Regional anaesthesia in patients taking anticoagulant drugs

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Abstract

Many surgical patients are taking drugs that impair normal coagulation, and this causes concern about the risk of perioperative bleeding events. The anaesthetist is particularly concerned about compressive vertebral canal haematomas, which may occur after spinal or epidural anaesthetic techniques. Fortunately, the risk of this complication is very low. The major risk factors are coagulopathy or technical difficulties with the block. There is also concern about perineural haematomas, which may be associated with peripheral nerve blocks. This article attempts to put the risks of these complications into context, with reference to different classes of anticoagulant drugs.

Keywords Aspirin; epidural; haematoma; low-molecular-weight heparin; warfarin

Royal College of Anaesthetists CPD Matrix: 1A02 and 2G01

Learning objectives

After reading this article, you should be able to:

- appreciate the incidence of vertebral canal bleeding complications associated with central neuraxial block
- understand the relative risk of bleeding complications associated with different classes of anticoagulant drugs
- understand the rationale for the existing guidelines for regional anaesthesia in patients taking drugs that interfere with normal coagulation

The advantages of central neuraxial block (CNB) are well known, but there is increasing concern that devastating vertebral canal bleeding may occur if these techniques are used in patients who are receiving anticoagulant drugs. These concerns are discussed below to help the anaesthetist make risk/benefit analyses of when to proceed with a regional technique in specific patients.

The incidence of vertebral canal haematoma (VCH) is extremely low. Tryba estimated the risk as 1 in 150,000 epidural anaesthetics and 1 in 220,000 spinal anaesthetics, after reviewing 1.5 million patients who had undergone one of the techniques.[1] However, the risk is almost certainly higher in patients who have received drugs that impair coagulation.

In 1994, Vandermeulen carried out a comprehensive literature review to identify case reports of VCH associated with CNB, and found only 61 cases published between 1906 and 1994.[2] Of these cases, 46 (75%) were associated with epidural techniques; 32 involved a catheter and 14 did not. Most of these cases (68%) occurred in patients who were taking anticoagulant drugs (most frequently intravenous unfractionated heparin) or had a coagulopathy. The other common risk factor identified was technical difficulties with block performance. Coagulation abnormalities and/or technical difficulties were associated with more than 87% of these cases.

The Royal College of Anaesthetists National Audit of major complications of CNB estimated that over 700,000 central neuraxial blocks are performed annually in the UK. Eight cases of VCH were reported over the year (six meeting audit inclusion criteria) all occurring after elective surgery in patients with an epidural catheter for postoperative pain management. Seven of these patients had received an antithrombotic drug (warfarin, aspirin and/or low-molecular-weight heparin (LMWH)) either at the time of epidural catheter insertion or removal. Increasing age, female sex, and significant co-morbidities also appeared to be risk factors. The estimate of the incidence of permanent harm from VCH was reported to be approximately 1 in 20,000 for perioperative epidurals, and 1 in 140,000 for all CNB.

Many surgical patients are now taking drugs that affect normal coagulation, which means that we must attempt to stratify the risk associated with each drug. Frequently used drugs that affect coagulation are shown in Table 1.

Thromboprophylaxis

Deep venous thrombosis and pulmonary embolism are common complications associated with surgical procedures, and are a major cause of morbidity and mortality. The risk factors are well known, but it is worth reinforcing that major lower limb or pelvic surgery and trauma put patients at high risk for these events. Malignancy increases the risk by sevenfold. Expert opinion based on extensive research in this area recommends anticoagulant thromboprophylaxis for these high-risk patients.[3] Because these patients will benefit the most from regional anaesthetic techniques we must look at sensible guidelines to allow us to proceed safely.

Central neuraxial block has been shown to significantly reduce the incidence of deep vein thrombosis after orthopaedic surgery, but additional prophylaxis is necessary to reduce the rate to acceptable levels.

Aspirin and non-steroidal anti-inflammatory drugs (NSAIDs)

These drugs impair platelet function by inhibiting platelet cyclo-oxygenase (COX). Aspirin inhibits COX irreversibly, while NSAIDs do so reversibly. This means that the antiplatelet effect of aspirin will persist until a new platelet population is manufactured (which will take at least 7 days), whereas platelet function will return to normal within 24–48 hours after stopping an NSAID. Despite the widespread use of these drugs for many years, there have been only five case reports of VCH in patients receiving aspirin or NSAIDs alone. Therefore, it is safe to proceed with CNB in patients taking these drugs; a view that has been endorsed by the American Society of Regional Anaesthesia.[4]

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Frequently used drugs that affect coagulation

Drug	Indications
Aspirin	Thromboprophylaxis in ischaemic heart disease or CVA
NSAIDs	Analgesics used widely in arthritis
Clopidogrel, Prasugrel & Ticagrelor	Potent antiplatelet activity; used in acute coronary syndrome
Unfractionated heparin	Thromboprophylaxis, therapeutic anticoagulation
Low-molecular- weight heparin	Thromboprophylaxis, therapeutic anticoagulation
Fondaparinux	Thromboprophylaxis
Warfarin	Thromboprophylaxis in atrial fibrillation, prosthetic heart valve, after DVT or PE
Rivaroxaban, dabigatran, apixaban	Thromboprophylaxis for TKR and THR, atrial fibrillation

CVA, cardiovascular accident; DVT, deep venous thrombosis; NSAIDs, non-steroidal anti-inflammatory drugs; PE, pulmonary embolism; THR, total hip replacement/arthroplasty; TKR, total knee replacement.

