given its narrow therapeutic range. High-alert medications carry an enhanced risk of causing significant patient harm. The leading adverse reaction associated with heparin is hemorrhage; bleeding can occur in any site. Heparin, therefore, is contraindicated in patients during and immediately after surgery of the eye, brain, or spinal column. Other adverse reactions include thrombocytopenia, heparin-induced thrombocytopenia, and hypersensitivity (eg, measles-like skin rash, urticaria, angioedema, bronchospasm).

Heparin also has been implicated in perioperative medication errors (Table 3), including at least one error that may have caused a patient’s death. Heparin is packaged in various concentrations, expressed as units per milliliters, and the total content of vials differ, two characteristics that predispose the agent to error involvement.

**Medication Interactions**

Nurses must recognize that concurrent use of other platelet-depressing agents is contraindicated because of the anticoagulant properties of...
heparin. Over-the-counter agents such as aspirin and aspirin-containing agents would clearly be contraindicated. Nutritional supplements such as garlic, ginkgo, and ginseng have less empirical evidence of significant drug-drug interactions but are generally contraindicated for the surgical patient.9

LOW-MOLECULAR-WEIGHT HEPARIN

The class of agents known as LMWH have shorter molecular chains and lower molecular weights than UFH agents. The molecules of LMWH are as effective as those of UFH; however, LMWH agents are generally easier to use as fixed dosages, and LMWH therapy requires less laboratory monitoring, which makes these agents ideal for outpatient use. Other approved uses are either prophylactic in nature, such as prevention of deep vein thrombosis after surgery and prevention of ischemia in certain cardiac conditions, or therapeutic uses, such as treatment of confirmed deep vein thrombosis.7

After subcutaneous administration, LMWH agents achieve high bioavailability because these agents bind minimally to plasma proteins or macrophages, which leaves more agent available to produce the anticoagulation effect.5,7 These agents work mainly by inactivating factor antifactor X (Xa)5,7 and by exerting weak antithrombin activities. The peak effect of a dose occurs after three hours, and the half-life is up to six times longer than for UFH.7 Metabolism occurs in the liver followed by renal elimination. Because of the predictability of LMWH effects, dosages can be administered either once or twice daily. Routine laboratory monitoring for anticoagulation is generally not indicated; however, laboratories can measure Xa levels to report the effect on clotting mechanisms.5

Adverse Effects

The risk of excessive bleeding remains the greatest adverse event; however, such effects are less likely to occur with LMWH than with UFH. Patients at greatest risk for hemorrhage

- have low body weight;
- are older than 70 years;
- have experienced trauma;
- are concomitantly using agents that affect hemostasis (eg, aspirin, nonsteroidal anti-inflammatory drugs); or
- have impaired renal function.

In addition, potential adverse effects are heightened in patients who are undergoing spinal anesthesia. Reversing the anticoagulant effect of LMWH can be accomplished by using protamine sulfate.5,7

<table>
<thead>
<tr>
<th>Products</th>
<th>N</th>
<th>%</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient surgery</td>
<td>36</td>
<td>1.9</td>
<td>Based on 2,979 records, 3,323 selections, and 384 unique products reported</td>
</tr>
<tr>
<td>Preoperative holding area</td>
<td>16</td>
<td>2.2</td>
<td>Based on 631 records, 719 selections, and 139 unique products reported</td>
</tr>
<tr>
<td>Operating room</td>
<td>143</td>
<td>3.9</td>
<td>Based on 3,298 records, 3,703 selections, and 343 unique products reported</td>
</tr>
<tr>
<td>Postanesthesia care unit</td>
<td>74</td>
<td>2.2</td>
<td>Based on 2,874 records, 3,312 selections, and 366 unique products reported</td>
</tr>
</tbody>
</table>

1. Rod Hicks, PhD, nurse researcher, written communication, February 21, 2011; data on file at US Pharmacopoeia.
Medication Interactions
The same medication interactions need to be considered for LMWH administration as for UFH administration. These include contraindicated use of over-the-counter, platelet-depressing agents (eg, aspirin, aspirin-containing agents, garlic, ginkgo, ginseng).

The MEDMARX report of perioperative medication errors noted instances in which LMWH agents were involved in errors. These agents were not reported as leading agents associated with errors in the outpatient surgery setting or in the OR; however, nine errors were reported in the preoperative holding area, and seven errors that involved elderly patients were reported in the postanesthesia care unit.

