2012-2013

NEWSLETTER

PAKISTAN SOCIETY OF ANAESTHESIOLOGISTS
KARACHI - CHAPTER

Volume 16:
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EDITOR'S NOTE

Introduction of new anticoagulants and the risk of stent thrombosis in patients with perioperative cessation of antiplatelet drugs present a dilemma to anaesthesiologists performing regional anaesthesia. Up-to-date knowledge of the newer generation of antiplatelet agents and different types of stents along with strict adherence to the recommended time intervals between the administration of anticoagulants, regional blocks and the removal of catheters will help reduce the risk of vertebral canal haematoma (VCH) and improve patient outcome.

It's my pleasure to dedicate this issue of the newsletter to present current and updated guidelines on regional anaesthesia and antithrombotic agents published by European Society of Anaesthesiology.

Dr Madiha Hashmi
Editor, PSA Newsletter

CONDUCT OF CENTRAL NEURAXIAL ANAESTHESIA IN PATIENTS RECEIVING ANTICOAGULANT MEDICATIONS

Neuraxial anaesthesia improves patient outcomes in terms of both mortality and morbidity, however, with an increasing number of patients receiving antithrombotic medication; concerns exist about the risk of perineural bleeding complications or neurological damage from compressive vertebral canal haematoma (VCH). Without rapid diagnosis and surgical decompression, VCH may result in permanent neurological damage.

Risk factors:
Risk factors associated with VCH occurring after CNB central neuraxial block were identified by Vandermeulen's review of case reports from 1906 to 1994. Of these 61 cases, 68% occurred in patients either taking anticoagulant drugs (25 received heparin) or those with a coagulopathy. An epidural technique was used in 75 patients, and 66% had an epidural catheter sited. In half of these patients, bleeding occurred immediately after catheter removal, demonstrating that this procedure is as important as catheter insertion. The other major risk factor was technical difficulty with the block.

An understanding of the mechanisms of blood coagulation, the pharmacological properties of the anticoagulant and antiplatelet medications, and also the clinical studies involving patients undergoing central neural block while receiving these medications is paramount in reducing the risk of spinal haematoma in patients undergoing neuraxial block. (Table 1)

Regional anaesthetic management of the patient on oral anticoagulants

- Discontinue oral anticoagulation and verify prothrombin time (PT) normalization before neuraxial block.
- Monitor the PT and INR daily.
- Remove indwelling neuraxial catheters when the INR is <1.5 in order to assure that adequate levels of all vitamin-K-dependent factors are present.
- There is no definitive recommendation for facilitating removal of neuraxial catheters in patients with INR >1.5 but <3.0. Removal of neuraxial catheters should be done with caution and neurological status assessed until the INR has been stabilized.
- In patients with an INR >3, warfarin should be withheld.
- No definitive recommendation can be made regarding the management to facilitate removal of neuraxial catheters (e.g. partial or complete reversal of anticoagulant effect, or discontinuation of warfarin therapy with spontaneous recovery of haemostasis). Individual factor levels might be helpful.

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UPCOMING CONFERENCES / MEETINGS / SYMPOSIA

APICON 2013
Nov 1-3, 2013
Bhurban - Pakistan

7th Dubai Anaesthesia 2014
March 6-8, 2014
Dubai, UAE

Pediatric Anesthesia Conference
May 2-4, 2014
USA

Aspen Anesthesia, 2014
Feburary 1 - 8, 2014
The Westin Snowmass Resort
Snowmass Village, Colorado

Maui Anesthesia, 2014
February 22 - March 1, 2014
The Hyatt Regency Maui
Hawaii

Cancun Anesthesia, 2014
March 29 - April 5, 2014
Cancun, Mexico

AAFPS 2014 2nd Asian Congress on Pain
March 27-30, 2014
Taipei, Taiwan

39th Annual Regional Anesthesiology and Acute Pain Medicine Meeting
April 3-6, 2014
Chicago, United States

NWAC 2014
April 30- May 3, 2014
Vienna, Austria

Euroanaesthesia 2014
May 31-June 3, 2014
Sweden

12th Annual Symposium on Regional Anesthesia, Acute Management and Perioperative Medicine
September 20-21, 2014
NY, USA

German Society of Anaesthesiology And Intensive Care 61st Annual Meeting 2014 (DAC 2014)
May 8-10, 2014
Leipzig

Regional anaesthetic management of the patient receiving unfractionated heparin

- Delay intravenous heparin administration for 1 h after needle/ catheter placement.
- Prolonged anticoagulation appears to increase risk of spinal haematoma formation, especially if combined with other anticoagulants or thrombolytics.
- If systematic anticoagulation therapy is begun with an epidural catheter in place, delay catheter removal for 24 h after heparin discontinuation and after evaluation of coagulation status.
- Remove indwelling catheters 1 h before a subsequent heparin administration.
- There is no contradiction to the use of neuraxial techniques during subcutaneous standard heparin at total doses <10, 000 units daily.
- The risk of spinal haematoma with larger daily subcutaneous doses is unclear; assess on an individual basis and implement more frequent neurological monitoring.
- Serial platelet counts are indicated for patients receiving subcutaneous heparin for >5 days.

