

Neuraxial block in patients with disturbed haemostasis: Brief version with recommendations (June 24,2009)

Scandinavian Society of Anaesthesiology and Intensive Care Medicine Task Force:

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Background for the SSAI recommendations

Perioperative thromboprophylaxis in patients under central neuraxial block (CNB), i.e. spinal (subarachnoid) anaesthesia/analgesia (SPA), continuous spinal analgesia (CSP), epidural anaesthesia/analgesia (EDA), combined SPA+EDA (CSE), has increased the risk of spinal haematoma (SH) and spinal cord damage. Nordic national guidelines on CNB in such patients vary. The Scandinavian Society of Anaesthesiology and Intensive Care Medicine (SSAI) established a task force to develop a Nordic consensus. This document contains brief tabulated consensus statements abstracted from a comprehensive review of the background, reasoning, and literature documentation (Breivik H et al Acta Anaesth Scand 2009). Recommendations are based on best available evidence, which mostly is experts' opinions, i.e. recommendation grade D with evidence category IV (weak evidence) see Table 2.

Indications for central neuraxial block (CNB)

These techniques should be considered when a patient is likely to have a more comfortable perioperative care, reduced perioperative morbidity (lower risk of complications), or reduced perioperative mortality compared with general anaesthesia (GA) and systemic analgesic medication for postoperative pain. Peripheral nerve blocks should also be considered as alternative to CNB. **The more likely CNB causes lower mortality and morbidity, the higher risk of spinal bleeding can be accepted.** **All hospitals practicing CNB must have protocol for handling early signs of intraspinal bleeding.**

Table 1. Surgical and obstetric procedures where CNB may improve perioperative outcome – compared with GA and systemic analgesics

Procedures for which CNB may improve perioperative outcome	Type of CNB ¹	Potential advantages of CNB compared with GA and postoperative opioid and nonopioid analgesia	Less pain, morbidity, mortality	Evidence category
Intraoperative pain (combined with general anaesthesia(GA), if necessary)	EDA SPA	Preventing early postoperative pain Reduce need for anaesthetics and analgesics	Comfort Morbidity	Ia Ia
Severe obstetric pain	EDA CSE/SPA	Optimal pain relief Improved neonatal Apgar and pH	Comfort Morbidity	Ia Ia
Postoperative pain relief (after CNB or CNB+GA for surgery)	EDA	Reduced postoperative pain, especially on moving Early mobilisation and gastrointestinal-recovery Reduced cardiovascular events and renal failure Reduced risk of respiratory failure Reduced risk of chronic pain after surgery	Comfort Morbidity Morbidity/Mortality Morbidity/Mortality Morbidity	Ia Ia Ia Ia III
Caesarean section	SPA/EDA	Avoidance of airway complication in the mother Maternal mortality reduced	Morbidity Mortality	IIb III
Hysterectomy	SPA	Less risk of chronic postoperative pain	Morbidity	III
TURProstate	SPA/EDA	Early detection and treatment of TURP syndrome	Mortality	IIb
Vascular surgery (extracranial)	EDA/SPA	Less graft occlusion, cardio-pulmon/renal complication	Morbidity	IIb
Alternative to (or combined) GA in pats for intermediate-high risk non-cardiac surgery	SPA/EDA	Reduced risk of cardiopulmonary complication Reduced 30 days mortality	Morbidity Mortality	Ia IIb
Tetraplegia+operation in the pelvic region	SPA/EDA	Inhibition of sympathetic hyper-reflexia	Morbidity Mortality	III IV

¹NOTE: SPA and EDA are not uniform terms: Low dose local anaesthetic drugs combined with an opioid and an alfa₂-receptor agonist, and with EDA continued after major surgery may entail more benefits on postoperative morbidity than single shot SPA or EDA. In the following text, a “strong indication” implies an indication with at least likely reduced perioperative morbidity

Table 2The grading scheme and hierarchy of evidence used in this guideline. Adapted from Eccles and Mason (2001).

Evidence category	Source of evidence:
Ia-b	• meta-analysis of randomised controlled trials (Ia), or • at least one randomised controlled trial (Ib)
IIa-b	• at least one controlled study without randomisation (IIa), or • at least one other type of quasi-experimental study (IIb)
III	non-experimental descriptive studies, comparative studies, correlation studies and case control studies
IV	expert committee reports, opinions or clinical experience of respected authorities
Recommendation grade	Evidence directly based on:
A	Category I evidence
B	• category II evidence, or • extrapolated recommendation from category I evidence
C	• category III evidence, or • extrapolated recommendation from category I or II evidence
D	• category IV evidence, or • extrapolated recommendation from category I, II, or III evidence

Reducing the risk of intraspinal bleeding from CNB in patients on antithrombotic drugs.

