Regional block and DVT prophylaxis

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The last few years have seen increasing concerns among anaesthetists about the risks of pharmacological prophylaxis for thromboembolic disease. Increased bleeding during or after surgery is one concern, but of greater significance is the possibility of an increased predisposition to haematoma formation when regional block is used. Most of the recent consideration of this problem has been in relation to vertebral canal haematoma formation after central nerve block. Some thought must be given also to the possibility of haematoma formation after peripheral techniques when the target nerve is deeply placed so that pressure cannot be used to control bleeding after needle insertion. However, this review will be focused on vertebral canal haematoma.

Vertebral canal haematoma

Vertebral canal haematoma is a potentially catastrophic complication, because permanent paraplegia will ensue unless the haematoma is both diagnosed and evacuated within 6-8 h. Even though it is a very rare complication, anxiety about it can mean that the patient is denied the benefits of either the regional anaesthetic technique or appropriate DVT prophylaxis. It is thus crucial that concerns about it do not lead to suboptimal management, which may well have greater total risks for the patient. Appropriate advice on the use of spinal or epidural block in patients receiving pharmacological prophylaxis for thromboembolism was published some years ago, but the concerns have been renewed by reports from the US of relatively large numbers of vertebral canal haematomas after spinal or epidural block.

Most cases of vertebral canal haematoma occur spontaneously, with an incidence estimated at only 1 in 1 million per year. Many of these cases are associated with disordered coagulation, which has been identified as one of the major aetiological factors in the cases reported after spinal or epidural block. Technical difficulty during instrumentation of the vertebral canal is another risk factor, with epidural block (especially with catheter insertion) appearing to carry a greater risk than spinal anaesthesia. Catheter removal is an important time of further risk.

It should be emphasized that the review by Vandermeulen and colleagues that produced these conclusions was able to identify only 61 case reports appearing in the literature between 1906 and 1994. However, this was before the widespread use of low-molecular-weight heparin (LMWH) in the UK and before the documentation of more than 40 cases of vertebral canal haematoma occurring in the US in patients receiving enoxaparin. Most cases followed spinal or epidural block, although a few followed diagnostic lumbar puncture. In addition to indicating an association with enoxaparin, the report confirmed the risk factors identified in the earlier review, notably that epidural catheters carried the highest risk and that the time of their removal was as important as the time of their insertion.

This American series is in direct contrast to experience in Europe, where enoxaparin has been available for much longer and only two cases of vertebral canal haematoma have been reported. However, we know of at least two unpublished cases that have occurred in the UK, including one in our own institution. The incidence of vertebral canal haematoma after spinal or epidural block in patients receiving enoxaparin has been estimated (albeit on an almost anecdotal basis) at 1 in 2.25 million in Europe and 1 in 14,000 in the US. Although there are many issues involved, the major contributory factor seems to have been the difference in the recommended dose of enoxaparin in the US. The European dose is only 40 mg once daily, starting 12 h before surgery, so that the peak effect of the drug (4–6 h after administration) will have diminished at the time of block administration and any risk reduced. In the US, the recommended dose was 30 mg twice daily, starting 1 h after surgery. This regimen results in no ‘safe window’ in which to carry out the block or remove an epidural catheter.

Key points
Vertebral canal haematoma is a rare but potentially devastating complication of central neuraxial block.
The main risk factors are clotting abnormalities and technical difficulties with performance of the block.
Most case reports have been associated with the use of low-molecular-weight heparin, thromboprophylaxis and epidural catheter techniques.
The patient’s clotting should be as close to normal as possible when the block is performed or indwelling catheter removed.
Careful planning of the timing of administration of thromboprophylactic drugs is important to minimize the risk of bleeding complications.
It would be easy to dismiss experience in the US as irrelevant to European practice; however, there are some important lessons if the risk of this dreadful complication is to be kept to a minimum. Not least of these lessons is that surgeons and anaesthetists must communicate properly regarding policies for the use of central nerve block and DVT prophylaxis. The following is an overview of the more general position.

- Vertebral canal haematoma is a rare complication of central nerve block, but its serious nature requires that some precaution is taken to minimize its incidence.
- The incidence seems to be related to the degree of coagulation disturbance. Interactions between drugs that affect coagulation – especially non-steroidal anti-inflammatory drugs (NSAIDs) and aspirin – may be particularly important.
- Technical difficulty during needle or catheter insertion has also been implicated in many cases. Therefore, the skill, experience and technique of the anaesthetist may be very relevant.
- The coagulation status of the patient at the time of catheter removal may be as important as that at its insertion.

Against this background, specific aspects of the various pharmacological agents that may be used in thromboprophylaxis will be considered below.

