Forward thinking in orthopaedic surgery prophylaxis

Mark Pownall

INTRODUCTION

Inadequate prophylaxis after orthopaedic surgery continues to put patients at risk of life-threatening thrombosis, Professor Simon Frostick, Professor of Orthopaedics at the University of Liverpool, warned at a debate at the Royal Society of Medicine, London, 3 February 2005.

Clinical practice is improving, Professor Frostick acknowledged in a review of the data on prophylaxis. In 1992, nearly a quarter of surgeons used nothing to prevent thromboembolic events, and only just over a half used pharmacological agents. In a subsequent follow-up survey 5 years later virtually all surgeons used some means of prophylaxis, and more than 85% used pharmaceutical treatments, with three quarters using effective low molecular weight heparins (LMWH).

PROPHYLAXIS: BENEFITS

Prophylaxis is important because deep vein thrombosis (DVT) is common after surgery, particularly orthopaedic surgery, where studies suggest that, if left without prophylaxis, as many as 75% of patients develop a DVT, and a significant percentage of these would develop into potentially fatal pulmonary embolism (Geerts et al, 2004). Professor Frostick revealed that the fatal pulmonary embolism rate in orthopaedic surgery ranges up to 6% in total hip replacements, 0.7% in total knee replacements and 12.9% in proximal femoral fractures (Callum et al, 2000; Geerts et al, 2004).

'Our best estimate is that there are between 100 and 350 pulmonary embolism deaths per year in the UK, and most of these patients probably die unnecessarily,' Professor Frostick said. 'As pulmonary embolism is identified at post-mortem in 80% of cases, and fewer post-mortems are now carried out, these figures are probably an underestimate as many thrombotic deaths are probably missed.'

But patients given prophylactic treatment aimed at preventing venous thromboembolism (VTE) appear to survive better. Three studies of a 5-week course of LMWH after surgery suggested that prophylaxis approximately halved the risk of DVT from 13–38% to 5–18% (Bergqvist et al, 1996; Dahl et al, 1997; Lassen et al, 1998) (*Figure 1*).

PROPHYLAXIS: RISKS

The main adverse effect of prophylaxis to VTE is bleeding, Professor Frostick explained. Warfarin seems to be worse in its bleeding risk than many other drugs, and has been associated with major bleeding in up to 4% of hospital patients (Paiement et al, 1993).

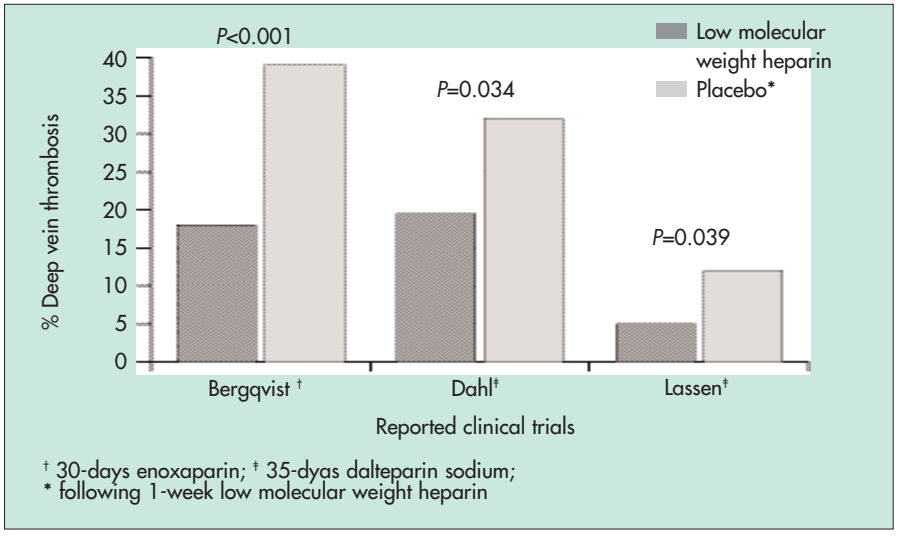
Unfractionated heparins were associated with an increased risk of bleeding compared with placebo in one meta-analysis of 10 000 hip replacement patients (Freedman et al, 2000). Most clinical trials, however, have found no difference in safety of LMWH compared with a variety of controls. There was very little major bleeding in patients given either a LMWH, or fondaparinux (Turpie et al, 2001). Concern was expressed, however, at the potential cost of treatment to reverse the anticoagulant effects of fondaparinux when bleeding complications occur with this agent.

Professor Frostick questioned whether there was any active drug available during surgery if LMWH was given more than a few hours before. Analysis of the risk of thromboembolic events suggested that the fewest number of DVTs occurred if LMWH was given 5–6 hours after surgery. In the UK, only one LMWH, bemiparin, is currently licensed for postoperative initiation in both general (Hidalgo and Figueroa, 2000) and orthopaedic (Navarro-Quilis et al, 2003) surgery.

EVIDENCE FOR OTHER PREVENTION TECHNIQUES?

There are no data to support the use of either mechanical pumps or stockings to prevent DVT in patients undergoing orthopaedic surgery. There was also little evidence of the benefits of mobilization of patients in the immediate

Figure 1. Thromboprophylaxis: benefit of 4–5 weeks low molcular-weight heparins (Bergqvist et al, 1996; Dahl et al, 1997; Lassen et al, 1998)



Mark Pownall is a Medical Writer, London NW5 1TX

post-operative period. Professor Frostick said that seven trials on a total of 419 patients had found no significant reduction in relative risk for low-dose aspirin (Geerts et al, 2004). In Professor Frostick's personal view, the dangers of aspirin as a prophylactic agent far outweigh any possible benefit. This view is supported by Geerts et al (2004). Professor Frostick said the best approach to prophylaxis was the 'just-in-time' concept where the dose of a prophylactic agent such as a LMWH was given as close as possible to the time of surgery.

