

Regional Anesthesia and newer Anticoagulants

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Introduction

New challenges in the management of the anticoagulated patient undergoing neuraxial blockade have arisen as prophylaxis for perioperative venous thromboembolism were on the rise because of increased awareness. Likewise, as more efficacious anticoagulants and antiplatelet agents have been introduced, patient management has become more complex. We have to be very careful in evolving a strategy to encourage safe and quality patient care.

Anesthetic Management of the Patient Receiving Thrombolytic Therapy

Patients receiving fibrinolytic/thrombolytic medications are at risk of serious hemorrhagic events, particularly those who have undergone an invasive procedure. Second Consensus Conference on Neuraxial Anesthesia and Anticoagulation (April 25-28, 2002) statements are based on the profound effect on hemostasis, the use of concomitant heparin and/or antiplatelet agents (which further increase the risk of bleeding), and the potential for spontaneous neuraxial bleeding with these medications.

Advances in fibrinolytic/ thrombolytic therapy have been associated with an increased use of these drugs, which will require further increases in vigilance. Ideally, the patient should be queried prior to the thrombolytic therapy for a recent history of lumbar puncture, spinal or epidural anesthesia, or epidural steroid injection to allow appropriate monitoring.

Preoperative evaluation should determine whether fibrinolytic or thrombolytic drugs have been used preoperatively, or have the likelihood of being used intraoperatively or postoperatively. Patients receiving fibrinolytic and thrombolytic drugs should be cautioned against receiving spinal or epidural anesthetics except in highly unusual circumstances. Data are not available to clearly outline the length of time neuraxial puncture should be avoided after discontinuation of these drugs.

In those patients who have received neuraxial blocks at or near the time of fibrinolytic and thrombolytic therapy, neurological monitoring should be continued for an appropriate interval. It may be that the interval of monitoring should not be more than two hours between neurologic checks. Furthermore, if neuraxial blocks have been combined with fibrinolytic and thrombolytic therapy and ongoing epidural catheter infusion, the infusion should be limited to drugs minimizing sensory and motor block to facilitate assessment of neurologic function.

There is no definitive recommendation for removal of neuraxial catheters in patients who unexpectedly receive fibrinolytic and thrombolytic therapy during a neuraxial catheter infusion. The measurement of fibrinogen level (one of the last clotting factors to recover) may be helpful in making a decision about catheter removal or maintenance.

Anesthetic Management of the Patient Receiving Unfractionated Heparin

Anesthetic management of the heparinized patient was established over two decades ago. Initial recommendations have been supported by in-depth reviews of case series, case reports of spinal hematoma and the ASA Closed Claims Project.

During subcutaneous (mini-dose) prophylaxis there is no contraindication to the use of neuraxial techniques. The risk of neuraxial bleeding may be reduced by delay of the heparin injection until after the block, and may be increased in debilitated patients after prolonged therapy. Since heparin-induced thrombocytopenia may occur during heparin administration, patients receiving heparin for greater than four days should have a platelet count assessed prior to neuraxial block and catheter removal.

Combining neuraxial techniques with intraoperative anticoagulation with heparin during vascular surgery seems acceptable with the following cautions: 1. Avoid the technique in patients with other coagulopathies. 2. Heparin administration should be delayed for 1 hour after needle placement. 3. Indwelling neuraxial catheters should be removed 2-4 hours after the last heparin dose and the patient's coagulation status is evaluated; re-heparinization should occur one hour after catheter removal. 4. Monitor the patient postoperatively to provide early detection of motor blockade and consider use of minimal concentration of local anesthetics to enhance the early detection of a spinal hematoma. 5. Although the occurrence of a bloody or difficult neuraxial needle placement may increase risk, there are no data to support mandatory cancellation of a case. Direct communication with the surgeon and a specific risk-benefit decision about proceeding in each case is warranted.

Currently, insufficient data and experience are available to determine if the risk of neuraxial hematoma is increased when combining neuraxial techniques with the full anticoagulation of cardiac surgery. Postoperative monitoring of neurologic function and selection of neuraxial solutions that minimize sensory and motor block is recommended to facilitate detection of new/progressive neurodeficits. The concurrent use of medications that affect other components of the clotting mechanisms may increase the risk of bleeding complications for patients receiving standard heparin. These medications include antiplatelet medications, LMWH and oral anticoagulants.

Anesthetic Management of the Patient Receiving Low Molecular Weight Heparin (LMWH)

Anesthesiologists in North America and Europe have done a lot of studies in this and formulated reasonable guidelines for the management of patients undergoing spinal and epidural blocks while receiving perioperative LMWH. Concern remains for higher dose applications, where sustained therapeutic levels of anticoagulation are present. Monitoring of the anti-Xa level is not recommended. The anti-Xa level is not predictive of the risk of bleeding and is, therefore, not helpful in the management of patients undergoing neuraxial blocks.