**Drugs used for thromboprophylaxis**

**Warfarin**

Frank anticoagulation is as absolute a contraindication to spinal or epidural block as there is. Most authorities recommend that the international normalized ratio (INR) should be 1.5 or lower for institution of a block or removal of a catheter. However, warfarin is used infrequently for perioperative thromboprophylaxis in the UK, and most patients presenting for anaesthesia are receiving the drug for other indications. Before elective surgery, such patients will have their coagulation managed to balance the risks of bleeding and thrombus formation appropriately. In principle, this involves stopping the warfarin and replacing it with unfractionated or LMWH thromboprophylaxis while the INR is less than 2.0. In most patients, it takes about 4 days for the INR to reach 1.5 after warfarin is stopped and about 3 days for it to return to 2.0 after it is started again.

**Emergency reversal of oral anticoagulant therapy**

If a patient requires emergency surgery and is at high risk of bleeding (particularly intracranial or spinal bleeding), current expert opinion recommends administration of factor IX concentrate (which contains factor II, IX and X) and also factor VIIa concentrate, if it is available. Fresh frozen plasma does not correct factor IX deficiencies, so it is less effective.

**Unfractionated heparin**

Thromboprophylaxis with low-dose (5,000 u) subcutaneous heparin given 2–3 times daily does not usually prolong the activated partial thromboplastin time (APTT), and large numbers of such patients have received spinal or epidural block without sequelae. However, the numbers of patients involved in these studies is small compared with the risk of vertebral canal haematoma. In addition, a transient elevation of the APTT may occur, so some anaesthetists prefer not to institute spinal or epidural block within 4–6 h of a dose, preferring to administer heparin after the block is performed. Similar considerations would apply to catheter removal. Because of the risk of heparin-induced thrombocytopenia (~3% of patients), the platelet count should be checked before performing the block or catheter removal if the patient has been receiving any heparin preparation for more than 48 h.

**LMWH**

The evidence suggests that the standard European dosing regimen (enoxaparin 20–40 mg once daily) is not associated with any increased risk as long as the block is performed, or the catheter removed, 12 h after drug administration. There is increasing evidence that postoperative dosing regimens provide effective thromboprophylaxis, so there is no reason why a first dose should not be given shortly after block administration or catheter removal.

However, current recommendations in the US ([http://www.asra.com/items_of_interest/consensus_statements/)] are more cautious, suggesting that 2 h should elapse before the next dose is given after an uneventful spinal or epidural block and that this interval should be extended to 24 h if the block has been difficult, traumatic or resulted in overt bleeding. These guidelines also recommend removing epidural catheters before initiating LMWH thromboprophylaxis and suggest a very cautious approach if the catheter is not removed.

**New drugs**

**Fondaparinux**

Fondaparinux is a recently licensed synthetic pentasaccharide that selectively inhibits factor Xa by binding to antithrombin III. Peak plasma concentrations are reached 2 h after subcutaneous administration. Its elimination half-life is 17 h in young healthy patients and 21 h in healthy elderly patients. It is further prolonged in patients with renal impairment. Elimination half-life is significantly longer than any of the LMWHs. It has been licensed for thromboprophylaxis in hip and knee arthroplasty and hip-fracture patients. This followed a series of large, prospective, randomized double-blind trials in which it was compared with enoxaparin. It is given 6 h after surgery, which makes decisions with respect to regional anaesthesia easier. However, its long
half-life means that it should be used with caution with indwelling epidural or spinal catheters, which certainly should not be removed within 24 h of a dose. Further experience may suggest that the interval should be even longer than this.

**Ximelagatran**

Ximelagatran is a direct thrombin inhibitor that can be given orally. It is currently under development and yet to receive a product licence. Unlike warfarin, it has predictable pharmacokinetics and no significant drug interactions. It does not require routine monitoring of coagulation and has the potential to replace warfarin in the future. Early clinical studies suggest that it has a thromboprophylactic efficacy comparative with that of enoxaparin in a variety of patient groups with similar rates of bleeding complications. The risk of vertebral canal bleeding in patients on this drug is obviously not known at present, but regional techniques not involving catheters should be safe because the first dose is administered after surgery.

**Antiplatelet agents**

**Aspirin, NSAIDs and dipyridamole**

Much concern has been expressed about the potential for the antiplatelet effect of aspirin, NSAIDs and dipyridamole to increase the risk of vertebral canal haematoma in patients receiving spinal or epidural block. However, there is little evidence to support this concern, although interactions with other agents such as LMWH may occur and should perhaps be avoided.

**Clopidogrel and platelet GP IIb/IIIa receptor antagonists**

Clopidogrel is a thienopyridine derivative that inhibits platelet aggregation mediated by ADP (adenosine diphosphate) and also interferes with platelet-fibrinogen binding. It is now licensed for prevention of thromboembolic events in patients with coronary or cerebrovascular disease, often in combination with low-dose aspirin therapy. Platelet function does not fully return to normal until at least 7 days after cessation of clopidogrel. There have been several case reports of both serious surgical bleeding and vertebral canal haematoma associated with this drug, and it is strongly recommended that clopidogrel is stopped at least 7 days before surgery. If these intervals have not been observed, a careful risk–benefit analysis should be considered before proceeding with central neuraxial block.

