

# Neuraxial Blockade and Anticoagulation

Recent advances in pharmacology, the formulation and continued evolution of thromboembolism prophylaxis, and increased use of regional anesthesia have created the need for formalized guidance. The American Society of Regional Anesthesia and Pain Medicine (ASRA) have formulated guidelines to assist the anesthesia provider in caring for the patient on anticoagulants. In 1998, the first Consensus Conference on Neuraxial Anesthesia and Anticoagulation was held. A second conference was held on April 25-28<sup>th</sup>, 2002. For updates, the ASRA web site can be accessed at [asra.com](http://asra.com).

Current medications prescribed for thromboprophylaxis for total joint replacement include the following:

## **Unfractionated heparin**

### **Low molecular weight heparin (LMWH)**

- Ardeparin sodium (Normoflo®)
- Dalteparin sodium (Fragmin®)
- Danaparoid sodium (Orgaran®)
- Enoxaparin sodium (Lovenox®)
- Tinzaparin (Innohep®)

## **Warfarin sodium**

Current medications prescribed for thromboprophylaxis for general surgery include the following:

## **Unfractionated heparin**

### **LMWH**

- Dalteparin sodium (Fragmin®)
- Enoxaparin sodium (Lovenox®)

Current medications prescribed for acute coronary syndrome and thromboembolism prophylaxis include the following:

- Enoxaparin sodium (Lovenox®)
- Dalteparin sodium (Fragmin®)
- Tinzaparin (Innohep®)

The major complication of anticoagulant therapy is bleeding. Bleeding can occur in the following anatomical areas: intraspinal, intracranial, intraocular, retroperitoneal, and mediastinal. This may result in hospitalization, transfusion, and death. Factors increasing the risk of bleeding while on anticoagulants include the following: intensity of anticoagulant effect, increased age, female gender, concomitant use of aspirin, history of gastrointestinal bleeding, and duration of anticoagulant treatment.

## **Spinal and Epidural Anesthesia and Hematoma Formation**

Hematoma formation may be the result of a spontaneous bleed or trauma induced by a needle. The epidural space is at particular risk for bleeding due to the rich epidural venous plexus. The anatomy surrounding the spinal cord is relatively fixed. As a result, excessive bleeding into the epidural space may lead to compression, ischemia, nerve trauma, or paralysis. A bleed into the intrathecal space is generally less devastating, secondary to dilution by the cerebral spinal fluid.

In relation to epidural or spinal anesthesia, the risk of epidural hematoma formation is rare. The true incidence is unknown. It has been estimated that the incidence of epidural hematoma formation related to epidural anesthesia is between 1:150,000 and 1:190,000. The estimated incidence for spinal anesthesia is 1:220,000. There is a relationship between regional anesthesia and patients that receive anticoagulant medications during surgery. The incidence of epidural hematoma formation increases to 33:100,000 for epidural anesthesia and 1:100,000 for spinal anesthesia.

### **Risk Factors for the Development of Epidural/Spinal Hematoma**

There are several risk factors for the development of an epidural/spinal hematoma related to the administration of spinal and epidural anesthesia. These factors include the following:

- Anatomic abnormalities of the spinal cord or vertebral column
- Vascular abnormalities
- Pathological or medication related alterations in homeostasis
- Alcohol abuse
- Chronic renal insufficiency
- Difficult and traumatic needle placement
- Epidural catheter removal

### **Signs and Symptoms of Epidural/Spinal Hematoma**

The anesthesia provider should maintain a high index of suspicion when he/she encounters the following signs and symptoms following neuraxial anesthesia/analgesia administration:

- Low back pain (sharp and may radiate)
- Sensory and motor loss (numbness and tingling/motor weakness long after the block should have worn off)
- Bowel and bladder dysfunction
- Paraplegia

In the past, persistent low back pain was thought to be the classic symptom for epidural hematoma. Recent research indicates that the first symptoms may include sensory or motor loss, bowel and bladder dysfunction, numbness and tingling, prolonged motor weakness, and paraplegia.

### **Diagnostic Testing, Treatment and Outcomes**

Diagnosis of an epidural hematoma is made by MRI (preferred), CT scan (may miss a small hematoma), and myelogram. Treatment is emergency decompressive laminectomy with hematoma evacuation. This must be done within 8-12 hours after the onset of signs and symptoms. The outcome is generally poor. There are three factors that affect the patient's recovery from this

devastating complication: size and location of the hematoma, speed of development, and severity/nature of pre-existing neurological problems.