Regional anaesthetic management of the patient receiving low molecular weight heparin

Preoperative LMWH

- Perform neuraxial techniques at least 10-12 h after a thromboprophylaxis dose and 24 h after a high therapeutic dose of LMWH.

Postoperative LMWH

- With twice daily dosing, administer the first dose of LMWH no earlier than 24 h after operation, regardless of anaesthetic technique, and only in the presence of adequate haemostasis.
- Remove indwelling catheters before initiation of LMWH thromboprophylaxis.
- The first dose of LMWH administered 2 h after catheter removal and 24 h after needle/catheter placement, whichever is later.
- Once daily dosing requires 6-8 h between needle/catheter placement and the first dose of LMWH. Subsequent dosing should occur no sooner than 24 h later

Regional anaesthetic management of the patient receiving antiplatelet medications

The concurrent use of medications that affect other components of clotting mechanisms, such as oral anticoagulants, standard heparin, and LMWH, increases the risk of bleeding complications for patients receiving antiplatelet agents.

- NSAIDs, by themselves, represent no significant risk for the development of spinal haematoma in patients having epidural or spinal anaesthesia.
- Allow platelet function to recover before neuraxial block after administration of ticlopidine, clopidogrel, and platelet GP IIb/IIIa receptor antagonists.
- The time to normal platelet aggregation after discontinuation of therapy is 14 days for ticlopidine, 5-7 days for clopidogrel, and 7-10 days for prasugrel. For the platelet GP IIb/IIIa inhibitors, the duration ranges from 8 h for eptifibatide and tirofiban to 48 h after abciximab administration.

General Recommendations Related to the Perioperative Use of Anticoagulants:

- Concurrent use of coagulation altering medications may increase the risk of bleeding without altering coagulation tests
- Always refer to latest guideline
- 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. Signs and symptoms include 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 and lastly paraplegia
- Frequent evaluation of neurological status of the patient should occur to aid in early detection of an epidural hematoma

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Table 1: Pharmacological activities of anticoagulants, antiplatelet and thrombolytics agents

Agent haemostasis	Effect on coagulation variables		Time to peak	Time to normal after discontinuation
	PT	APTT		
I.V. heparin	↑	↑↑↑	Minutes	4-6 h
Subcutaneous heparin	—	↑	40-50 min	4-6 h
Low molecular weight heparin	—	—	3-5 h	12-24 h
Warfarin	↑↑↑	↑	4-6 days	4-6 days
Dabigatran	↑	↑↑	2 h	4-7 days
Antiplatelet agents				
Aspirin	—	—	Hours	5-8 days
Other NSAIDs			Hours	1-3 days
Ticlopidine,clopidogrel,prasugrel			Hours	5-14 days
Platelet glycoprotein IIb/IIIa receptor inhibitors			Minutes	8-48 h
Fibrinolytics	↑	↑↑	Minutes	24-36 h

References:
1. Anticoagulants and spinal-epidural anesthesia. AnesthAnalg 1994; 79: 116577.
2. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. Eur J Anaesthesiol 2010;27:999-1015.
3. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). Reg Anesth Pain Med 2010;35:64-101.

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STENT THROMBOSIS VS. SPINAL HAEMATOMA- Balancing The Risks And Benefits

Coronary artery stents, bare-metal (BMS) or drug-eluting (DES), are used in the majority of patients who undergo percutaneous coronary intervention (PCI) to improve symptoms in patients with obstructive coronary artery disease.

Stent restenosis and stent thrombosis are potential complications of coronary artery stenting; their incidence is highest in the first year after PCI. Stent restenosis is defined as gradual re-narrowing of the stented segment that occurs mostly between 3 to 12 months after stent placement and usually presents as recurrent angina but can present as acute MI in approximately 10 percent of patients. In contrast, stent thrombosis is an abrupt thrombotic occlusion of a previously widely patent stent. It is a catastrophic complication that presents as sudden death or large myocardial infarction in most patients.

In order to avoid these complications, almost all patients who receive an intracoronary stent receive dual antiplatelet therapy (DAPT). DAPT is typically the combination of aspirin plus clopidogrel, ticlopidine, prasugrel, or ticagrelor, all of which are referred to as platelet $P2Y_{12}$ receptor blockers. At least **12 months** of DAPT after placement of either bare metal or drug-eluting stents (BMS or DES) is recommended in patients not at high risk of bleeding and in whom surgery requiring discontinuation of DAPT is not anticipated. The minimum duration of uninterrupted therapy (ie, before which every effort to not stop therapy should be made) is **one month** for patients who receive BMS and **six months** for patients who receive DES.