ROLES AND RESPONSIBILITIES OF THE PERIOPERATIVE NURSE
Perioperative nurses can easily incorporate the ACCP guidelines into practice. The ACCP guidelines recommend obtaining appropriate laboratory tests before surgery to minimize the risk of excessive bleeding. Identifying that a patient has inadequate prothrombin time (PT), PTT, and INR levels disrupts the surgical schedule, disrupts the surgeon’s clinic schedule, and negatively affects patient satisfaction if this occurs during preoperative care.

Scheduling
One of the most difficult areas in which to incorporate the guidelines is in the scheduling department. Surgical scheduling must take into consideration the patient’s access to a laboratory, the laboratory’s ability to report results in a timely fashion, and the surgical team’s ability to take action on the results. Such coordination requires more than just calling the scheduling desk and obtaining the appointed time for the procedure. Until seamless transfer of medical records between providers’ offices and health care facilities is functional and fully in place, there remains the need to enhance the type of information collected at the point of scheduling to identify patients on VKA therapy. Research opportunities include investigating whether these patients are best suited to be scheduled as the first procedure of the day or should routinely be scheduled as a later procedure of the day.

Documentation and Communication of Patient Information
At the point of intake, such as an outpatient surgery setting or another location (eg, preregistration and testing center), documentation of the patient’s medical and surgical history and medication reconciliation can provide safeguards. Information reviewed should include the primary care provider’s and surgeon’s respective consultation notes pertaining to VKA therapy. Nurses must recognize the underlying conditions that require VKA therapy. Merely asking questions such as “What medications are you currently taking?” is not adequate. Rather, the interview process must be sufficient to identify whether the VKA is on hold and for how long, or whether the patient has transitioned or should transition to bridge therapy. Information obtained at this stage must be documented and shared with other members of the surgical team and throughout the perioperative continuum of care.

Preoperative Assessment
During the preoperative assessment phase, the nurse should review the patient’s pertinent laboratory results. A sudden decrease in the PTT, PT, or INR may be reported by the laboratory system. The nurse must carefully consider and communicate these findings. If patients are arriving early to have laboratory work done, then how the nurse completes the laboratory requisitions is important. Rather than merely putting “preoperative” or a similar designation in the indication for the laboratory test, the nurse should complete the form with detailed information, such as “holding anticoagulant before surgery.” The reason for this detailed documentation is that many laboratory systems track trends in patient results. Detailed documentation also provides sufficient rationale
for the test, which has financial implications for billing practices.

**Storage and Retrieval**
Institutions are encouraged to have detailed storage and retrieval policies related to heparin given its high-alert status and the various concentrations and packaging sizes on the market. Although independent double checks of heparin remain an important task, perhaps a stronger safety net would be to have bar-code verification at the point of stocking and retrieving from storage devices. The emphasis here is slightly different than for bedside bar-code medication administration. Bar-code verification during the process of stocking the storage device reinforces that the correct strength of the agent is in the right storage bin and, ultimately, in the hands of the practitioner. Perioperative nurses should be prepared to collaborate with pharmacists to ensure that the safest and most practical policies are developed and then implemented to support this process.

**Perioperative Considerations**
Within the OR itself, vial concentrations again must be affirmed as the medication is moved between the circulating nurse and scrub person or other members of the surgical team. All original containers should be retained until the patient exits the operating suite. Also, within the OR, nurses must recognize the hazards of prolonged procedures and patient positioning as risk factors for complications.3

An additional perioperative consideration for the care of patients who are at risk for experiencing a thromboembolic event centers around the potential effect of intentional use of clotting agents to support hemostasis during surgery. This practice is a concern for patients already at risk for clotting who have had their VKA temporarily withheld because this could place these patients at risk for clots. Circulating nurses should have protamine sulfate readily available for administration to counter the residual effects of VKA therapy and augment hemostasis for these vulnerable patients.11 From the intraoperative phase through discharge, it is essential that all perioperative practitioners closely observe these patients’ laboratory values (eg, PT, PTT) to address acute adjustments to the patient’s medical regimen when VKA therapy is resumed.

Postanesthesia care unit nurses may be involved in administering either UFH or LMWH. The nurse should verify medication orders with a pharmacist. Furthermore, nurses should understand why the agent was ordered and review pertinent laboratory results before administering additional doses. Finally, the nurse must clearly document all doses administered.

