REGIONAL ANAESTHESIA, THERAPY AGAINST PAIN AND COAGULATION DISORDERS

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Introduction

Since the early 80,s most patients having surgery receive prophylaxis against thromboembolism, usually unfractioned or low molecular weight heparins (LMWH).

Recent meta-analyses and large- scale multicenter trials show that LMWH give a significantly lower rate of thromboembolic complications than usual doses (10,000-15,000U) of unfractioned heparins (UFH). Moreover, LMWH make routine prophylaxis simpler, because the approved dosage schedules require only once daily administration and no need for laboratory monitoring.

In the same time, in last decade nomerous studies demonstrated beneficial effects of central regional anaesthetic techniques epidural and spinal anaesthesia in vascular patients, patients with coronary arthery diseases and specialy thoracic surgery patients(1).

Thoracic epidural anaesthesia (TEA) improves cardiac performance, have beneficial effects on oxygen delivery/demand ratio, catecholamines, nitrogen balance and coagulation. In patients at risk of coronary ischemia, TEA should dilate constricted coronary vessels, decrease heart rate and myocardial metabolism and reduce pre and after load (2).

In general hemodynamic satbility and reduced stress response should provide and improve outcome.

Sympatectomy induced by local anesthetic may increase infrainguinal blood flow up to 50% and therefore lower the incidence of reoperation due to inadequate tissue perfusion.

In thoracic surgical patients TEA improve diaphragmatic function, postoperative dynamic pain control, reduce significanly postoperative pulmonary complications.

The most serious complication of central nerve blockade (CNB) but very rare is paraplegia. Reported causes include: cord ischaemia resulting from hypotension, direct needle trauma, infection, injection of neurotoxic chemicals and **spinal haematoma**.

Spinal haematoma

Symptomatic spinal haematoma are exceedingly rare. Reported causes and risk factors include:

- Anticoagulant therapy- approximately 70% of all reported cases
- Major blunt trauma
- Blood dyscrasias
- Vascular spinal anomalies or neoplasms
- Antiplatelet or fibrinolytic therapy
- Needle or catheter insertion into the vertebral canal

Most spinal haematoma complicating epidural block develop in the epidural space, and are commonly attributed to needle or catheter trauma, causing bleeding from large, fragile veins of the epidural venous plexus of Batson.

This mechanism cannot account for bleeding into the subdural or subarachnoid spaces, which is where spinal haematoma usually develop following subarachnoid puncture.

In these cases, bleeding probably originates from the radicular vessels that accopmany each nerve root, the largest being the radicular-medullary artery and vein of Adamkiewicz.

The risk of spinal haematoma complicating anaesthetic practice

When assesing cases of spinal haematoma wich have been reported in association with CNB, it is important to realize the rarity of this complication in conventional anaesthetic practice (3).

Scott and Hibbard 1990. reported only one case after surveying a total of 505000 epidural blocks, while seven separate surveys , comprising over 65000 spinal blocks, failed to isolate a single case(4).

Schmidt and Nolte demonstrated that the highest risk of clinically important spinal bleeding occurs with epidural catheters, the lowest risk with single- shot spinals(5). Based on large mostly retrospective case series the maximum incidence of clinically important spinal bleeding after epidural catheter blocks without specific risk factors is approximalety 1: 190,000-200,000(6).

Aproximately 60-80% of all clinically important episodes of spinal bleeding are associated with haemostatic disordersor a bloody tap.

Removal of epidural catheter carries a significant risk of spinal haematoma. Case series suggest that 30-60% of clinically important spinal haematomas occur after catheter removal (7,8).

Further important risk factors are technical problems, repeated punctures, anatomical problems (M. Bechterew), age of patients and anticoagulants.

Traumatic neuroaxial blockade on itself increases the relative risk of incidence spinal haematoma eleven fold 1.20,000 , 1:29,000 respectively, and anticoagulant LMWH therapy to 1: 10 000 and lower.

The most important way to detect risk factors for spinal haematoma are careful clinical examination, testing for coagulation abnormalities, the use of hight standard technique and protocol.

