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## Pharmacological thromboprophylaxis and epidural anaesthesia

Neuraxial blocks offer several benefits over General Anaesthesia (GA) in surgical practice, due to their effect on endocrine and metabolic activity during the perioperative period. They are also known to provide improved outcomes with regard to intraoperative complications like bleeding,<sup>[1,2]</sup> high quality postoperative analgesia, greater patient comfort and reduced post-operative morbidity and mortality.<sup>[3]</sup> Few of the studies have shown reduction in Deep vein thrombosis (DVT) with neuraxial block compared to GA.<sup>[4]</sup> These distinct advantages and efficacy of these neuraxial techniques over GA force the anaesthetist to lean more in favor of these blocks, whenever possible.<sup>[5]</sup>

The team of experts appointed to establish a Nordic consensus on recommendations for best clinical practice, observed that there is a strong evidence to suggest that neuraxial blocks improve the patient's comfort and reduce the post-operative morbidity and mortality.<sup>[6]</sup> Also, withholding perioperative epidural analgesia denies the patient, about the possible benefits such as early resolution of post-operative ileus, early ambulation, decreased vascular graft thrombosis, and decreased hospital stay among others.<sup>[7]</sup>

The Japanese study team observes that westernisation of food habits and increased expectancy of life all across the globe and specially in Japan, has led to an increase in the risk of DVT and Pulmonary embolism (PE).<sup>[8]</sup> Their multicentre study revealed that perioperative DVT and PE following joint replacement surgeries and major abdominal surgeries was in the range of 3.36 and 4.41 per 10000 operations respectively.<sup>[8]</sup> The risk of PE following spine deformity surgery was estimated to be as high as 2.2% and it was not influenced by age, gender, intraoperative blood loss, operative time and

number of fusion levels.<sup>[9]</sup>

The pathogenesis of DVT is multifactorial, which includes Virchow's triad of hypercoagulability, venous stasis and endothelial damage.<sup>[10]</sup> The patients with extended recumbence and limited mobility after major surgical procedures are at increased risk of DVT.<sup>[11]</sup>

Though there is a global alarm regarding the increased reporting of epidural hematoma, the real incidence in any part of the globe is really not well known.<sup>[11]</sup> It is an undeniable fact that any incidence of pulmonary embolism following DVT remains one of the commonest preventable causes of death in post-operative patients.<sup>[12]</sup> It is important to know that, there is a strong evidence which indicates that spinal bleeding is influenced by several other risk factors such as elderly patients, patients with hepatic and renal diseases, anatomical variations in spines and spinal canal vessels and subclinical haemostatic disorders including antihaemostatic drugs.<sup>[6]</sup> The other risk factors include traumatic epidural needle or catheter placement, and therapeutic levels of anticoagulation during catheter removal.<sup>[13]</sup>

The perioperative thromboprophylaxis measures include both mechanical and pharmacological methods. The mechanical thromboprophylaxis measures include compression stockings, bilateral intermittent pneumatic calf compression devices, and subsequent monitoring with duplex ultrasonography of lower limbs and when necessary even lung perfusion scintigraphy to confirm the diagnosis, so that appropriate treatment can be initiated when necessary.<sup>[14]</sup>

But the study by Kobayashi and others has revealed that mechanical prophylaxis is inadequate to prevent

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PE and they further suggested that, advanced thromboprophylaxis by anticoagulants is essential.<sup>[8]</sup>

But the administration of pharmacological thromboprophylaxis in surgical patients with cardiovascular diseases or peripheral vascular diseases is on the rise and is posing an everyday challenge to Anaesthesiologist, when administration of epidural analgesia is considered beneficial.<sup>[7]</sup> The wide spread use of central neuraxial block and equally high prevalence of anticoagulation methods in the perioperative period have led to an inevitable overlap of the two practices.<sup>[14]</sup>

The DVT and PE are considered as the most fearsome complications, in view of the high degree of morbidity and even mortality. The incidence of post-operative epidural hematoma is reported very rarely, thus leading to uncertainty of real versus perceived risk of this complication. Hence, the fear of epidural hematoma is one of the major disincentives to start pharmacological thromboprophylaxis in post-operative period. In the world literature, there is

insufficient published data available to precisely set the evidence based guidelines.<sup>[11]</sup> Also the rarity of this complication makes the prospective randomised study very difficult and currently there is no laboratory model available to study this,<sup>[15]</sup> in addition to the ethical issues involved. Even the Angiologists believe that the available data certainly do not support the routine use of pharmacological thromboprophylaxis, at least in identified low DVT risk group. Rather, individualised risk benefit assessment is needed in such patients.<sup>[12]</sup>

It should be realised that spontaneous Epidural hematomas can occur due to intrinsic problems, which appear as a clinically significant neurological deficiency, especially during concomitant thromboprophylaxis. The available evidence suggests a neurological deficiency is observed in 1:1,50,000 epidurals and 1:2,20,000 spinal anaesthetics.<sup>[15]</sup> This incidence is found to be about 1 in 2,00,000 in obstetric patients.<sup>[3]</sup>