Antiplatelet or oral anticoagulant medications administered in combination with LMWH may increase the risk of spinal hematoma. Concomitant administration of medications affecting hemostasis, such as antiplatelet drugs, standard heparin, or dextran represents an additional risk of hemorrhagic complications perioperatively, including spinal hematoma. Education of the entire patient care team is necessary to avoid potentiation of the anticoagulant effects. The presence of blood during needle and catheter placement does not necessitate postponement of surgery. However, initiation of LMWH therapy in this setting should be delayed for 24 hours postoperatively. Traumatic needle or catheter placement may signify an increased risk of spinal hematoma, and it is recommended that this consideration be discussed with the surgeon.

Preoperative LMWH

Patients on preoperative LMWH thromboprophylaxis can be assumed to have altered coagulation. In these patients needle placement should occur at least 10-12 hours after the LMWH dose.

Patients receiving higher (treatment) doses of LMWH, such as enoxaparin 1 mg/kg every 12 hours, enoxaparin 1.5 mg/kg daily, dalteparin 120 U/kg every 12 hours, dalteparin 200 U/kg daily, or tinzaparin 175 U/kg daily will require delays of at least 24 hours to assure normal hemostasis at the time of needle insertion.

Neuraxial techniques should be avoided in patients administered a dose of LMWH two hours preoperatively (general surgery patients), because needle placement would occur during peak anticoagulant activity.

Postoperative LMWH

Patients with postoperative initiation of LMWH thromboprophylaxis may safely undergo single-injection and continuous catheter techniques. Management is based on total daily dose, timing of the first postoperative dose and dosing schedule.

Twice daily dosing. This dosage regimen may be associated with an increased risk of spinal hematoma. The first dose of LMWH should be administered no earlier than 24 hours postoperatively, regardless of anesthetic technique, and only in the presence of adequate (surgical) hemostasis. Indwelling catheters should be removed prior to initiation of LMWH thromboprophylaxis. If a continuous technique is selected, the epidural catheter may be left indwelling overnight and removed the following day, with the first dose of LMWH administered at least two hours after catheter removal.

Single daily dosing. This dosing regimen approximates the European application. The first postoperative LMWH dose should be administered 6-8 hours postoperatively. The second postoperative dose should occur no sooner than 24 hours after the first dose. Indwelling neuraxial catheters may be safely maintained. However, the catheter should be removed a minimum of 10-12 hours after the last dose of LMWH. Subsequent LMWH dosing should occur a minimum of 2 hours after catheter removal.

Regional Anesthetic Management of the Patient on Oral Anticoagulants

The management of patients receiving warfarin perioperatively remains controversial. Consensus statements are based on warfarin pharmacology, the clinical relevance of vitamin K coagulation factor levels/deficiencies, and the case reports of spinal hematoma among these patients.

Caution should be used when performing neuraxial techniques in patients recently discontinued from chronic warfarin therapy. The anticoagulant therapy must be stopped, (ideally 4-5 days prior to the planned procedure) and the PT/INR measured prior to initiation of neuraxial block. Early after discontinuation of warfarin therapy, the PT/INR reflect predominantly factor VII levels, and in spite of acceptable factor VII levels, factors II and X levels may not be adequate for normal hemostasis. Adequate levels of II, VII, IX, and X may not be present until the PT/INR is within normal limits.

The concurrent use of medications that affect other components of the clotting mechanisms may increase the risk of bleeding complications for patients receiving oral anticoagulants, and do so without influencing the PT/INR. These medications include aspirin and other NSAIDs, ticlopidine and clopidogrel, unfractionated heparin and LMWH.

For patients receiving an initial dose of warfarin prior to surgery, the PT/INR should be checked prior to neuraxial block if the first dose was given more than 24 hours earlier, or a second dose of oral anticoagulant has been administered.

Patients receiving low dose warfarin therapy during epidural analgesia should have their PT/INR monitored on a daily basis, and checked before catheter removal, if initial doses of warfarin are administered more than 36 hours preoperatively. Initial studies evaluating the safety of epidural analgesia in association with oral anticoagulation utilized mean daily doses of approximately 5 mg of warfarin. Higher dose warfarin may require more intensive monitoring of the coagulation status. As thromboprophylaxis with warfarin is initiated, neuraxial catheters should be removed when the INR is <1.5. This value was derived from studies correlating hemostasis with clotting factor activity levels greater than 40%.

Neurologic testing of sensory and motor function should be performed routinely during epidural analgesia for patients on warfarin therapy. The type of analgesic solution should be tailored to minimize the degree of sensory and motor blockade. These checks should be continued after catheter removal for at least 24 hours, and longer if the INR was greater than 1.5 at the time of catheter removal.

An INR > 3 should prompt the physician to withhold or reduce the warfarin dose in patients with indwelling neuraxial catheters. No definitive recommendation could be made for removal of neuraxial catheters in patients with therapeutic levels of anticoagulation during neuraxial catheter

infusion. Reduced doses of warfarin should be given to patients who are likely to have an enhanced response to the drug.

