Anticoagulation and Regional Anesthesia

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Neurologic complications associated with spinal or epidural anesthesia can result from toxic effects of the injected agent, incorrect placement of a needle or catheter causing direct neural tissue damage, infectious agents, or spinal cord compromise because of ischemia or mass effect (Table 1). Adverse events related to the surgical procedure, positioning, or a patient's underlying medical condition can also present as "complications" of regional anesthesia. Anticipation and prevention of complications, along with their early diagnosis and treatment, are the most important factors in dealing with regional anesthetic risks.

Epidural hematomas present as neurologic deficits in the postoperative period as a result of cord compression. Epidural needles and catheters frequently (2.8% to 11.5%) cause vascular trauma associated with minimal bleeding that usually resolves without sequelae. Patients with abnormal coagulation are at increased risk, although coincidental hematoma development is also possible. In a review of the literature between 1906 and 1994, Vandermeulen et al. (1) reported 61 cases of spinal hematoma associated with epidural or spinal anesthesia. In 42 of the 61 patients (68%), the spinal hematomas occurred in association with hemostatic abnormality. Twenty-five of the patients had received IV or subcutaneous heparin, whereas an additional five patients were presumed to have received heparin, as they were undergoing vascular surgery. In addition, 12 patients had evidence of coagulopathy or thrombocytopenia or were treated with antiplatelet medications, oral anticoagulants, thrombolytics, or dextran 70 immediately before or after the spinal or epidural anesthetic. Needle and catheter placement was reported to be difficult in 15 (25%) patients and bloody in 15 (25%) patients. Thus, in 53 of the 61 cases (87%), either a clotting abnormality or needle placement difficulty was present.

Several large studies have confirmed the rarity of permanent neurologic injury associated with centroneuraxial blockade (2,3). However, new challenges in the management of the anticoagulated patient undergoing these procedures have arisen, largely as a result of pharmacologic advances in the prevention of perioperative venous thromboembolism. Risk management is based on appropriate timing of needle placement and catheter removal relative to the timing of anticoagulant drug administration. Familiarity with the pharmacology of antithrombotic agents, clinical studies involving patients undergoing neuraxial blockade while receiving these medications, as well as spinal hematoma case reports, help guide the clinician in management decisions. The following recommendations for managing patients on medications affecting hemostasis are based on the present available knowledge and may change as further information becomes available. Updated (2002) recommendations for neuraxial blockade in the presence of anticoagulant therapy are present on the American Society of Regional Anesthesia (ASRA) web site (www.asra.com).

Antiplatelet Agents

Fully anticoagulated patients are usually not candidates for central neural blockade. However, antiplatelet drugs are often self-administered for pain relief or prescribed for a wide variety of preventative or therapeutic reasons. Although the effects of most nonsteroidal anti-inflammatory drugs are measured in days, the antiplatelet effects of aspirin may last for a week or longer. A large retrospective study suggesting that central neural blockade is safe in patients taking these medications has been confirmed prospectively (4–6). The bleeding time is not a good predictor of the risk of bleeding.

Newer antiplatelet agents such as ticlopidine and clopidogrel (thienopyridine derivatives) and platelet glycoprotein (GP) IIb/IIIa antagonists (abciximab, eptifibatide, and tirofiban) exert diverse effects on platelet function and have not been extensively studied. The relative risk of bleeding with these drugs is unknown; however, case reports of bleeding after administration of these agents suggest that discontinuation of these drugs before performing regional anesthesia might be prudent. The recommended time interval between discontinuation of thienopyridine therapy and neuraxial blockade is 14 d for ticlopidine and 7 d for clopidogrel. For the platelet GP IIb/IIIa inhibitors,

Table 1. Differential Diagnosis of Epidural Abscess, Epidural Hemorrhage, and Anterior Spinal Artery Syndrome

	Epidural Abscess	Epidural Hemorrhage	Anterior Spinal Artery Syndrome
Age of patient	Any age	50% over 50 yr	Elderly
Previous history	Infection*	Anticoagulants	Arteriosclerosis/ hypotension
Onset	1–3 d	Sudden	Sudden
Generalized symptoms	Fever, malaise, back pain	Sharp, transient back and leg pain	None
Sensory involvement	None or paresthesias	Variable, later	Minor, patchy
Motor involvement	Flaccid paralysis, later spastic	Flaccid paralysis	Flaccid paralysis
Segmental reflexes	Exacerbated,* later obtunded	Abolished	Abolished
MRI/CT/Myelogram	Signs of extradural compression	Signs of extradural compression	Normal
Cerebrospinal fluid	Increased cell count	Normal	Normal
Blood data	Rise in ESR	Coagulopathy	Normal

* Infrequent findings.
ESR = erythrocyte sedimentation rate.

the duration ranges from 8 h for eptifibatide and tirofiban to 48 h after abciximab administration. COX-2 inhibitors do not have antiplatelet effects and therefore should not increase the risk of spinal hematoma.

Coumadin Treatment

Coumadin has a good safety profile when used postoperatively in orthopedic patients for antithrombosis (7). A small dose is usually given the day before surgery and continued in the postoperative period. A neuraxial technique can be used, but the catheter should be discontinued before an international normalized ratio (INR) of 1.5 (8). Patients on long-term Coumadin therapy should have a normalized INR before needle placement. The INR is a measure of factor VII activity, which is the factor with the shortest half-life. Therefore, low levels of Factors II, IX, and X may persist when the INR is only slightly prolonged (representing normalization of factor VII) when discontinuing Coumadin therapy. Conversely, the early prolongation of INR in a patient beginning Coumadin therapy can be associated with adequate levels of other factors. Individual factor levels may be helpful.

