Risk of spinal haemorrhage in neuroaxial blocks given to critically ill patients with direct-acting oral anticoagulants

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Risk of spinal haemorrhage in neuraxial blocks given to critically ill patients treated with direct-acting oral anticoagulants.

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Introduction: neuraxial blocks may reduce morbidity and mortality in patients with various critical conditions, including orthopaedic injuries and abdominal emergencies requiring laparotomy. Patients already treated with New/Direct-acting Oral AntiCoagulatns (NOAC's or DOAC's) present for intensive care more often now that these drugs are routinely prescribed as long-term thrombosis-prophylaxis.

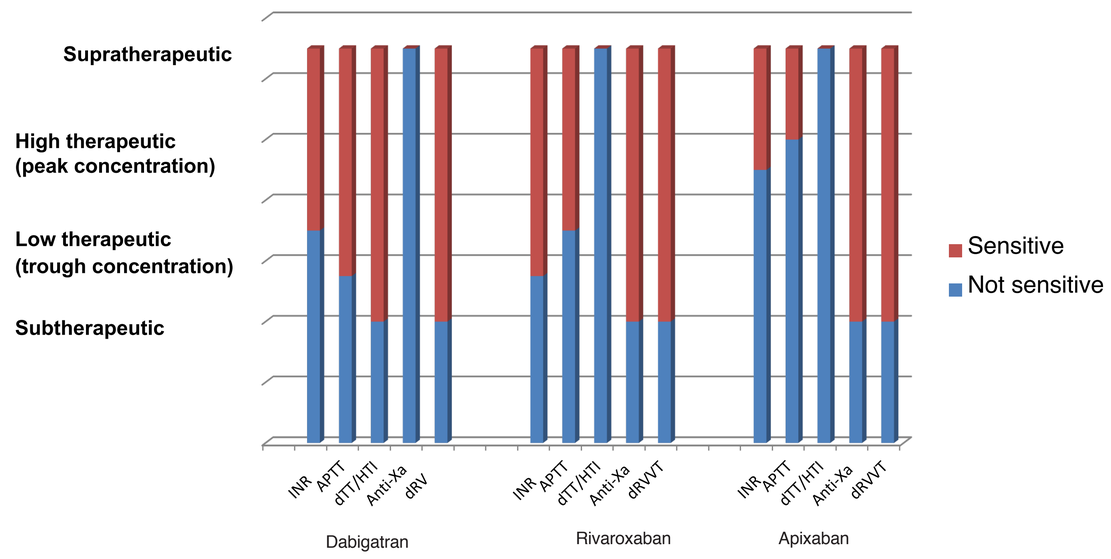
Objectives/Aims: A literature review was conducted using PubMed, with the objective of presenting current guidelines and assays, and explaining how hepatic and renal insufficiency affect their elimination and thereby risk of spinal haemorrhage from neuraxial block.

Results: Guidelines and pharmacokinetics: Current guidelines pertain mainly to elective neuraxial blocks and not those in the critically ill. They rely on data concerning elimination half-lives: after 5 half-lives, 97% of a drug should be eliminated. In particular, dabigatran's half-life is drastically increased by renal failure, which is very relevant in the setting of critical care.

Varying recommendations for time interval (h) between last dose of DOAC and central neuraxial block procedure						
	Renal clearance	$T_{1/2}$ (h)	ASRA	ESA	SSAI	PRAP (Denmark)
Dabigatran (Pradaxa®)	85%	12-16	96-144	34	48-120	75
Apixaban (Eliquis®)	30%	8-15	72-120	26-30	48	40-75
Rivaroxaban (Xarelto®)	30%	5-13	72	~24	48	25-65
ASRA: American Soc. of Regional Anesthesia, ESA: European Society of Anaesthesiology, SSAI: Scandinavian Society of Anaesthesia and Intensive Care, PRAP: Danish Society of Thrombosis and Haemostasis.						

Results: Monitoring: See diagram. APTT and PT/INR are not recommended for monitoring these drugs, although a low aPTT ought to indicate low dabigatran activity. Dabigatran can be monitored by anti-IIa assay, diluted thrombin time and ecarin based assays, while apixaban, rivaroxaban and edoxaban can be monitored by anti-Xa assays. Whether these tests can be used to exclude significant risk of neuraxial block is, however, controversial since most are insensitive at low levels of antithrombotic activity. Assays validated for unfractionated heparin or low molecular weight heparin are not necessarily validated for DOACs.

Which tests for each NOAC?



Swedish Medical Products Agency 2017:1

Results: Clinically relevant interactions: NOAC's have several clinically relevant interactions: for example clarithromycin, amiodarone and verapamil prolong dabigatran's half-life. Case-reports exist describing dabigatran being eliminated by continuous renal-replacement therapy in the ICU.

Results: Antidotes: At present dabigatran is the only NOAC with an available specific antidote (Idarucizumab / Praxbind®). A specific antidote for apixaban and rivaroxaban, andexanet alfa (Ondexxya®), has been granted conditional marketing authorization in the EU. These drugs are currently very expensive. Prothrombin complex concentrate can be given to reverse some of the effects of DOACs, but how much to administer in the context of needing to give a central block to a critically ill patient, and how to assess its effect is unclear.

Results: Estimating the risk of haemorrhagic complications: Limited previous experience of 'non-complicated blocks' in patients recently treated with NOAC may give a false sense of confidence, since the statistical upper-limit of the 95% confidence interval for the actual unknown risk of an event that has not been observed in a series of n observations is 3/n ("Hanley's Rule of Three").

Conclusion(s): In order to assess when it is safe to administer a neuraxial block, clinicians should be well-acquainted with NOAC's pharmacology, and be aware of how this is affected by critical illness.

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