## **General Recommendations Related to the Perioperative Use of Anticoagulants**

Specific recommendations will be reviewed for each classification of anticoagulant. The ASRA does provide some general guidelines concerning perioperative use of anticoagulants.

- Concurrent use of coagulation altering medications may increase the risk of bleeding without altering coagulation tests.
- When providing postoperative analgesia with an epidural catheter, the anesthesia provider should utilize opioids or dilute concentrations of local anesthetic to allow for neurological evaluation.
- Remove epidural catheters at the lowest point of anticoagulant activity. Do not administer additional doses of anticoagulant immediately after epidural catheter removal.
- In high risk cases, the patient should be monitored for neurological complications for 24 hours post epidural catheter removal.
- Frequent evaluation of neurological status of the patient should occur to aid in early detection of an epidural hematoma.

## **Anticoagulants**

Common anticoagulants that may be encountered include the following:

- Antiplatelet medications
- Oral anticoagulants
- Standard heparin
- LMWH
- Thrombolytic and fibrinolytic therapy
- Herbal preparations
- New anticoagulants

### **Antiplatelet Medications**

#### **1. Aspirin:**

Mechanism of action: blocks cyclooxygenase. Cyclooxygenase is responsible for the production of thromboxane A<sub>2</sub>, which induces platelet aggregation causing vasoconstriction.

Duration of action: irreversible effect on platelets. The effect will last for the life of the platelet (7-10 days). Long term use of large doses may lead to a decrease in prothrombin production lengthening the PT (prothrombin time).

#### **2. NSAIDS:**

Mechanism of action: inhibits cyclooxygenase by decreasing tissue prostaglandin synthesis.

Duration of action: reversible. Duration of action depends on half life of the medication and ranges from 1 hour to 3 days.

ASRA recommendations related to aspirin and NSAIDs: either medication alone should not increase the risk of epidural/spinal hematoma. However, dosages should be scrutinized and the duration of therapy should be taken into consideration. There are no laboratory tests that are accepted for preoperative testing. This includes bleeding time. A normal bleeding time does not necessarily indicate normal platelet function. On the other hand, an abnormal bleeding time does not necessarily indicate abnormal clotting function. Careful consideration should be given to other medications/conditions that may affect platelet function. Conditions that should increase the anesthesia providers' concern would include a history of bruising easily, history of excessive bleeding, female gender, and increased age.

### **3. Thienopyridine Derivatives- ticlopidine (Ticlid®) and clopidogrel (Plavix®):**

Mechanism of action: Thienopyridine derivatives interfere with platelet membrane function by inhibition of adenosine diphosphate (ADP) induced platelet-fibrinogen binding.

Duration of action: Thienopyridine derivatives exert an irreversible effect on platelet function for the life of the platelet.

The ASRA recommends the discontinuation of ticlopidine 14 days prior to neuraxial blockade. Clopidogrel should be discontinued 7 days prior to neuraxial blockade. There are no accepted preoperative tests for these two medications.

### **4. Platelet GP IIb/IIIa inhibitors- abciximab (Reopro®), eptifibatide (Integrilin®) and tirofiban (Aggrastat®):**

Mechanism of action: reversibly inhibits platelet aggregation by preventing the adhesion of ligands to glycoprotein IIb/IIIa, including plasminogen and von Willebrand factor.

Duration of action: time to normal platelet aggregation for abciximab is 24-48 hours. For eptifibatide and tirofiban normal platelet function should occur in 4-8 hours.

The ASRA recommends that neuraxial blockade should not be administered until there is normal platelet function. GP IIb/IIIa inhibitors are contraindicated within 4 weeks of surgery. If a GP IIb/IIIa inhibitor is administered postoperatively, after a spinal/epidural anesthetic, there should be careful neurological monitoring of the patient.

## **Oral Anticoagulants**

### **1. Warfarin (Coumadin®)**

Mechanism of action: inhibits vitamin K formation. Depletion of the vitamin K dependent proteins (prothrombin and factors VII, IX and X) occurs.

Duration of action: onset is 8-12 hours with a peak at 36-72 hours.

ASRA recommendations concerning patients using warfarin include the following:

- Evaluate patients for use of concurrent medications that affect clotting, in addition to warfarin.
- Warfarin should be stopped 4-5 days before surgery. A PT and INR should be measured prior to the initiation of neuraxial blockade.