In a patient with disturbed haemostasis, CNB carries an increased risk of spinal bleeding. This risk must be carefully evaluated against any benefits from a CNB. In addition to a history of any bleeding tendency, intake of antihaemostatic drugs should be documented. If CNB is indicated in a patient on such medication, the recommended time intervals between neuraxial puncture (or manipulation of a CNB catheter) and drug intake, that are indicated in tables below, will reduce, but not eliminate the risk of spinal bleeding. When difficulties are encountered due to abnormal anatomy, several attempts, or bloody tap, alternatives to CNB should be reconsidered.

Table 3. Recommendations when CNB is indicated: heparins, Xa-inhibitors, vitamin K-antagonists, and platelet inhibitors

Recommended minimum time intervals between the last dose of a certain drug and CNB, and between CNB and first dose or iteration of the drug. **The same recommendations apply for manipulation or removal of an epidural catheter.**

Patients with delayed drug elimination (e.g. renal impairment) may require longer intervals.

Combinations of antithaemostatic drugs increase the risk of bleeding. **All are recommendation grade D, based on experts' opinions (evidence category IV)**

Antithaemostatic drug	Drug ⇒ CNB or catheter manipulation	CNB or cath. manipulation ⇒ Drug
Heparins/Xa-inhibitors	Recommended minimum time-interval	Recommended minimum time-interval
Unfractionated heparin -UFH ≤5000 U(70U/kg)/day	4 h, normal APTT and platelets ¹	1 hour ^{2,3}
>5000 U(70-100U/kg) /day	4 h, normal APTT and platelets ^{1,2}	6 h recommended ³ , 1-2 h is common practice
>100U/kg/day	4 h, normal APTT and platelets ^{1,2}	6 h recommended ³ , EDA the evening before ^{2,3}
Low mol. weight heparin-LMWH (dalteparin or enoxaparin) ≤5000 U or ≤40 mg/day	10 h ⁴	6 h recommended, 2-4 h is common practice ⁵
>5000 U or >40 mg/day	24 h	6 h recommended, 2-4 h is common practice ⁵
Fondaparinux ≤2.5 mg/day (Xa+at)	36 h	6 h
Rivaroxaban pi/oral)(Xa-inh)	18 h	6 h
Apixaban (pi/oral- Xa-inh)	Data not available	6 h
Vitamin K antagonists		
Warfarin; phenprocoumon	(1-4 days, dose-dependent) ⁶ INR ≤1.4-2.2 –see Table 5	Restart after catheter removal ⁶
Platelet inhibitors		
Acetyl salicylic acid (ASA)	12 h in patients on secondary prevention ⁷ 3 days in patients on primary prevention (but 1 week in patients taking doses >1 g/day)	Resume as soon as possible after surgery Resume after surgery
Dipyridamol	No interval required	No interval required
NSAID	See Table 5	2 h ⁸
Clopidogrel	5 ⁹ days (50% of normal platelets have regenerated)	After catheter removal
Ticlopidin	5 ⁹ days (50% of normal platelets have regenerated)	After catheter removal
Prasurgel	?5 days –insufficient experience for recommendation	After catheter removal
Abciximab	48 hours	2 hours
Tirofiban	8 hours	2 hours
Eptifibatid	8 hours	2 hours

¹ **After 5 days of UFH** daily platelet count to rule out Heparin Induced Thrombocytopenia (HIT-II).

² **If surgery requires intraoperative UFH >5000 U**, consider inserting the epidural catheter in the evening before.

³ 1-2 h after CNB, an i.v. dose of 50-100 U/kg is **common practice during extracranial vascular surgery**, but an increased risk of bleeding is possible

⁴ **Emergency cases** on LMWH 2500 U or 20 mg twice daily, and strong indication for SPA (benefit/risk is high (Table 1); e.g. hip fractures, urgent CSection): **0 h (i.e. CNB can be given when indicated)**.

⁵ The balance between risk of bleeding and thrombosis is optimal when the **first dose is given 6 h after end of elective surgery** in nonthrombogenic patients. Major cancer surgery, prolonged surgery in very ill patients, and those > 75 years may need preoperative or intraoperative thromboprophylaxis .

⁶ Start LMWH prophylaxis when INR <2.0 in patients at high risk of a thromboembolic episode (e.g. mechanical mitral valve, aortic valve, recent (<6months) arterial or venous thromboembolic episode).