A retrospective study of 306 vascular surgery patients

**Table 1: Drugs used for thromboprophylaxis**

Medications	Mechanism of action	Duration of action	Recommendations
<b>Antiplatelets</b>			
Aspirin/NSAIDs	Blocks cyclooxygenase, reduces thromboxane A2, thus inhibiting platelet aggregation	7-10 days (aspirin) 1hr - 3 days NSAIDS	None
Ticlopidine Clopidogrel	Interferes with platelet membrane function by inhibiting platelet fibrinogen bonding	Irreversible effect on platelet function (for life of platelet)	Discontinue clopidogrel – 7 days and Ticlopidine – 14 days
Abciximab Eptifibatide Tirofiban	Reversibly inhibits platelet aggregation by preventing adhesion of ligands (factor VIII & vWF) to glycoprotein IIb/IIIa	Abciximab – 24-48 hrs and 4-8 hrs for Eptifibatide and Tirofiban	Avoid till platelet function returns to normal
<b>Anticoagulants</b>			
Warfarin	Inhibits vitamin K formation and depletion of factors II, VII, IX and X	Onset at 8-12 hrs with peak at 36-72 hrs	Discontinue 4-5 days before. Monitor patient for 24 hr post spinal, epidural or removal of catheter
Heparin Subcutaneous Intravenous	Binds to anti thrombin III, factor II, X	T1/2 (IV) – 56 min. Duration of action intravenous – 2-4 hrs, subcutaneous 6-12 hrs	Delay s.c heparin till block IV- delay until 1 hr after block, remove 2-4 hrs after last dose
Low molecular weight heparin Adreparin Dalteparin Enoxaparin Tinzaparin Danaparoid	Inhibits factor X	Elimination half life – 4-6 hrs, duration of action – 12-24 hrs	Pre op: Nerve blocks 10-12 hrs after last dose: delay for 24 hrs if high dose used Post op: remove catheter 10-12 hrs after last dose twice daily dose, delay first dose for 24 hrs; Once daily dose 1st dose 6-8 hrs post op, 2 hrs delay after catheter removal
<b>New anticoagulant drugs</b>			
Bivalirudin Lepirudin	Direct inhibitor of both free and bound thrombin (factor IIa)	Short half-life – 30 min for bivalirudin, 2 hrs for lepirudin	Unknown, assess risk
Fondaparinux	Inhibits factor Xa	Elimination half-life – 15-17 hrs	Extreme caution; Atraumatic needle placement; no catheters

continuously receiving clopidogrel, did not detect any incidence of neurological complications after epidural catheter placement. As this report is based on small sample size it cannot be considered as recommendation<sup>[7]</sup> and cautious approach may be desirable. But recent surveys are projecting very high incidences. The ever increasing use of anticoagulants either for pre-existing cardiovascular diseases, or as a post-operative thromboprophylaxis, are challenging the anaesthesiologists to update themselves with current guidelines, to minimise or avoid incidences of epidural hematoma and neurological complications.

Among Asian population, it is reported that, the incidence of perioperative DVT and PE undergoing hip surgeries is considered to be very low.<sup>[16]</sup>

The FDA approval of Low molecular weight Heparin (LMWH) in 1993 for perioperative thromboprophylaxis, no doubt has benefitted the patients with regard to PE, but it has also increased the perceived risk of epidural hematoma. The study by Neimark and others observed that prophylactic LMWH in patients undergoing spinal anaesthesia is unnecessary due to higher risk of epidural hematoma.<sup>[17]</sup> It is presumed that a bleed from intrathecal space is likely to be less devastating due to cerebrospinal fluid dilution.

There are no laboratory tests that are generally accepted for preoperative testing of these patients receiving thromboprophylaxis. A normal bleeding time does not necessarily indicate normal platelet function and the contrary is also true. A normal prothrombin time (PT) or International normalised ratio (INR) though used in patients on oral anticoagulants, they cannot be considered as the bench marks. The thromboelastography may be able to detect and quantify the effect of unfractionated heparin.<sup>[18]</sup>

Since minimal risk can never be same as elimination of risk, several issues like duration and reversibility of action of each drug, are to be considered before instituting a neuraxial block in anti-coagulated patients [Table 1]. Simultaneously, it does not appear ethical altogether to avoid a neuraxial technique, which can offer several advantages. Thus it is prudent to weigh the risk and benefits of neuraxial techniques and discuss them openly with the patients

The other options such as continuous peripheral nerve blocks can be used whenever possible. Any signs of

spinal cord compression, such as severe back pain, progressive weakness or numbness of lower limbs, bladder and bowel dysfunction, in the post-operative period should warrant immediate attention. Probably a large multicentre prospective observational study to identify the incidence of epidural hematoma, in various ethnic groups may be beneficial.

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