Anticoagulants

Values of haemostatic parameters allowing institution of CNB

Test	Without problem	Afetr individual evaluation
Protrombin Time	> 50% (INR <1,5)	40-50% (INR 1,5-1,7)
Activated partial Thrombopl. Time	Upper limit of normal	Exceeding upper limit by 1-4 s
Platelet count	>80 000-100 000	50 000-80 000

Vandermuelen et all. 1997.

Low dose heparin therapy (UFH)

The currently recommended regimen fot thromboprophylaxis with UFH for at risk surgical patients is:

Preoperative 2h – 5000 IU subcutaneously

Postoperative 5000 IU subcutaneously every 8-12h untile patient mobile.

UFH have not been associated with more spinal bleeding, if daily doses do not exceed 15000 IU in patients with normal weight, without liver disease and others risk factors.

Despite theese considerations some patient may be overely sensitive even to the low dose heparin. Plasma heparin levels peak at 2-8 hours may show marked variability, sometimes resulting in significant concentrations at 2h. So caution slould be exercised even when neuroaxial block is contemplated in patients on UFH and it may be wise to perform the activated partial thrombplastin time(APTT) before and during the thromboprophylaxis.

LMWH

Unlike conventional heparin, LMWH possess a greater ability to inhibite factor Xa than thrombin, and theoretically present bleeding risk for any given antithrombotic effect. They also only require once daily subcutaneous injection when used as venous thrombo-embolic prophylaxis, because bioavailability approaches 100%, and plasma half-life is 2-4 times longer than that of unfragmented heparin.

After analyzing controlled trials, Bergquist found that no symptomatic spinal haematoma had complicated over 10 000 blocks performed after administration of LMWH. He therefore concluded that this practice was safe (9).

Data from recent large prospective studies with enoxaparine (total number of patients 12,448, dana on file, Rhone Poulenc Rorer) showed that in general surgery about 20% and in orthopedic surgery about 30% of the patients were anaesthetised with CNB.

The mean duration of prophylaxis treatment with LMWH is 7 days in general surgery and 14 days in orthopedic surgery with usual dose od 30 mg / day of enoxaparine. Only two (2) patients with significant spinal bleeding associated with CNB and enoxaparine were reported to the manufacturer. To validate these data Tryba and coworkers have independently analyzed all cases of spinal bleeding with LMWH which have been reported to the Drug Commission of German Physicians. No further spinal bleeding after enoxaparine treatment has been reported. Thus, in Europe the probable incidence of significant spinal bleeding with enoxaparine in patients with CNB is about 1:2,500000.

Experience with higher dosage regimes of LMWH in the USA 60 mg enoxaparine twice daily, has shown an increase of clinically important spinal haematomas. Based on these dana the probable risk of spinal bleeding associated with LMWH and CNB in teh USA is in the range of 1:3000-9000. The important message of this study of hight risk patients (total hip replacement) is that dose only influenced the risk of wound haematomas, but not the risk of thrombotic complications (10).

	Total	1993-98
USA	39	39
Scandinavia	6	5
All other cauntries	6	2

Consistent practice guidelines among European societies have been established.

Recomendations included:

1. A delay in needle or catheter placement of at least 12h after LMWH injection
2. Subsequent administration of LMWH was postponed 8-12h after CNB
3. The catheter should not be removed until at least 12h after the last dose of LMWH
4. Traumatic needle placement resulted in the additional delay in LMWH administration or in use of another thromboprophylactic method.

There are no indications that any of the available LMWH preparations differ significantly in the risk of spinal haematomas.

The thromboembolic prophylaxis with LMWH should be started on the evening before surgery and continued on the evening of the day of surgery.

Spinal and epidural anaesthetic techniques lower the incidence of deep venous thrombosis (DVT)because of vasodilatation and increased venous blood flow in the legs after sympatetic blockfor 45-55%. This moderate effect could be sufficient to prevent DVT could be sufficient to prevent DVT during surgery , so that the first LMWH injection in some patients could be postponed until after the operation (11).