⁷ In patients with unstable angina and after stroke/TIA, MI, PCI or CABG – see Table 11A.

⁸ In a patient with an indwelling EDA catheter and simultaneous LMWH or other antithaemostatic treatment, NSAIDs should be avoided when catheter manipulations are indicated; COX-2 inhibitor may be preferable.

⁹ 5 days after discontinuing clopidogrel or ticlopidin more than about 50% of platelets have regenerated which is sufficient for primary haemostasis

Table 4. Acceptable number of platelets and levels of INR for CNB at different levels of benefit from CNB: Recommendation grade D.

Test (reference values)	Potential benefit of neuraxial block (see Table 1)					
	Single shot spinal anaesthesia			Epidural and CSE		
	Comfort	Morbidity	Mortality	Comfort	Morbidity	Mortality
Platelet count x10 ³ (150 – 350)	>100	>50	>30	>100	>80	>50
INR (0.9 - 1.2)	≤1.4	<1.8	<2.2	≤1.2	<1.6	<1.8

Table 5. Half lives and recommendations regarding discontinuation of some NSAIDs

Drug	T _{½B}	Recommended interval from last dose till CNB
Diclofenac	1-2 hrs	0 ¹ -12 hrs
Ibuprofen	2 hrs	0 ¹ -12 hrs
Ketoprofen	2 hrs	0 ¹ -12 hrs
Indomethacin	4.5 hrs	0 ¹ -24 hrs
Ketorolac	4-6 hrs	0 ¹ -24 hrs
Naproxen	10-17 hrs	0 ¹ -48 hrs
Lornoxicam	4 hrs	0 ¹ -24 hrs
Piroxicam	10-70 hrs	2 weeks
Tenoxicam	72 hrs	2 weeks
COX-2 specific inhibitors	Various	No clinical effect on platelets

¹No interval in emergency cases.

Table 6. Recommendations when CNB is indicated: Thrombolytics, activated protein C, thrombin inhibitors

– all are recommendation grade D, based on experts' evaluation of pharmacokinetics

Recommended minimum time intervals between the last dose of a certain drug and CNB (left column), and between CNB and first dose or iteration of the drug (right column). The same recommendations apply for manipulation or removal of a catheter.

Patients with delayed drug elimination (e.g. renal impairment) may require longer intervals.

Combinations of antithrombotic drugs increase the risk of bleeding.

Antithrombotic drug	Drug ⇒ CNB or cath. manipulation	CNB or cath. manipulation ⇒ Drug
Thrombolytic drugs		
Streptokinase	24 h ¹	At least 2 hours, but clots are not completely stabilized until about 10 days, and risk of bleeding is probably increased if a thrombolytic drug is given before 10 days
Alteplase	6 h ¹	
Retepase	24 h ¹	
Tenecteplase	Data not available	
Activated protein C		
Drotrecogin alfa	Data not available	12 hours
Thrombin inhibitors (treatment of HIT and VTE-prevention)		
Dabigatran	Data not available	6 hours
Bivalirudin	Data not available;	Data not available;
Argatroban	Data not available;	Data not available;
Lepirudin	Data not available	Data not available
Epoprostenol	Data not available	Data not available

¹Monitoring of fibrinogen levels may be helpful.

Table 7. Properties of some commonly used anti-haemostatic drugs

Drug/class	Target factor(s)	Time to peak effect	Plasma half life	Monitoring	Antidote	Antithrombotic effect
Heparin (i.v.)	II and X (1/1)	< 30 min	1-2 h	APTT	Protamine	Moderate/severe ¹
LMWH (s.c.)	II and X (1/3)	3-4 h	4-7 h	Anti Xa activity	(Protamine)	Moderate/severe ¹
Fondaparinux	X	2-3 h	17-20 h	Anti Xa activity	-	Moderate/severe ¹
ASA	Platelets (irreversible)	~1 h	0.5 h ²	Platelet Function Analyser®/Multiplate®	Desmopressin	Mild
NSAID	Platelets (reversible)	Variable	See table 3	Platelet Function Analyse®r/Multiplate®	Desmopressin	Mild
ADP-receptor blocker (e.g. clopidogrel)	Platelets (irreversible)	3-7 days	8 h ²	Platelet Function Analyser®/Multiplate®	Platelets	Moderate
VKA drugs (e.g. warfarin)	II, VII, IX, and X	5 days (oral intake)	Variable	INR	Vit K/Factor concentrate Human plasma	Moderate at INR 2-3 Severe at INR >3

¹Prophylactic/therapeutic doses

²Duration of haemostatic effects are more dependent on platelet regeneration than drug half life

Combinations of drugs with effects on haemostasis

Theoretically, combinations of drugs with different pharmacodynamics have additive effects on haemostasis. In patients on more than one anti-haemostatic drug, indication for a CNB must be strong.