Continuation of antiplatelet therapy in perioperative period becomes a limiting factor for placement of central neuraxial block and deep peripheral nerve blocks due to the risk of bleeding. Factors which increase the risk of vertebral canal haematoma (VCH) include, combination therapy, bloody and traumatic punctures, spinal anomalies, such as spina bifida and Bechterews disease, older patients, female gender and renal failure. Risk of haematoma is lowest in spinal anaesthesia and higher with epidural catheter anaesthesia, and may be more common in lumbar region compared to thoracic neuraxial block. Nearly half of bleeding occurs during removal of an epidural catheter and this procedure should be considered as critical as catheter insertion. The interplay between spinal haematoma and antithrombotic drugs is a challenge for anesthesiologists. The cardinal principle to follow is that the plasma level of drug must be minimal whenever any intervention in spine is being done. These interventions include needle placement, placement of epidural catheter, manipulation of epidural catheter or removal of epidural catheter, and same must be observed for spinal and deep nerve blocks. Smaller the dose and longer delay between drug administration, lower the risk of bleeding. The rule of thumb adopted by most anaesthesiology societies is that the time interval between cessation of medications and neuraxial blockade must be at least two times the elimination half-life of the drug. A comprehensive knowledge of pharmacology of all antithrombotic drugs is mandatory for the anaesthesiologist contemplating the block.
Team approach involving surgeon, cardiologist, anaesthesiologist and intensivists is a must for a successful outcome.

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GUIDELINES

Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology

RECOMMENDED TIME INTERVALS BEFORE AND AFTER NEURAXIAL PUNCTURE OR CATHETER REMOVAL

	Time before puncture/catheter manipulation or removal	Time after puncture/catheter manipulation or removal	Laboratory tests
Unfractionated heparins (for prophylaxis, ≤15 000 IU per day)	4-6 h	1 h	Platelets during treatment for more than 5 days
Unfractionated heparins (for treatment)	i.v. 4–6 h s.c. 8–12 h	1 h 1 h	aPTT, ACT, platelets
Low-molecular-weight heparins (for prophylaxis[b])	12 h	4 h	Platelets during treatment for more than 5 days
Low-molecular-weight heparins (for treatment)	24 h	4 h	Platelets during treatment for more than 5 days
Fondaparinux (for prophylaxis, 2.5 mg per day)	36–42 h	6–12 h	(anti-Xa, standardised for specific agent)
Rivaroxaban (for prophylaxis, 10 mg q.d.)	22–26 h	4–6 h	(PT, standardised for specific agent)
Apixaban (for prophylaxis, 2.5 mg b.i.d.)	26–30 h	4–6 h	?
Dabigatran (for prophylaxis, 150–220 mg)	Contraindicated according to the manufacturer	6 h	?
Coumarins	INR ≤1.4	After catheter removal	INR
Hirudins (lepirudin, desirudin)	8–10 h	2–4 h	aPTT, ECT
Argatroban[c]	4 h	2 h	aPTT, ECT, ACT
Acetylsalicylic acid	None	None	
Clopidogrel	7 days	After catheter removal	
Ticlopidine	10 days	After catheter removal	
Prasugrel	7–10 days	6 h after catheter removal	
Ticagrelor	5 days	6 h after catheter removal	
Cilostazol[c]	42 h	5 h after catheter removal	
NSAIDs	None	None	

DOSE RECOMMENDATIONS FOR VENOUS THROMBOEMBOLISM PROPHYLAXIS IN HIGH-RISK PATIENTS

Generic	Max. prophylactic dose per day
Unfractionated heparin	Heparin (3 × 5000 IU or aPTT in normal reference range)
Certoparin	1 × 3000 anti-Xa U s.c.
Dalteparin	1 × 5000 anti-Xa U s.c.
Enoxaparin	1 × 40 mg s.c.
Nadroparin	2850 anti-Xa U (0.3 ml) or weight-adjusted, max. 5700 anti-Xa U s.c. (0.6 ml)
Reviparin	1 × 1750 anti-Xa IU s.c.
Tinzaparin	1 × 4500 anti-Xa U s.c.
Fondaparinux	1 × 2.5 mg s.c.
Danaparoid	2 × 750 IU s.c.
Desirudin	2 × 15 mg s.c.
Rivaroxaban	1 × 10 mg p.o.
Apixaban	2 × 2.5 mg p.o.
Dabigatran	1 × 220 mg (first dose 110 mg) 1 × 150 mg p.o. in the elderly patient >75 years (first dose 75 mg)

Eur J Anaesthesiol 2010;27:999-1015.

33rd Annual Conference of PSA-Karachi chapter April 13-14, 2013

Courtesy by: **Akhai Pharmaceuticals**