Unfractionated Heparin

The safety of continuous epidural techniques in the presence of standard unfractionated heparin therapy during major vascular surgery has been well documented (9,10). The recommendations for neuraxial blockade in the presence of unfractionated heparin include the following: 1) wait 1 h after needle/catheter placement before administering heparin; 2) wait 4–6 h after stopping heparin and check aPTT before needle placement; 3) follow aPTT or ACT to avoid excessive heparin effect; and 4) manage catheter removal with the same safety precautions used for placement.

Minidose heparin, usually given twice daily as a 5000-U subcutaneous dose, does not appear to increase the risk of epidural hematoma (11,12). The use of neuraxial techniques in the presence of full heparinization during cardiopulmonary bypass has been studied and in the limited data available has not been associated with a high risk of complications. However, this technique must be considered controversial; important clinical outcome advantages have not been demonstrated.

Fractionated Heparin: Low Molecular Weight Heparin

Several cases of spinal hematoma in patients receiving low molecular weight heparin (LMWH) who underwent epidural or spinal anesthesia have been reported (13–19). A total of 60 cases are in the Medwatch series as of 2002. Enoxaparin is the most commonly prescribed LMWH in the US; the recommended dosage is larger than that used in Europe, and a two dose per day regimen is often recommended. The first dose of LMWH is given 10–12 h after surgery; however, this time interval may decrease as antithrombotic efficacy studies are completed. If LMWH has been administered, a waiting period of 10–12 h is recommended before block placement, and single-shot spinal is considered the safest alternative. Removal of catheters should occur before the first postoperative dosing. The risk of bleeding has been shown to be lower with a single-shot small needle (i.e., spinal). These recommendations are evolving as the use of these drugs expands and new agents are released. Addition of other anticoagulants, such as nonsteroidal anti-inflammatory drugs, increases the risk. Measurement of Xa activity has not been helpful in determining an appropriate course of action.

More recently, the FDA has approved single daily dosing with LMWH in some clinical situations. This option allows more flexibility in managing perioperative regional anesthesia. The European guidelines and clinical experience suggest that an epidural catheter can be maintained postoperatively with single daily

dosing. The catheter should be discontinued 10–12 h after the LMWH dose is given, and the next does should be held at least 2 h after the catheter is removed.

Thrombolytic Agents

Spinal hematomas associated with indwelling epidural catheters and intrathecal bleeding with continuous spinal anesthesia in patients receiving thrombolytic agents (streptokinase, urokinase, t-PA) have been reported (20). Spinal and epidural anesthesia should be avoided in these patients. If a catheter is in place and these agents are given, the safest course would be to allow the effects of the thrombolytic agent to dissipate (at least 24 h) before removing the catheter (21–23).

New Antithrombotics

Newer anticoagulants such as hirudin and the pentasaccharide Fondaparinux (24,25) present serious risks of bleeding. Hirudin is primarily used in patients with heparin allergy and induces irreversible antithrombin activity. Fondaparinux has recently been approved by the FDA for use for perioperative antithrombosis. This highly effective anti-Xa drug is the active portion of the heparin molecule. The current recommendation, based on the pharmacologic profile of this drug, is that no neuraxial technique be performed in its presence. Clinical experience may modify this recommendation.

Herbal Medications

Herbal medications enjoy widespread use in the surgical population (26,27). There are no data suggesting that these medications are a risk when taken alone. However, combination with other anticoagulants has not been studied, and the theoretical risk of bleeding might be increased. Three commonly used herbals are associated with anticoagulant activity: ginseng, garlic, and ginkgo. Both garlic and ginkgo have antiplatelet effects; ginseng has been shown to increase PT/aPTT in animals. Ideally, these herbals should be discontinued preoperatively (garlic 7 days, ginkgo 36 h, ginseng 24 h).

Postoperative Neurologic Complications

The decision to perform spinal or epidural anesthesia/analgesia and the timing of catheter removal in a patient receiving thromboprophylaxis should be made on an individual basis, weighing the small, but definite risk of spinal hematoma with the benefits of regional anesthesia for a specific patient. Alternative anesthetic and analgesic techniques exist for patients who are considered to have an unacceptable risk profile. The patient's coagulation status should be optimized at the time of spinal or epidural needle/catheter placement, and the level of anticoagulation should be carefully monitored during the period of epidural catheterization. Indwelling catheters should not be removed in the presence of therapeutic anticoagulation, as this appears to increase the risk of spinal hematoma. In addition, communication with other clinicians (e.g., surgeons) involved in the perioperative management of patients receiving anticoagulants is essential.

Finally, identification of risk factors and establishment of guidelines will not completely eliminate the complication of spinal hematoma. Vigilance in monitoring is essential to ensure early evaluation of neurologic dysfunction and prompt intervention. Allowing the local anesthetic to wear off before instituting continuous postoperative infusions and using low-dose local anesthetic and/or narcotic infusions (when appropriate) permit ongoing evaluation of the patient's neurologic status. Neurologic complications associated with regional anesthetics are usually discovered after the patient has left the recovery room. Persistent motor blockade during recovery from sensory anesthesia may indicate anterior spinal artery occlusion or spasm. Lack of recovery from spinal or epidural blockade in the expected time interval may indicate spinal cord compression resulting from epidural hematoma. Because early intervention, preferably <12 h, is the key to success in managing these potentially devastating complications, prompt diagnosis (MRI) and early surgical management is indicated.

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