

Neuraxial blockade in the anticoagulated patient: Brief version with recommendations

Scandinavian Society of Anaesthesiology and Intensive Care Medicine Guidelines

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Background

An increased use of perioperative thromboprophylaxis and central neuraxial blockade (CNB) for postoperative pain relief have increased the risk of spinal haemorrhage and spinal cord damage. Nordic national guidelines on CNB in anticoagulated patients diverge. Therefore, the Scandinavian Society of Anaesthesiology and Intensive Care Medicine (SSAI) established a task force to propose common Nordic understanding of best practice in this area. This first part of the document contains brief tabulated consensus statements and will be followed by a document describing the background, reasoning, and literature documentation (to be published). Recommendations are based on evidence, and the overall evidence grade (Bell et al. 2005) is indicated. Unfortunately, frequently the best evidence in this area is experts' opinion.

Indications for CNB: Spinal (subarachnoid) anaesthesia/analgesia (SPA), continuous spinal analgesia (CSP), epidural anaesthesia/analgesia (EDA), or combined SPA/EDA (CSE)

These techniques should be considered when the patient is likely to have more comfortable perioperative care, reduced peri- and postoperative morbidity (lower risk of complications), or reduced peri- and postoperative mortality compared with general anaesthesia (GA) and systemic analgesic medication for postoperative pain. Continuous peripheral nerve blocks must also be considered as alternative intra- and postoperative pain relief.

The stronger the indication for CNB (the more likely there are morbidity or mortality benefits from a CNB), the higher risk can be accepted of bleeding into the spinal canal.

Table 1.

Some indications for central neuraxial blockade (CNB) where benefits may be expected

Indication	CNB ¹	Potential advantages	Benefit of CNB	OEG ²
Intraoperative pain (combined with general anaesthesia,(GA) if necessary)	EDA and SPA	Preventing early postoperative pain Reduce need for anaesthetics and analgesics	Comfort Morbidity	A A
Severe obstetric pain	EDA CSE	Optimal pain relief	Comfort Morbidity	A A
Postoperative pain relief (after CNB or CNB+GA for surgery)	EDA	Reduced dynamic acute pain Early mobilisation and gastrointestinal-recovery Less risk of cardiovascular events and renal failure Reduced risk of respiratory failure Reduced risk of chronic pain after surgery	Comfort Morbidity Morbidity/Mortality ³ Morbidity/Mortality ³ Morbidity	A A A A C
Caesarean section	SPA EDA	Avoidance of airway complication in the mother	Morbidity Mortality	A B
Hysterectomy	SPA	Less risk of chronic postoperative pain	Morbidity	D
TURProstate	SPA EDA	Early detection and treatment of TURP syndrome	Morbidity Mortality	E E
Vascular surgery – abdominal aortic and lower extremity	EDA SPA	Reduced risk of graft occlusion, cardio-pulmonary and renal complication	Morbidity	A
Alternative to (or combined with) GA in selected patients with severe cardiopulmonary dysfunction	SPA EDA	Reduced risk of cardiopulmonary complication	Morbidity Mortality	A ³ C-E ³
Tetraplegia+operation in the pelvic region	SPA	Inhibition of sympathetic hyper-reflexia	Morbidity Mortality	E E

¹ NOTE: SPA and EDA are not generic terms: Low dose local anaesthetic drugs combined with an opioid and an alfa₂-receptor agonist, and with EDA continued after major surgery may be more beneficial for postoperative morbidity than single shot SPA or EDA.

² Overall Evidence Grade (A – E, Table 7 (Bell et al 2005)).

³ In recent reviews less morbidity and need for intensive care are documented, mortality-differences are not statistically significant.

In the following text, a “strong indication” implies an indication with at least a likely benefit on morbidity.

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

In a patient with disturbed haemostasis, CNB carries an increased risk of spinal bleeding. This risk has to be carefully evaluated against any possible benefits from a CNB at the preanaesthetic visit. In addition to a history of any bleeding tendency, intake of antihaemostatic drugs should be carefully 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, indicated in tables 2 - 4 below, will reduce, but not eliminate the risk of spinal bleeding.