A desire by orthopaedic surgeons to 'do something' to prevent VTE complications had, in some way, backfired because as many surgeons use aspirin as use LMWHs.

When given, effective treatment may not be administered for long enough and is often stopped prematurely at discharge, typically about 6–7 days after surgery, when there is an increased risk of VTE for up to 35 days after surgery.

Mr Arpit Patel, a locum consultant orthopaedic surgeon at Hinchingbrooke Hospital said postoperative prophylaxis could be extended by patients self-injecting LMWH after discharge. 'Most patients can do it themselves. We categorize patients into medium and high risk, and those considered high risk are given stockings and an injectable LMWH for 4 weeks. In other western European countries patients may self-inject prophylaxis for up to 6 weeks after surgery,' he observed. In Professor Frostick's view, few orthopaedic surgeons are using extended prophylaxis, when as many as 10% of patients are having a VTE complication several weeks after surgery.

'It is only done for hip replacements, but there is the same prevalence of symptomatic DVT causing readmission for other orthopaedic procedures.' Professor Frostick called on surgeons to follow evidence-based guidance, such as that produced by the American College of Chest Physicians (Geerts et al, 2004). For hip and knee replacements, these guidelines recommend LMWH or fondaparinux and/or warfarin. But the strongest recommendation is against the use of aspirin.

For cost reasons LMWH were likely to be a popular option. While some had theoretical advantages, clinical trial evidence had not established significant differences between varieties of LMWH. Cost and licensing considerations, such as the time of initiation and the duration of prophylaxis, were likely to be important factors in the choice of prophylaxis.

The need for consistency was emphasized when Peter Bates, a specialist registrar at the Royal National Orthopaedic Hospital in Stanmore, north London, said there were different policies on prophylaxis between hospitals, but also between consultants within individual hospitals. Practice ranged from mechanical prophylaxis alone, to aspirin use and mechanical prophylaxis, to extended use of LMWH.

Professor Frostick's recommendation to orthopaedic surgeons was administration of a LMWH or fondaparinux 4–6 hours postoperatively because 'this gets round the problem of perioperative bleeding and problems of spinal or epidural anaesthesia'.

GUIDELINES

The National Institute for Clinical Excellence is about to start work on guidance on prevention of venous thromboembolism in surgical patients. The guidance will look at mechanical interventions, including graduated elastic compression stockings, intermittent pneumatic compression devices and mechanical foot pumps. And pharmaceutical interventions including aspirin, low-dose unfractionated heparin, low molecular weight heparin oral anticoagulants (warfarin) and dextrans will also be considered. Although no precise date has been set, the guidance is expected to be published in 2007. **HM**

Bergqvist D, Benoni G, Bjorgell O et al (1996) Low-molecular weight heparin (enoxaparin) as prophylaxis against venous thromboembolism after total hip replacement. *N Engl J Med* **335**(10): 696–700

Callum KG Whimster F, Dyet JF et al (2001) The Report of the National Confidential Enquiry into Perioperative Deaths for Interventional Vascular Radiology. *Cardiovasc Intervent Radiol* **24**(1): 2–24

Dahl OE, Andreassen G, Aspelin T et al (1997) Prolonged thromboprophylaxis following hip replacement surgery: results of a double-blind, prospective, randomised, placebo-controlled study with dalteparin (Fragmin). *Thromb Haemost* **77**(1): 26–31

Freedman KB, Brookenthal KR, Fitzgerald RH Jr, Williams S, Lonner JH (2000) A meta-analysis of thromboembolic prophylaxis following elective total hip arthroplasty. *J Bone Joint Surg Am* **82**(7): 929–38

Geerts WH, Pineo GF, Heit JA et al (2004) Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* **126**(Suppl): S338–S400

Hidalgo M, Figueroa JM (2000) Prophylaxis of venous thromboembolism in abdominal wall surgery. *Hernia* **4**: 242–47

Lassen MR Borris LC, Anderson BS et al (1998) Efficacy and safety of prolonged thromboprophylaxis with a low-molecular weight heparin (dalteparin) after total hip arthroplasty – the Danish Prolonged Prophylaxis (DaPP) Study. *Thromb Res* **89**(6): 281–7

Navarro-Quilis A, Castellet E, Rocha E, Paz-Jimenez, Planes A: Bemparin Study Group in Knee Arthroplasty (2003) Efficacy and safety of bemiparin compared with enoxaparin in the prevention of venous thromboembolism after total knee arthroplasty: a randomized, double-blind clinical trial. *J Thromb Haemost* 1: 425–32

Paiement GD, Wessinger SJ, Hughes R, Harris WH (1993) Routine use of adjusted low-dose warfarin to prevent venous thromboembolism after total hip replacement. *J Bone Joint Surg Am* **75**(6): 893–8

Turpie AG, Gallus AS, Hoek JA (2001) A synthetic pentasaccharide for the prevention of deep vein thrombosis after total hip replacement. *N Engl J Med* **344**(9): 619–25

KEY POINTS

- The evidence for the benefit of prophylaxis against thromboembolic events after orthopaedic surgery is strong and convincing.
- Post-operative dosing overcomes practical problems of administering prophylaxis at the same time as anaesthesia.
- Post-operative dosing should be initiated within 4–6 hours of surgery.
- Prophylaxis should be extended to 4–6 weeks after surgery.
- Low molecular weight heparins appear to be clinically equivalent to each other. Simple cost-effective presentations of prophylaxis are preferred.
- UK clinical guidance needs to be developed. Until the National Institute for Clinical Excellence publishes its recommendations (due in 2007), the American College of Chest Physician's advice in *Chest* (2004) is a useful guide.