Should antifibrinolytics be used in orthopaedic surgery?

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Greater appreciation of the risks of blood transfusion, coupled with concerns about the future availability and cost of donor blood, have led to increased interest in techniques to reduce transfusion requirements. Aprotinin and tranexamic acid are antifibrinolytic agents which are used to reduce blood loss. In cardiac surgery aprotinin has been shown to reduce blood transfusion requirements and mortality without any increase in thrombotic complications. Although less evidence exists to support the safety and efficacy of tranexamic acid, its use results in a similar reduction in transfusion during cardiac surgery (Hardy, 2001).

HOW DO ANTIFIBRINOLYTICS WORK?

Trauma, blood loss and other stimuli during surgery, such as the use of a tourniquet, can activate the coagulation and inflammatory cascades. This in turn may result in excessive fibrinolysis, platelet activation, clotting factor consumption and prolonged bleeding.

Tranexamic acid is a lysine analogue that occupies the lysine binding site on plasminogen rendering it unable to bind to fibrin. Existing fibrin clots are thus prevented from being lysed. Aprotinin is a serine protease inhibitor. These are naturally occurring proteins that regulate the activity of proteases in numerous processes. Aprotinin exerts its beneficial effect in several ways (Royston, 1998):

1. Mimicking the native plasmin inhibitor alpha-2-antiplasmin thus preventing bleeding associated with excess fibrinolytic activity
2. Inhibition of platelet activation by thrombin at a protease-activated receptor, protecting platelets from excessive consumption and producing a weak anticoagulant effect
3. Anti-inflammatory actions including inhibition of white cell activation and reduced vascular permeability.

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ANTIFIBRINOLYTICS IN ORTHOPAEDIC SURGERY

Several trials have found tranexamic acid to be effective in knee replacement surgery. Benoni and Fredin (1996) conducted a randomized, double-blind study involving 86 patients. Either tranexamic acid 10 mg/kg or placebo was given just before tourniquet deflation and again at 3 hours. The number of patients receiving blood and the total number of units transfused were reduced to one third with tranexamic acid. Total blood loss was reduced and postoperative haemoglobin concentrations were higher in the treatment group. There was no increase in thromboembolic complications.

Aprotinin has been found to be beneficial in pelvic, hip, spinal and orthopaedic cancer surgery (Erstad, 2001). For example, a randomized double-blind trial of 301 patients undergoing primary unilateral hip replacement by Murkin et al (2000) examined aprotinin at three different doses *vs* placebo. Even a single dose of 500 000 units of aprotinin was found to be effective. Blood loss and allogeneic transfusion requirement were reduced and mean postoperative haemoglobin concentrations were higher. Again, no increase in the rate of thromboembolism was found.

CONCLUSION

The prophylactic use of antifibrinolytics is effective in reducing transfusion requirement in orthopaedic surgery. This is unsurprising given the data from cardiac surgery. However, only small numbers of patients have been studied. Administration of aprotinin carries a risk of hypersensitivity reactions and is more costly than tranexamic acid.

Are these concerns outweighed by the potentially beneficial anti-inflammatory effects of aprotinin and the rising cost of blood? Tranexamic acid lacks the anticoagulant effect associated with aprotinin, which may be important in orthopaedic patients. Until more evidence is available the use of these drugs should be targeted to patients at high risk for bleeding and transfusion. HM

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