**CONCLUSION**
To summarize the clinical practice guidelines for antithrombotic therapy from the viewpoint of perioperative nursing, it is important to identify which patients are taking VKA or are undergoing antiplatelet therapy before surgery. This identification must occur in a timely fashion to prevent adverse outcomes for the patient and disruption of the surgical schedule. Part of the identification process includes knowing the patient’s underlying pathology and determining the patient’s level of risk for either bleeding or experiencing a thromboembolic event. The type of therapy directs practitioners regarding the need for and frequency of laboratory monitoring. Perioperative nurses should be familiar with the various coagulation tests available and schedule procedures in a manner that allows sufficient time to review any laboratory data. Communication of clinical information among all members of the health care team about patients taking VKA remains a priority to reduce risk of hemorrhage or untoward thromboembolic events.

**Editor’s note:** The views expressed are those of the authors and do not reflect the official policy...
or position of the Uniformed Services University of the Health Sciences, the Department of the Defense, or the US Government.

References


Rodney W. Hicks, PhD, RN, FNP-BC, FAANP, FAAN, is a nurse researcher and consultant, Lubbock, TX. Dr Hicks has no declared affiliation that could be perceived as posing a potential conflict of interest in the publication of this article.

Linda J. Wanzer, MSN, RN, CNOR, COL (Ret), is the director of the Perioperative Clinical Nurse Specialist Program and assistant professor of nursing at the Uniformed Services University of the Health Sciences, Graduate School of Nursing, Bethesda, MD. COL Wanzer has no declared affiliation that could be perceived as posing a potential conflict of interest in the publication of this article.

BradLee Goeckner, MSN, RN, CNOR, LCDR, NC, USN, is a perioperative clinical nurse specialist and directorate of surgical services at NAVMEDCEN, San Diego, CA. LCDR Goeckner has no declared affiliation that could be perceived as posing a potential conflict of interest in the publication of this article.
CONTINUING EDUCATION PROGRAM

www.aorn.org/CE

PERIOD OPERATIVE PHARMACOLOGY: BLOOD COAGULATION MODIFIERS

PURPOSE/GOAL

To educate perioperative nurses about perioperative use of blood coagulation modifiers.

OBJECTIVES

1. Identify types of blood coagulation modifiers.
2. Discuss practice guidelines for perioperative management of antithrombotic therapy.
3. Discuss considerations of vitamin K antagonist (VKA) therapy.
4. Differentiate between low-molecular-weight heparin (LMWH) and unfractionated heparin (UFH).
5. Explain nursing responsibilities for perioperative use of blood coagulation modifiers.

The Examination and Learner Evaluation are printed here for your convenience. To receive continuing education credit, you must complete the Examination and Learner Evaluation online at http://www.aorn.org/CE.

QUESTIONS

1. Blood coagulation modifiers include agents commonly known as
   a. anticoagulants.
   b. antifibrinolytics.
   c. antiplatelet agents.
   d. beta-adrenergic blockers.
   e. thrombolytics.
   a. 1 and 2  b. 3, 4, and 5  c. 1, 2, 3, and 5  d. 1, 2, 3, 4, and 5

2. According to a British guideline, risk originates from the
   a. patient.
   b. disorder.
   c. therapy.
   a. 1 and 2  b. 2 and 4  c. 1, 2, and 3  d. 1, 2, 3, and 4

3. The American College of Chest Physicians (ACCP) practice guidelines provide direction regarding
   a. how to assess the risk for a thromboembolic event against the risk for bleeding.
   b. how to identify which patients may require bridge therapy.
   c. how to select agents to treat specific clinical scenarios.
   d. when to discontinue the agent before surgery.
   e. when to resume the agent after surgery.
   a. 4 and 5  b. 1, 2, and 3  c. 1, 2, 4, and 5  d. 1, 2, 3, 4, and 5
4. For patients on VKA therapy who are considered to be at low risk for a thromboembolic event, the ACCP guidelines recommend resuming the VKA agent between _____________ after the surgical procedure, when there is evidence that adequate hemostasis has been achieved.
   a. the conclusion of the procedure and 12 hours
   b. 12 and 24 hours
   c. 24 and 36 hours
   d. 36 and 48 hours