Intraoperative heoarinization

Heparin is often administered during vascular reconstructive surgery, to prevent thromboembolism and graft occlusion, to patients who also benefit from the sympathetic blockade and excellent analgesia resulting from CNB (12,13).

In the three large series, which specifically reported the absence of haematoma complications from 6000 blocks (using catheter techniques) performed prior to vascular surgery, heparin was administred at least 50 min after block insertion, ist effects was monitored via the ACT or APTT and preoperative screening was meticulous.

Intraoperative heparinization is therefore compatible with CNB, but a cautious approach (12,13).

1. Preoperative screenig should be meticulous, and factors such as aspirin ingestion, renal failure, alcoholism and serious conccurent illness, wich predispose to heparin induced bleeding, should be viewed with caution.
2. Heparin should not be administred within 1h of block insertion
3. Larger heparin doses > 5 000 IU and infusions should be monitored
4. Cancellation of surgery following a blood tap should to be considered
5. Catheter should be secured firmly, heparin infusion discontinued at least 2h prior to their removal, and recommenced 1h later.
6. Operator skill is obligatory.

Fibrinolytic agents

Streptokinase, tissue plasminogen activator and urokinase are used in the management of actualy thrombosed limbs, and during vascular surgery. As fibrinolytic therapy has adverse prothrombotic effect, these patients are simutaneously treated with heparin. Therefore, these patients are not good candidates for CNB, they are hight risk patients for development of hemorrhagic complicationsand the official recommendation is to avoid use of these drugs within 10 days of puncture of noncompressible vessels.

Other drugs affecting haemostasis

Another group of drugs that may interfere with safe neuroaxial block are antiplatelet drugs. There are three groups of platelet inhibitors used more frequently.

Inhibitors of cyclooxygenase (aspirin, NSAID) produce a modest inhibition of platelet aggregation by inhibiting enzyme cyclooxygenase and prevents thromboxane synthesis.

However, this is a very mild inhibition as body produces other prothrombotic substances not inhibited by ASA (serotonin, thrombin, epinephrine) (14,15).

Platelet adenosin diphosphate receptor antagonist (ADP) ticlopidin and clopidogrel has plasma half –life of about 7 days , but even after 10-14 days we can stll have a low level inhibition of pletelet aggregation, so during this time it may be prudent not to perform CNB.

Platelet glycoprotein (GP) II B/IIIa receptor antagonist abciximab is usually given intravenously for 24h to patients who underwent high risk PTCA. Abciximab prolongs bleeding time and although its effects last only 2-3 days, low level platelet aggregation blockade can be present for up to 10 days.

In trying to reduce the risk of spinal haematoma in regional epidural anaesthesia with catheter, the following guidelines considere avoiding of medications is proposed:

Tryba, ESRA Varsawa 2001.

1.	Aspirin	> 1gr/day	7 days
2.	Aspirin	300 mg/ day	3 days
3.	Aspirin	100 mg/day	24 hours
4.	NSAID	(COX 1 inhibitors)	1-3 days
5.	NSAID	(COX2 inhibitors) is could be continue till operation	
6.	Ticlopind, Clopidogrel		7-10 days.

Dextran

Dextran are used as plasma expanders, and in the prophylaxis of thromboembolic complications following surgery. Following the infusion of these solutions bleeding time may be prolonged, polymerization of fibrin impaired and plateletfunction reduced.

Dextrans should be avoided as plasma expanders in patients receiving any form of heparin therapy, because of an increased tendency to bleed. This combination has been implicated in a further spinal haematoma complication (16).

Two tests which are based on measurements of viscoelastic properties of blood thromboelstogram TEG and Sonoclot ("time to peak"), may be used to asses platelet function.

Leprudin and recombinat hirudin, a highly specific thrombin inhibitor, are anticoagulants presently used as an alternative to heparin in patients with heparin induced thrombocytopenia.Half- life of these drugs is about 2 hours, so it would be resonable to measure APTT before proceeding with any neuraxial blockade.

So fare there are no reports associated with spinal or epidural haematomas with these antikoagulants.

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