- If the patient has received warfarin preoperatively; PT and INR should be measured if warfarin was administered more than 24 hours prior to surgery or a second dose has been administered.
- Patients receiving postoperative low dose warfarin and epidural analgesia should have PT/INR monitored daily. Epidural catheters should be removed only when INR is < 1.5. Neurological testing should be performed routinely during epidural analgesia and continued for 24 hours after catheter removal if the INR is >1.5. In patients with an INR of >3.0 with an indwelling epidural catheter, the dose of warfarin should be held.

## 2. Standard Heparin

Mechanism of action: binds with antithrombin III, neutralizing the activated factors of X, XII, XI and IX.

Duration of action: for IV heparin the elimination half life is 56 minutes.

For patients receiving heparin, the ASRA has the following recommendations:

- No contraindication to use of neuraxial blocks in patients receiving mini-dose, subcutaneous heparin. The administration of subcutaneous heparin should be held until after block administration. Patient should be screened for concurrent medications that may impact clotting.
- Patients on heparin for more than 4 days should have a platelet count checked prior to the administration of neuraxial blockade secondary to the risk of heparin induced thrombocytopenia.

Precautions for vascular surgery and heparin use are as follows:

- Do not use neuraxial techniques in patients with coagulopathies.
- Heparin administration should be delayed for 1 hour after neuraxial access.
- Indwelling catheters should be removed 2-4 hours after the last dose and reevaluation of coagulation status. Heparin should not be reinitiated until at least 1 hour has passed.
- Patients receiving postoperative analgesia with local anesthetics should be monitored for hematoma formation.
- If a 'bloody tap' is encountered communicate with the surgeon. No data currently supports mandatory cancellation of the surgical case.

## 3. LMWH- ardeparin (Normiflo®), dalteparin (Fragmin®), enoxaparin (Lovenox®), tinzaparin (Innohep®), danaparoid (Organran®):

Variables associated with hematoma formation in patients receiving neuraxial anesthetics and LMWH include: female gender, the elderly, traumatic needle/catheter placement, and an indwelling catheter present during LMWH administration. The risk of epidural hematoma in patients on LMWH has been estimated to be 1:3000 for continuous epidural anesthesia and 1:40,000 for spinal anesthesia.

Mechanism of action: derived from standard heparin but the fragments are 1/3<sup>rd</sup> the size of heparin molecules. LMWH affects factor X. It does not alter the patient's PTT. Currently there are no laboratory measures of its action.

General ASRA recommendations:

- Assess the patient for concurrent medications that may alter coagulation.
- “Bloody tap” does not necessitate the cancellation of surgery. Communicate with the surgeon. LMWH initiation should be delayed for 24 hours.

Preoperative LMWH considerations:

- LMWH should be held for 10-12 hours prior to neuraxial blockade for normal dosing.
- Careful consideration should be given to total dosing and timing of LMWH. A delay of 24 hours prior to the initiation of neuraxial blockade should occur in the following dosing regimens: enoxaparin 1 mg/kg every 12 hours or 1.5 mg/kg every 24 hours; dalteparin 120 U/kg every 12 hours or 200 U/kg every 24 hours; tinzaparin 175 U/kg every 24 hours.

Postoperative LMWH considerations:

- Twice daily dosing- the first dose should not be administered until after 24 hours postoperatively. Indwelling catheters should be removed prior to the initiation of LMWH. If a continuous technique is used, then the catheter should be removed the next day with the first dose of LMWH occurring at a minimum of 2 hours after catheter removal.
- Single daily dosing- the first dose may be given 6-8 hours postoperatively. The second dose should occur at least 24 hours after the first dose. An indwelling epidural catheter should be removed 10-12 hours after the last dose of LMWH. Additional doses of LMWH should not occur for at least 2 hours after catheter removal.

## Thrombolytic and Fibrinolytic Medications

Original recommendations related to the use of these medications were to avoid therapy if neuraxial puncture occurred in the last 10 days. The patient should be queried as to whether they received these medications recently. There is no data that details the length of time that neuraxial puncture should be withheld. If a patient has received a neuraxial block and fibrinolytic/thrombolytic therapy is unexpectedly initiated in the postoperative patient, the patient should be monitored closely for neurological complications. There are no recommendations for the removal of indwelling catheters in patients who unexpectedly receive thrombolytic/fibrinolytic therapy.

## Herbal Preparations

Of concern to the anesthesia provider is the side effect of bleeding in the patient who consumes herbal preparations.