Table 2. Recommendations on antithrombotic treatment when central neuraxial block (CNB) is indicated –frequently used drugs

Anticoagulant	Drug ⇒ CNB or cath. manipulation	OEG	CNB or cath. manipulation ⇒ Drug	OEG
Unfractionated heparin ≤2500 U-UFH /day ≥2500 U-UFH /day	4 hours, normal APTT and platelets ¹ 4 hours, normal APTT and platelets ^{1,2}	A A	1 hour ² 6 hours ²	E E
Low mol. weight heparin (dalteparin or enoxaparin) ≤5000 U or ≤40 mg/day >5000 U or >40 mg/day	10 hours ^{1,3} 24 hours ¹	A A	6 hours 6 hours	A A
Fondaparinux (Arixtra®) ≤2.5 mg/day	36 hours	A	6 hours	A
Anti-vitamin K drugs				
Warfarin; phenprocoumon	(1-4 days, dose-dependent) ⁴ INR ≤1.4-2.2 –see Table 5	E	INR ≤1.4 ⁴ (restart after catheter removal)	E
Platelet inhibitors				
Acetyl salicylic acid (ASA)	1 day in high risk patients ⁵ 3 days in others (1wk at doses >1 g/day)	A B	1 day	C
Dipyridamol	No interval required	B	No interval required	B
NSAID (see Table 3)	1 day (piroxicam and tenoxicam 2 weeks)	E	2 h	E
Clopidogrel (Plavix®)	5 days	B	0 h After catheter removal	E
Tiklopidin (Ticlide®)	5 days	E	0 h After catheter removal	E

¹ After 5 days of UFH/LMWH, a platelet count is mandatory to rule out Heparin Induced Thrombocytopenia (HIT).

² If surgery requires intraoperative >2500 IU-UFH, consider inserting the epidural catheter in the evening before. It has been common practice in peripheral vascular and abdominal aortic surgery to give about 100 U/kg i.v. intraoperatively, and to our knowledge there has been no apparent increase in neurological complications, but the series have been relatively small.

³ Emergency cases on LMWH ≤2500 U/20 mg twice daily and strong indication for CNB (hip fracture, urgent C-section): 0 hr.

⁴ Start LMWH prophylaxis when INR <2.0.

⁵ High risk patients should maintain their ASA up to the day before surgery. These are patients with:

- Unstable coronary disease
- Previous cardiovascular episode:
 - myocardial infarction
 - coronary intervention:
 - CABG
 - mechanical dilatation
 - bare metal stents
 - drug eluting stents
 - stroke/TIA

CNB is contraindicated when ASA + clopidogrel (or ticlopidin) are maintained up to the day before surgery,

Table 3. Half lives and recommendations regarding discontinuation of some NSAIDs

Drug	T _{½B}	Recommended interval from last dose till CNB	OEG
Ketorolac	4-6 hrs	24 hrs	E
Diklofenac	1-2 hrs	24 hrs	E
Ibuprofen	2 hrs	24 hrs	E
Ketoprofen	2 hrs	24 hrs	E
Indomethacin	4.5 hrs	24 hrs	E
Naproxen	10-17 hrs	24 hrs	E
Piroxicam	10-70 hrs	2 weeks	E
Tenoxicam	72 hrs	2 weeks	E
COX-2 inhibitors		No effects on platelets	A

Table 4. Recommendations on antithrombotic treatment when central neuraxial block (CNB) is indicated – less often used drugs

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) require longer intervals. Combinations of antithrombotic drugs increase the risk of bleeding.		
Anticoagulant	Drug ⇒ CNB or cath. manipulation	CNB or cath. manipulation ⇒ Drug
Thrombolytic drugs		
Streptokinase	24 hours ¹	Clots are not completely stabilized until about 10 days and risk of bleeding is increased if a thrombolytic drug is given before
Alteplase (Actilyse®)	6 hrs ¹	
Retepase (Rapilysin®)	6 hrs ¹	
Tenecteplase (Metalyse®)	Data not available ¹	
Platelet inhibitors		
Abciximab (ReoPro®)	48 hours ²	2 hours
Tirofiban (Aggrastat®)	8 hours ²	2 hours
Eptifibatid (Integrilin®)	8 hours ²	2 hours
Activated protein C		
Drotrecogin alfa (Xigris®)	Data not available	12 hours
Thrombin inhibitors (for treatment of HIT)		
Bivalirudin (Angiox®)	Data not available;	Data not available;
Argatroban (Novastan®)	Data not available;	Data not available;
Levirudin (Refludan®)	Data not available	Data not available
Epoprostenol (Flolan®)	Data not available	Data not available

¹ Monitoring of fibrinogen levels may be helpful.

² Platelet function test (e.g. thromboelastogram) can be used in urgent cases with a and strong indication for CNB
Overall Evidence Grade for given time limits: E

Table 5. Recommended levels of INR or platelet count for neuraxial block at different levels of benefit from CNB

Test (normal range)	Potential benefit of neuraxial block (see Table 1)					
	Single shot spinal anaesthesia			EDA, CSP, 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

All recommendations have OEG = E

If two or more laboratory tests indicate a haemostatic disorder, extra caution is required.