Table 1

COX-2 inhibitors

Celecoxib, parecoxib and etoricoxib are anti-inflammatory drugs that selectively inhibit COX-2, which is not expressed in platelets. Therefore, these agents do not affect platelet function. Although safe when used alone, they can potentiate the effect of warfarin by increasing the prothrombin time.[5]

Clopidogrel and prasugrel

These thienopyridine derivates are potent antiplatelet agents: ADP-induced platelet aggregation and platelet–fibrinogen binding are inhibited. These effects are irreversible and platelet function will not return to normal until at least 7 days after stopping the drug. Since the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) study was published in 2001, there has been a move to use clopidogrel in combination with aspirin in patients with acute coronary syndrome.[6] However, there have been several reports of increased and even fatal surgical bleeding complications associated with clopidogrel. For example, in one observational study in patients undergoing coronary artery bypass grafting, the re-exploration rate for bleeding in patients taking clopidogrel and aspirin was 10.4% versus 2.2% in those on aspirin alone.[7]

To date, there have been four cases of VCH associated with CNB in patients taking clopidogrel and two cases (one of which was fatal) of major bleeding after lumbar sympathetic block. The risk of VCH in patients on clopidogrel is unknown. The datasheet states that the drug should be discontinued 7 days before surgery, and this interval should also be observed before carrying out any central neuraxial or peripheral block. It is recommended that individual hospitals adopt policies to ensure that clopidogrel and prasugrel are discontinued before surgery. If an antiplatelet effect must be maintained, aspirin can be substituted. Consultation with a cardiologist is recommended before discontinuing clopidogrel or prasugrel in patients with coronary stents.

Ticagrelor

Ticagrelor is a new potent antiplatelet agent licensed for use in acute coronary syndrome and high risk percutaneous coronary intervention. It has a reversible effect on ADP-mediated platelet aggregation and 80% of its effect will wear off within 3 days of discontinuing therapy. It is recommended that it is discontinued for at least 5 days prior to planned invasive procedures to reduce the risk of bleeding complications.

Platelet glycoprotein IIb/IIIa antagonists

Abciximab, eptifibatide and tirofiban are used to prevent coronary ischaemic events in high-risk patients. CNB should be avoided until platelet aggregation has returned to normal, which will take a minimum of 8 hours after tirofiban and eptifibatide and 24–48 hours after abciximab dosing. The datasheets for these drugs state that they are contraindicated within 4–6 weeks of trauma or major surgery.

Dipyridamole

Dipyridamole has antiplatelet and vasodilating actions and is often used in combination with aspirin in the management of cerebrovascular disease. The half-life is approximately 10 hours. There is a lack of data in the literature with regards to regional anaesthesia and dipyridamole and current guidelines suggest that when used alone there is no need to discontinue before CNB.

Unfractionated heparin

This agent has been used for many years, for both thromboprophylaxis and therapeutic anticoagulation. Subcutaneous thromboprophylactic doses have rarely been associated with bleeding complications, and are not considered to significantly increase the risk of VCH. Expert opinion recommends performing CNB 4 hours after administration of unfractionated heparin or giving the drug at least 1 hour after the block has been carried out. Patients who have been receiving the drug for more than 4 days should have a platelet count, because the incidence of heparin-induced thrombocytopenia is up to 3%.

Therapeutic anticoagulation with heparin is a contraindication to regional block. An intravenous heparin infusion should be discontinued for 4 hours, and the activated partial prothrombin time should be normal before attempting a block or removing a catheter. Thoracic epidural analgesia after cardiac surgery with full anticoagulation remains controversial and a review article by Chaney makes some useful recommendations about how to manage this scenario.[8]

Low-molecular-weight heparin (LMWH)

LMWHs have longer half-lives than unfractionated heparin, which makes once-daily administration possible. They have fibrinolytic properties as well as anti-Xa activity when used prophylactically at a low dose.[9] There is no LMWH monitoring test currently available for routine clinical use. More than 40 cases of vertebral canal haematoma following CNB in patients receiving LMWH occurred in North America in the late 1990s. This may have occurred because North American dose guidelines were for twice-daily LMWH administration, which means that there was no 'safe' time to perform a block or remove an epidural catheter. During the same time, no such problem was reported in Europe despite the fact that LMWHs had been