Mechanism of action: varies with the preparation.

- Garlic, ginger, feverfew: inhibit platelet aggregation
- Ginseng: antiplatelet components
- Alfalfa, chamomile, horse chestnut, ginseng: contain a coumadin component
- Vitamin E: reduces platelet thromboxane production
- Ginko: inhibits platelet activating factor

The risk for epidural/spinal hematoma is unknown. Surgical patients should be advised to stop herbal products 5-7 days before surgery. One of the crucial aspects of preoperative assessment is

the concomitant use medications that alter coagulation. In addition, the patient should be screened for bleeding tendencies.

## **New Anticoagulants**

New medications are continually being developed. New thrombin inhibitors such as bivalirudin and lepirudin have no specific recommendations. Caution should be maintained. Careful assessment of confounding medications, patient history, and risk and benefits ratio should be assessed.

Fondaparinux (Arixtra®) is an antithrombotic medication used for DVT prophylaxis. It binds with antithrombin III and neutralizes factor Xa. Peak effect is in 3 hours and half life is 17-21 hours. Its effects are irreversible. Extreme caution should be used with this medication until further clinical experience can help guide the anesthesia provider in the timing of neuraxial blockade. A black box warning similar to that of LMWH is included.

Bivalirudin and lepirudin are two new thrombin inhibitors. Bivalirudin is used in interventional cardiology and lepirudin is used to treat heparin-induced thrombocytopenia. There are no current recommendations for neuraxial blockade.

## **Anticoagulation and Peripheral Nerve Blocks/Plexus Blocks**

It has been recommended that the ASRA guidelines to neuraxial blockade be applied to plexus and peripheral nerve blocks. This appears to be rather restrictive. Good clinical judgment should guide the anesthesia provider's decision making. The most serious complication of non-neuraxial regional techniques in anticoagulated patients is hemorrhage. Case reports highlight major bleeding occurring with psoas compartment and/or lumbar sympathetic blocks. In patients with neurological deficits, it has been found that complete recovery occurred in 6-12 months. The key to the reversal of neurological deficits is the fact that the bleeding occurs in an expandable site as opposed to bleeding associated with neuraxial blockade.

## Current Recommendations for Spinal/Epidural Anesthesia and Anticoagulants

Classification	Medications	Recommendations	Laboratory
<b>Antiplatelet's</b>	Aspirin/NSAIDS Ticlopidine Clopidogrel Abciximab Eptifibatide Tirofiban	None DC 14 days before DC 7 days before Avoid	None None None None
<b>Anticoagulants</b>	Warfarin	DC 4-5 days before Monitor patient for 24 hours post spinal, epidural or removal of catheter	PT/INR prior to needle placement or catheter removal; INR <1.5
<b>Heparin</b>	Subq heparin  IV heparin	Delay until after block  Delay until 1 hour after block; remove catheter 2-4 hours after last dose.	>4 days check plt count  Measure PTT
<b>LMWH</b>	Ardeparin Dalteparin Enoxaparin Tinzaparin Danaparoid	*Preop: block 10-12 hrs after last dose; high dose delay 24 hrs. (enoxaparin)  *Postop: Twice daily dose delay 1 <sup>st</sup> dose for 24 hrs; 2 hr delay after catheter removal. Once daily dose 1 <sup>st</sup> dose 6-8 hrs post op; remove catheter 10-12 hr after last dose and wait 2 hrs till next dose. (enoxaparin)	None
<b>Herbal Preparations</b>	Garlic Ginkgo Ginseng Ginger Feverfew Vitamin E	DC 5-7 days before surgery	None
<b>New Anticoagulants</b>	Bivalirudin Lepirudin  Fondaparinux	Unknown; assess risk  Extreme caution; atraumatic needle placement; no catheters	None  None

## References

Morgan G.E., Mikhail M.S., & Murray M.J. (2006). Spinal, epidural, and caudal blocks. In G.E. Morgan et al *Clinical Anesthesiology*, 4<sup>th</sup> edition. New York: Lange Medical Books.

Clairhout A.J., Johnson M., Radtke J.D., & Zaglaniczny, K.L. (2004). Anticoagulation and spinal and epidural anesthesia. *AANA Journal*. 72.

2<sup>nd</sup> Consensus Conference on Neuraxial Anesthesia and Anticoagulation. April 25-28<sup>th</sup>, 2002.  
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