Anesthetic Management of the Patient Receiving Antiplatelet Medications

Antiplatelet medications, including NSAIDs, thienopyridine derivatives (ticlopidine and clopidogrel) and platelet GP IIb/IIIa antagonists (abciximab, eptifibatide, tirofiban) exert diverse effects on platelet function. The pharmacologic differences make it impossible to extrapolate between the groups of drugs regarding the practice of neuraxial techniques.

There is no wholly accepted test, including the bleeding time, which will guide antiplatelet therapy. Careful preoperative assessment of the patient to identify alterations of health that might contribute to bleeding is crucial. These conditions include a history of easy bruisability/excessive bleeding, female gender, and increased age.

NSAIDs appear to represent no added significant risk for the development of spinal hematoma in patients having epidural or spinal anesthesia. The use of NSAIDs alone does not create a level of risk that will interfere with the performance of neuraxial blocks. At this time, there do not seem to be specific concerns as to the timing of single-shot or catheter techniques in relationship to the dosing of NSAIDs, postoperative monitoring, or the timing of neuraxial catheter removal.

The actual risk of spinal hematoma with ticlopidine and clopidogrel and the GP IIb/IIIa antagonists is unknown. Based on labeling and surgical reviews, the suggested time interval between discontinuation of thienopyridine therapy and neuraxial blockade is 14 days for ticlopidine and 7 days for clopidogrel.

Platelet GP IIb/IIIa inhibitors exert a profound effect on platelet aggregation. Following administration, the time to normal platelet aggregation is 24-48 hours for abciximab and 4-8 hours for eptifibatide and tirofiban. Neuraxial techniques should be avoided until platelet function has recovered. GP IIb/IIIa antagonists are contraindicated within four weeks of surgery. Should one be administered in the postoperative period (following a neuraxial technique), the patient should be carefully monitored neurologically.

The concurrent use of other medications affecting clotting mechanisms, such as oral anticoagulants, unfractionated heparin, and LMWH, may increase the risk of bleeding complications. Cyclooxygenase-2 inhibitors have minimal effect on platelet function and should be considered in patients who require anti-inflammatory therapy in the presence of anticoagulation

New Anticoagulants (Direct Thrombin Inhibitors and Fondaparinux)

New antithrombotic drugs which target various steps in the hemostatic system, such as inhibiting platelet aggregation, blocking coagulation factors, or enhancing fibrinolysis are continually under

development. The most extensively studied are antagonists of specific platelet receptors and direct thrombin inhibitors. Many of these antithrombotic agents have prolonged half-lives and are difficult to reverse without administration of blood components.

Thrombin Inhibitors

Recombinant hirudin derivatives, including desirudin, lepirudin, and bivalirudin inhibit both free and clot-bound thrombin. Argatroban, an L-arginine derivative, has a similar mechanism of action. Although there are no case reports of spinal hematoma related to neuraxial anesthesia among patients who have received a thrombin inhibitor, spontaneous intracranial bleeding has been reported. Due to the lack of information available, no statement regarding risk assessment and patient management can be made.

Fondaparinux

Fondaparinux produces its antithrombotic effect through factor Xa inhibition. The FDA released fondaparinux with a black box warning similar to that of the LMWHs and heparinoids. The actual risk of spinal hematoma with fondaparinux is unknown. Consensus statements are based on the sustained and irreversible antithrombotic effect, early postoperative dosing, and the spinal hematoma reported during initial clinical trials. Close monitoring of the surgical literature for risk factors associated with surgical bleeding may be helpful in risk assessment and patient management.

Until further clinical experience is available, performance of neuraxial techniques should occur under conditions utilized in clinical trials (single needle pass, atraumatic needle placement, avoidance of indwelling neuraxial catheters). If this is not feasible, an alternate method of prophylaxis should be considered.

Summary

Practice guidelines or recommendations summarize evidence-based reviews. However, the rarity of spinal hematoma defies a prospective-randomized study, and there is no current laboratory model. As a result, these consensus statements represent the collective experience of recognized experts in the field of neuraxial anesthesia and anticoagulation. They are based on case reports, clinical series, pharmacology, hematology, and risk factors for surgical bleeding. An understanding of the complexity of this issue is essential to patient management; a "cookbook" approach is not appropriate. Rather, the decision to perform spinal or epidural anesthesia/analgesia and the timing of catheter removal in a patient receiving antithrombotic therapy should be made on an individual basis, weighing the small, though definite risk of spinal hematoma with the benefits of regional anesthesia for a specific patient. Alternative anesthetic and analgesic techniques exist for patients considered an unacceptable risk. The patient's coagulation status should be optimized at the time of spinal or epidural needle/catheter placement, and the level of anticoagulation must 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 significantly increase the risk of spinal hematoma. It must also be remembered that identification of risk factors and establishment of guidelines will not completely eliminate the complication of spinal hematoma. Vigilance in monitoring is critical to allow early evaluation of neurologic dysfunction and prompt intervention. We must focus not only on the prevention of spinal hematoma, but also optimization of neurologic outcome.

References

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