Thromboprophylaxis in elective orthopaedic surgery – what is the purpose?

The need for thromboprophylaxis after elective orthopaedic surgery is uncertain. Chemical prophylaxis, usually with subcutaneous heparin, is known to reduce the relatively common episodes of deep-vein thrombosis detected by fibrinogen scanning and venography after surgery, but it is not yet clear whether this represents a major gain in reducing clinical thrombosis and fatal and non-fatal pulmonary embolism (PE) after operation.

There are two separate controversies. First, does the meta-analysis of heparin published in 1994, based on large numbers of trials which used both surrogate and clinical end-points, provide a firm positive indication for the routine use of subcutaneous heparin? Secondly, are the clinical complications of fatal and non-fatal PE, deep-vein thrombosis and the post-phlebitic syndrome sufficiently common to justify routine thromboprophylaxis? The evidence from Fender et al in this journal (p. 896), and others, suggests that mortality from postoperative venous thrombosis is exceedingly rare.

In contrast to the absence of large randomised trials with clinical end-points, the number of Consensus and guideline documents on thromboprophylaxis continues to increase. These documents rely largely on the same data from clinical trials, mainly the early International Multicentre Trial of heparin prophylaxis in elective surgical patients and the subsequent meta-analysis of heparin prophylaxis. Some surgeons consider that the conclusion of these documents, namely that anticoagulant prophylaxis should be given to all moderate and high-risk patients, was based on insufficient clinical evidence.

In the most recent Consensus document a welcome note of doubt was introduced. The authors state: “A number of orthopaedic surgeons believe that with modern practice, the frequency of fatal PE in patients having elective total hip replacement (THR) is lower than previously assumed without pharmacological prophylaxis”. They called for a careful prospective audit to establish the mortality and incidence of fatal PE after THR.

Fender et al, in this issue of the Journal, supplied precisely that audit. They confirm that the incidence of fatal PE is very low at about 0.2% to 0.3%. In their study, there were four patients with fatal PE in over 2000, two of whom had heparin. But non-randomised observational studies do not provide reliable evidence of the effects of thromboprophylaxis. Indeed, Fender et al estimate that the fatal PE rate may have been 0.5% (95% CI 0.2 to 0.9%) and that some cases may not have been detected.

Why is there such a large discrepancy between the Consensus documents on thromboprophylaxis and the clinical practice of orthopaedic surgeons, of whom only about 36% considered low-dose anticoagulants to be a necessity in THR? Of these surgeons, a number used thromboprophylaxis only for fear of medicolegal repercussions, rather than from a conviction of the benefit to the patient, after a stentorian article on that topic. This is no way to practise good medicine. The gap between recommendation and practice has risen due to the lack of firm evidence for the clinical benefits of thromboprophylaxis. The case in favour of subcutaneous heparin (either unfractionated or low-molecular-weight) rests with the meta-analysis of anticoagulants. This meta-analysis was positive, showing that heparin gave an approximately 50% benefit in reducing non-fatal and fatal PE, but its conclusions were not generally adopted. Why?

First, many of the trials relied on the surrogate endpoints of radioactive fibrinogen scanning and venography for the diagnosis of deep-vein thrombosis and clinical endpoints were not recorded as primary end-points for some of the trials. Secondly, given the very low mortality rates observed in these recent observational studies of elective orthopaedic surgery, it is clear that a halving in risk after THR is likely to translate, at best, into avoidance of fatal PE in only a few patients per thousand of those given prophylaxis.

The value of a treatment depends not only on the proportional reduction of events that it produces compared with no treatment, but also on the incidence of the clinical events in the population studied. This low potential for clinical gain must be balanced against haemorrhagic complications. Do the clinical benefits of thromboprophylaxis outweigh the risk (and, nowadays, justify the financial cost)
of the treatment? Perhaps most surgeons will ask a common-sense question: can a prospective randomised controlled clinical trial be done to resolve this problem? If the answer is no, as the numbers of patients required are too high, between 20 000 and 50 000, what is the surgeon to conclude? Probably, that the treatment is not worth giving. The extensive studies needed to demonstrate the small reduction in death rate from this cause may not be worthwhile.

This argument hides the possibility that a sub-group of patients at particularly high risk may benefit, whereas the low-risk majority do not. Unfortunately, at present we have no way of knowing how this theoretical high-risk minority can be identified.

The situation today is summarised by the 1993-94 NCEPOD report which states that the position regarding thromboprophylaxis for orthopaedic surgery is still unresolved.

By contrast, patients undergoing surgery for fractured neck of femur remain at high risk of death (5% to 10%) due to cardiovascular causes including PE. This is a welcome reduction from the 10% for PE alone originally quoted by Sevitt and Gallagher. In acute fracture patients, even quite moderate proportional reductions in the risk of such deaths may well be worthwhile.

The situation regarding thromboprophylaxis for operations for fractured neck of femur may be clarified next year. In 1994 the Antiplatelet Trialists Collaboration carried out a meta-analysis of aspirin as thromboprophylaxis for surgery. The conclusion, that there was an approximate 50% reduction in fatal and non-fatal complications, was similar to that obtained previously for subcutaneous heparin. Very few surgeons, however, use aspirin compared with subcutaneous heparin, reflecting perhaps that there is no commercial gain in promoting the use of aspirin. The aspirin meta-analysis has prompted the organisation of a very large randomised controlled trial of 162 mg of aspirin daily started preoperatively and continued for five weeks after surgery, compared with placebo. This will assess the effects of aspirin on vascular mortality, vascular morbidity (both venous and arterial) and total mortality at five weeks, as well as mortality at one year.

The Pulmonary Embolism Prevention (PEP) trial is being carried out internationally and has over 60 participating centres in the UK. It has already recruited 11 000 of its goal of 15 000 patients. Aspirin has the added advantage of reducing adverse arterial events; it has already been established that over 80% of the vascular complications after surgery are arterial rather than venous. This trial may help to answer the question that every patient should ask the surgeon about thromboprophylaxis: “Does your treatment improve my chances of staying alive after my operation?”

As a long-term goal, the best treatment in the PEP trial (aspirin or placebo) could be compared against subcutaneous heparin and the combined treatment regime. This trial may be feasible in patients having operations for fractured neck of femur; there are a large number of cases, and the high rates of both postoperative death and vascular complications make them a high-risk group, but the number required in THR would be very large. At least, surgeons would then have clinical evidence from a substantial trial on which to base their practice of thromboprophylaxis.

In the meantime the jury is still out.

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REFERENCES