

## Correspondence

### Low-molecular weight heparin as prophylaxis against thromboembolism after total hip replacement—is it worth the price?

It is well-known today that low-molecular weight heparin for thromboprophylaxis is the highest cost of drugs for orthopedic hospital patients. It was introduced in Sweden in 1993, replacing Macrodex. Since the remarkable metaanalysis by Murray et al. (1996), it has been questioned whether thromboprophylaxis really reduced mortality at all. In 130,000 total hip patients, followed for 3 months after surgery, there was no significant difference in mortality between heparin, warfarin, aspirin and no prophylaxis at all, but no studies were randomized. The explanation was supposed to be that some patients die of thromboembolism after stopping of the prophylaxis within the 3 months of the study and that other patients die from side-effects of gastrointestinal, cerebral or other internal bleedings. With a 3-month mortality around 0.3% and a mixture of other unrelated causes of death, it is difficult to solve the problem by prospective randomized studies. Therefore thrombosis, as demonstrated by phlebography or ultrasound, has been put in focus to show the value of prophylaxis. Such studies have shown the prevalence of deep vein thrombosis on day 7 as about 16% and on day 35 as 32% in placebo treated patients, compared to 19% in heparin-treated patients (Dahl et al. 1997, Dahl 1998). In the same randomized study of 308 patients, the incidence of symptomatic pulmonary embolism was 3% in the placebo-treated group (including 1 who died), compared to 0 in the heparin group. On the basis of this they recommend 5 weeks of prophylaxis. This conclusion is similar to that of Bergqvist et al. (1996) and Planes et al. (1996), but is it convincing? In both studies, the occurrence of deep vein thrombosis was checked around the last day of treatment, i.e., 3 weeks after prophylaxis was stopped in the placebo group and about 1 day after in the heparin group. It is astonishing that this is

scientifically accepted as a proof of efficacy because there must be some effect of withdrawal with an increased risk of thrombosis 3 weeks after the end of treatment, compared to immediately after, and this may occur after prolonged prophylaxis as well. These patients are ambulant from the day after surgery.

I have found no article that analyzes such effects of withdrawal after low-molecular heparin treatment. With a clinical occurrence of thrombosis of a few percent only among total hip patients and a phlegographically-proven occurrence of about 10–20% it can be questioned whether the cost of using heparin prophylaxis is worthwhile. There is no single study showing a reduced mortality, but several indications of a somewhat increased wound secretion.

Recently, in the August 1999 issue of JBJ Surg 81A, Lawton and Morrey from the Mayo Clinic showed that heparin used for treatment of suspected pulmonary embolism more than doubled the risk of revision. Loosening increased from 5% to 12% and revision less than 10 years postoperatively from 6% to 15%. Hematomas increased from 0 to 9%, but the rate of infection was not affected. The study analyzed 150 patients for whom treatment had been started because of suspected pulmonary emboli after a total hip arthroplasty and it was concluded that heparin should not be used until a pulmonary embolism has been proven by ventilation perfusion scanning or otherwise. The risk of local hematoma also is high if heparin for such treatment is administered before the 6th postoperative day (Patterson et al. 1989). The possible mechanism is bleeding at the bone-cement interface (Majkowski et al. 1994).

This extensive report does not discuss the use of heparin for prophylaxis only. However, it is not unlikely, that a few patients are more sensitive

than others. The body weights differ by a factor of two, but the doses are usually the same for all.

The Swedish National Register of total hip arthroplasties in Gothenburg has reported a tendency to inferior results with the third generation cementing technique that is difficult to understand. Is the use of heparin for the prophylaxis of thromboembolism a possible cause? In the annual reports from Gothenburg, the methods of prophylaxis are not mentioned at all, but this can be retrospectively analyzed if some years before 1993 are compared to some years after 1993 concerning the 5-year revision rates for aseptic loosening.

In summary, if there is no proven reduction of mortality and a reduced occurrence of venous thrombosis only as long as the prophylaxis continuous, does this outweigh the possible loss in primary wound healing and prosthetic fixation?

Perhaps low molecular weight heparin prophylaxis should be used only if a diagnosis of thrombosis has been established earlier for the patient and his relatives and in such cases continued during 1 month. This could be a more evidence-based and cost-effective care program to follow until further facts have been presented.

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Bergqvist D, Benoni G, Bjorgell O, Fredin H, Hedlundh U, Nicolas S, Nilsson P, Nylander G. Low-molecular weight heparin as prophylaxis against venous thromboembolism after total hip replacement. *N Engl J Med* 1996; 335: 696-700.

Dahl O E. Thromboprophylaxis in hip arthroplasty. *New frontiers and future strategy. Acta Orthop Scand* 1998; 69: 339-42.

Dahl O E, Andreassen G, Aspelin T, Muller C, Mathiesen P, Nyhus S, Abdelnoor M, Solhaug J H, Arnesen H. Prolonged thromboprophylaxis following hip replacement surgery. *Thromb Haemost* 1997; 1: 26-31.

Lawton R L, Morrey B F. The use of heparin in patients in whom a pulmonary embolism is suspected after total hip arthroplasty. *J Bone Joint Surg (Am)* 1999; 81: 1063-71.

Majkowski R S, Bannister G C, Miles A W. The effect of bleeding on the cement-bone interface. An experimental study. *Clin Orthop* 1994; 229: 293-7.

Murray D W, Britton A R, Bulstrode C J. Thromboprophylaxis and death after total hip replacement. *J Bone Joint Surg (Br)* 1996; 76: 863-70.

Patterson B M, Marchand R, Ranawat C. Complications of heparin therapy after total joint arthroplasty. *J Bone Joint Surg (Am)* 1989; 71:1130-4.

Planes A, Voshelle N, Darmon J Y, Fagola M, Bellaud M, Huet Y. Risk of deep venous thrombosis after hospital discharge in patients having undergone total hip replacement: double-blind comparison of enoxaparin versus placebo. *Lancet* 1996; 348: 224-8.