NSAIDs are used widely as adjuncts to epidural pain treatment in patients on simultaneous LMWH, with no known reports of increased spinal bleeding complications. However, there are no data to support the safety of this practice, either.

Based on pharmacologic properties of the drugs, we recommend paracetamol or a COX-2 inhibitor as safe adjuncts in this context.

However, although low dose ASA and NSAIDs have minor impact on haemostasis themselves, they (including COX-2-inhibitors) may aggravate an already impaired kidney function and thereby cause accumulation of LMWH and other drugs excreted by the kidneys.

Specific serotonin reuptake-inhibiting drugs (SSRI) have some effects on platelet aggregation. Together with ASA or NSAID medication, their effects may be additive, but clinical significance is uncertain.

Certain "health preparations" (in particular omega3 enriched products) are weak cyclooxygenase inhibitors, and have some effects on platelet aggregation. However, this is most likely of no clinical significance, not even in combination with ASA.

Emergency cases

In patients with *low or moderate risk of thromboembolic complications* after surgery, who have taken an ASA or NSAID within the last 12 hours, a CNB may be administered when indicated, but the first dose of LMWH should be delayed until 6 hours after surgery.

If a haemostatic disorder is suspected, *desmopressin* (0.3 µg/kg) may be given in combination with *tranexamic acid*.

In patients at *high risk of thromboembolic complications*, LMWH should be started as soon as possible after admission to the hospital, with half the daily dose (i.e. dalteparin 2500 U or enoxaparin 20 mg) every 12 hours.

In these patients, the CNB may be administered without delay if the patient requires immediate surgery, provided there is a **strong** indication for CNB.

Spinal vessel trauma, and hence risk of bleeding, is minimized if a single shot SPA is chosen, compared with an epidural catheterization.

In *emergency CSections*, the risks of neuraxial complications should be weighted against the risks of general anaesthesia in a particular patient. SPA may be considered if the LMWH dose is ≤2500 U every 12 h and the platelet count is >50 000.

Obstetric patients at term, who receive prophylactic LMWH 5000 U daily, should be given this in divided doses of 2500 U every 12 hr, and CNB for elective CSection or vaginal delivery should wait until 10 hours after the last dose.

Parturients on higher LMWH-doses need special attention by a coagulation specialist.

Reducing risk of neurological complications during CNB

Every department where CNBs are carried out should have strict protocols for handling spinal bleeding (and infections):

Prerequisites for safe CNB practice:

A robust monitoring regime is mandatory for detecting early signs and symptoms of an intraspinal expansion due to bleeding or abscess, and a high alert for verification of diagnosis and evacuation of such an expansion.

A single shot SPA with a small calibre spinal needle carries a lower risk of spinal haematoma than insertion of an epidural catheter.

Therefore, lower platelet counts and higher INR levels are accepted for single shot SPA than other CNB-techniques (Table 4).

If an indwelling epidural catheter is deemed necessary, the following measures facilitate detection of early signs of a haematoma and reduce the risk of permanent neurological damage:

- Make sure that the catheter position is in the segmental epicentre of the operation area.
- Use the lowest possible concentration of a local anaesthetic in the postoperative setting. Combinations with opioids and adrenaline reduce dose requirements of each drug and their dose-related side effects. Adrenaline also increases platelet stickiness and may thereby reduce bleeding tendency.
- Assess leg weakness every 4 hours during ongoing epidural analgesia, and for 24 hours after removal of an epidural catheter.
- Inform the patient of the significance of leg weakness and loss of sensation in the perineum.
- Do not manipulate the catheter when the patient has a haemostatic abnormality.

Take immediate action to verify diagnosis if any clinical sign of intraspinal bleeding occurs (**new or severe back pain, increasing leg weakness, sensory loss, urine retention**):

- Do MRI (or CT if MRI is not possible)
- and consult a neurosurgeon or an orthopaedic surgeon.
- Avoid unnecessary patient transport and loss of time: The most effective treatment is decompressing laminectomy within 12 hours of appearance of symptoms of intraspinal bleeding.

The comprehensive review of background, indications for neuraxial blocks, risk factors of intraspinal bleeding, recommendations for protocols, monitoring regimens, and how to minimize risks and maximize safety of neuraxial blocks is published in **Breivik H et al. Acta Anaesth Scand 2009;53**:(in press).