The platelet GP IIb/IIIa receptor antagonists abciximab, eptifibatide and tirofiban are used to prevent coronary ischaemic events in high-risk patients. Central neuraxial block should be avoided until platelet aggregation has returned to normal, which will be a minimum of 8 h after tirofiban or eptifibatide and 24–48 h after abciximab administration. The data sheets for these drugs state that they are contraindicated within 4–6 weeks of trauma or major surgery.

**Specific recommendations**

Definitive recommendations should be based on the results of randomized double-blind studies. However, none are available. Given the incidence of vertebral canal haematoma, it is unlikely that such evidence will ever become available. Clinicians should take a common-sense approach to the problem and the evidence reviewed briefly above and practice within a framework of agreed local policies. It is hoped that Table 1 will be of use in the development of such policies. However, it has to be recognized that there are no easy answers to this problem and that individual decisions about specific patients may be needed.

**Obstetric considerations**

It is more difficult to lay down guidelines for the obstetric patient in labour, or presenting for emergency surgery, who has already received a thromboprophylactic drug. The agent used, the dose and the time interval since its last administration should be noted and related to the above recommendations. Any decision should be based on the balance of risks and benefits, which will often require discussion with the patient and with the surgeon. These discussions should be documented fully. Departments of anaesthesia should agree policies with their surgical and obstetric colleagues for dealing with emergency (and elective) situations likely to arise in their local settings.

### Table 1 Options for instituting central nerve block before elective surgery in patients receiving pharmacological thromboprophylaxis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Proceed normally, but remember interactions</td>
</tr>
<tr>
<td>Low-molecular-weight heparin</td>
<td>Administer 12 h beforehand or start after surgery</td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>Either (a) administer at least 4–6 h before block</td>
</tr>
<tr>
<td></td>
<td>(b) delay first dose until after block performed, or until after surgery</td>
</tr>
<tr>
<td></td>
<td>(c) proceed normally, but with caution (see text)</td>
</tr>
<tr>
<td>Warfarin</td>
<td>If INR &lt; 1.5: proceed normally</td>
</tr>
<tr>
<td></td>
<td>If INR &gt; 1.5: either (a) delay surgery</td>
</tr>
<tr>
<td></td>
<td>(b) consider alternative anaesthetic/analgesic technique if surgery urgent</td>
</tr>
<tr>
<td></td>
<td>(c) consider reversal with factor IX concentrate in an emergency (see text)</td>
</tr>
</tbody>
</table>

Similar considerations apply to spinal or epidural catheter removal.

Mechanical methods of DVT prophylaxis (e.g. intermittent calf compression boots or foot pumps) are effective alternatives in any situation where there is a wish to avoid pharmacological methods completely.
These proposals are thought to represent appropriate advice for the experienced anaesthetist. Departments should also ensure that trainees understand the issues and seek advice from a consultant if they are in any doubt. Because many of the reported cases were associated with a ‘difficult’ or ‘traumatic’ procedure, and with disordered coagulation, the need for a cautious, gentle technique is self-evident. When there is difficulty or bleeding during the block procedure (or any other unusual risk factor), it is essential that this is recorded and greater vigilance in regard to monitoring of neurological function ensured during the postoperative period. It may also be advisable to omit or delay the next dose of thromboprophylactic agent. In the face of difficulty occurring during a block procedure, it may even be appropriate to review the situation and switch to an alternative anaesthetic method.

**Combinations of thromboprophylactic drugs**

It is important to recognize that combinations of thromboprophylactic drugs may cause greater disturbance of coagulation and require more caution. The commonest situation is the patient who is already on aspirin and is to undergo an operation where the local protocol would require administration of a heparin preparation. Whether aspirin alone is sufficient as an effective DVT prophylactic agent is doubtful, but there may be no need to give any other agent before surgery, particularly in view of evidence that spinal and epidural block have beneficial effects in preventing postoperative hypercoagulation and reducing the incidence of thromboembolism. For example, profound epidural block maintained for 24 h will reduce the incidence of asymptomatic DVT after lower limb joint replacement surgery to about 25%. Further, the combination of epidural block with aspirin therapy (with or without sequential calf compression) has been shown to produce very low DVT rates. There is a need for further research to define the role of spinal and epidural block, particularly in association with mechanical and pharmacological agents, in preventing DVT and pulmonary embolism after surgery.

**Key references**

- Tryba M, Wedel DJ. Central neuraxial block and low molecular weight heparin (enoxaparine): lessons learned from different dosage regimens in two continents. *Acta Anaesthesiol Scand* 1997; **41**: 100–3

See multiple choice questions 36–38.