Combinations of drugs with effects on haemostasis

Combinations of drugs with different pharmacodynamics have additive effects on haemostasis and coagulation. In patients on more than one anti-haemostatic drug, the utmost caution when considering a CNB is recommended. NSAID drugs are used widely as adjuncts to epidural pain treatment in patients on simultaneous LMWH, with no 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, paracetamol is probably a safe adjunct in this context, and COX-2 inhibitors do not have a direct effect on platelets. However, although low dose ASA and NSAIDs have minor impact on haemostasis themselves, they (including COX-2-inhibitors) reduce renal function and may cause accumulation of LMWH and other drugs excreted by the kidneys. This is of most clinical importance in patients with already reduced kidney function, to a creatinine clearance of 30 ml/min or less.

Serotonin reuptake-inhibiting drugs (SSRI) have some effects on platelet aggregation. Together with ASA or NSAID medication, this effect may become aggravated somewhat. Some “health preparations” (e.g. Omega-3 enriched products) are weak cyclooxygenase inhibitors, and have some effect on platelet aggregation. However, this is most likely of no clinical significance, not even in combination with ASA or NSAID (OEG = A).

Emergency cases

In patients with low or moderate risk of thromboembolic complications after surgery, who have been treated with ASA or NSAID recently, a CNB may be administered when indicated, and the first dose of LMWH should be delayed until 6 hours after surgery. If a haemostatic disorder is suspected, *desmopressin* (0.3 mikrog/kg) may be

given in combination with *tranexamic acid*. Concerns about associations between desmopressin administration and postoperative myocardial infarction are unfounded.

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. 2500 U/20 mg), repeated 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 the CNB. Spinal vessel trauma, and hence risk of bleeding, is minimized if a single shot SPA is chosen, compared with an epidural catheterization (see below).

In *emergency C-sections*, SPA may be given at any time to patients who are on prophylactic treatment with LMWH 2500 every 12 hr (provided platelet counts are > 50 000).

Obstetric patients, who receive prophylactic LMWH 5000 U daily, should **have** 2500 U every 12 hr at term, and CNB for elective C-section or vaginal delivery should wait until 10 hours after the last dose (Table 2). Parturients on higher LMWH-doses need special attention by coagulation specialist.

Reducing risk of complications during CNB

Prerequisites for safe CNB practice: A robust monitoring regime for detecting early signs and symptoms of intraspinal bleeding and a high alert for verification of diagnosis and evacuation of the haematoma.

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 5).

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 the needed dose of each drug and their dose-related side effects.
- Adding adrenaline also increases platelet stickiness and may reduce risk of bleeding
- Assess leg weakness (e.g. with Bromage scale) 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, or sphincter dysfunction): 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 only effective treatment is decompressive laminectomy within 6-12 hours of appearance of symptoms of intraspinal bleeding.

Table 6. Properties of some commonly used anti-haemostatic drugs

Drug/class	Target factor(s)	Plasma half life	Monitoring	Antidote	Antithaemostatic effect
Heparin	II and X (1/1)	1-2 h	APTT	Protamine	Moderate/severe ¹
LMWH	II and X (1/3)	4-7 h	Anti Xa activity	-	Moderate/severe ¹
Fondaparinux	X	17-20 h	Anti Xa activity	-	Moderate/severe ¹
ASA	Platelets (irreversible)	0.5 h ³	Bleeding time	Desmopressin	Mild
NSAID	Platelets (reversible)	See table 3	Bleeding time	Desmopressin	Mild
ADP-rec. blocker (clopidogrel)	Platelets (irreversible)	8 h ³	Bleeding time	Platelets	Moderate
AVK drugs (e.g. warfarin)	II, VII, IX, and X	Variable	PK INR	Vit K/Factor conc. Human plasma	Severe ²

¹Prophylactic/therapeutic doses ²At therapeutic levels (PK INR >2)

³ Duration of haemostatic effects are more dependent on platelet regeneration than drug half life

Table 7. Grading system of strength of evidence and recommendations

(according to Bell DD, Brindley PG, Forrest D, Al Muslim O, Zygun D: Can J Anaesth 2005;52:309-22)

Grading of evidence	Grading of recommendations
I. Large, randomized trials with clear-cut results; low risk of false-positive (alpha) error or false-negative (beta) error	A. Supported by at least two level I investigations
II. Small, randomized trials with uncertain results; moderate-to-high risk of false positive (alpha) and/or false negative (beta) error	B. Supported by one level I investigation
III. Nonrandomized, contemporaneous controls	C. Supported by level II investigations only
IV. Nonrandomized, historical controls, and expert opinion	D. Supported by at least one level III investigation
V. Case series, uncontrolled studies, and expert opinion	E. Supported by level IV or V evidence