5. The advantages of LMWH over UFH include that LMWH agents
   1. can be administered in the outpatient setting.
   2. do not necessitate close laboratory monitoring.
   3. have uniform dosing, regardless of age or weight.
   4. achieve peak effect faster.
      a. 1 and 2
      b. 2 and 4
      c. 1, 2, and 3
      d. 1, 2, 3, and 4

6. Characteristics that make it difficult to ascertain the optimal safe dose of UFH include that
   1. after hepatic metabolism, heparin is excreted through the renal system in about six hours.
   2. the half-life of heparin is approximately 60 minutes.
   3. the peak effect of a single IV dose of heparin can occur within two minutes after injection.
      a. 1 and 2
      b. 1 and 3
      c. 2 and 3
      d. 1, 2, and 3

7. The anticoagulant effect of UFH can be rapidly reversed by using
   a. choline salicylate.
   b. papaverine.
   c. protamine sulfate.
   d. streptokinase.

8. Low-molecular-weight heparin agents achieve high bioavailability because these agents bind minimally to plasma proteins or macrophages, thus leaving more agent available for producing the anticoagulation effect.
   a. true
   b. false

9. The risk of excessive bleeding is the greatest adverse event from heparin administration; however, such effects are less likely to occur with
   a. LMWH.
   b. UFH.

10. At the point of intake, information that the nurse should review includes
    1. the patient’s currently prescribed medications.
    2. whether the patient transitioned or should transition to bridge therapy.
    3. whether a VKA agent is on hold and for how long.
    4. underlying conditions that require VKA therapy.
    5. the primary care provider’s and surgeon’s consultation notes that pertain to VKA therapy.
       a. 4 and 5
       b. 1, 2, and 3
       c. 1, 2, 3, and 4
       d. 1, 2, 3, 4, and 5
LEARNER EVALUATION

CONTINUING EDUCATION PROGRAM

Perioperative Pharmacology: Blood Coagulation Modifiers

This evaluation is used to determine the extent to which this continuing education program met your learning needs. Rate the items as described below.

OBJECTIVES

To what extent were the following objectives of this continuing education program achieved?

1. Identify types of blood coagulation modifiers.
   Low 1. 2. 3. 4. 5. High

2. Discuss practice guidelines for perioperative management of antithrombotic therapy.
   Low 1. 2. 3. 4. 5. High

3. Discuss considerations of vitamin K antagonist therapy. Low 1. 2. 3. 4. 5. High

   Low 1. 2. 3. 4. 5. High

5. Explain nursing responsibilities for perioperative use of blood coagulation modifiers.
   Low 1. 2. 3. 4. 5. High

CONTENT

6. To what extent did this article increase your knowledge of the subject matter?
   Low 1. 2. 3. 4. 5. High

7. To what extent were your individual objectives met? Low 1. 2. 3. 4. 5. High

8. Will you be able to use the information from this article in your work setting? 1. Yes 2. No

9. Will you change your practice as a result of reading this article? (If yes, answer question #9A. If no, answer question #9B.)

9A. How will you change your practice? (Select all that apply)
   1. I will provide education to my team regarding why change is needed.
   2. I will work with management to change/implement a policy and procedure.
   3. I will plan an informational meeting with physicians to seek their input and acceptance of the need for change.
   4. I will implement change and evaluate the effect of the change at regular intervals until the change is incorporated as best practice.
   5. Other: _______________________

9B. If you will not change your practice as a result of reading this article, why? (Select all that apply)
   1. The content of the article is not relevant to my practice.
   2. I do not have enough time to teach others about the purpose of the needed change.
   3. I do not have management support to make a change.
   4. Other: _______________________

10. Our accrediting body requires that we verify the time you needed to complete the 1.7 continuing education contact hour (102-minute) program: _______________________

This program meets criteria for CNOR and CRNFA recertification, as well as other continuing education requirements.

AORN is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center’s Commission on Accreditation.
AORN recognizes these activities as continuing education for registered nurses. This recognition does not imply that AORN or the American Nurses Credentialing Center approves or endorses products mentioned in the activity.
AORN is provider-approved by the California Board of Registered Nursing, Provider Number CEP 13019. Check with your state board of nursing for acceptance of this activity for relicensure.

Event: #11509; Session: #0001 Fee: Members $8.50, Nonmembers $17
The deadline for this program is June 30, 2014.
A score of 70% correct on the examination is required for credit. Participants receive feedback on incorrect answers. Each applicant who successfully completes this program can immediately print a certificate of completion.