Acta orthop. scand. 52, 77–80, 1981

# LOW-DOSE HEPARIN IN PROXIMAL FEMORAL FRACTURES

## *Failure to Prevent Deep-Vein Thrombosis*

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The effect of heparin, 5000 units every 8 hours, on deep venous thrombosis in patients with proximal femoral fractures was investigated in a controlled, double blind, randomised study. Heparin or placebo was administered as soon as possible after the fracture, and before 6 hours had passed, and was continued for 14 days. The diagnosis of deep venous thrombosis was made using daily $I_{125}$ fibrinogen scans. A total of 130 patients entered the trial and the results were registered on a sequential diagram. This showed that the 0-hypothesis could not be rejected, and that consequently no difference in the frequency of deep-vein thrombosis was detected.

*Key words:* femoral fractures; heparin; thrombosis

Accepted 3.vi.80

Deep-vein thrombosis is a frequent complication after fractures of the proximal femur (Smyrnis et al. 1973). Fatal pulmonary embolism is one of the major causes of death in these patients (Sevitt & Gallagher 1959). Since the introduction of low dosage heparin prophylaxis by Sharnoff & De Blasio (1970) many authors have demonstrated a reduction in the frequency of deep-vein thrombosis in patients undergoing a variety of surgical procedures (Kakkar et al. 1971, Gordon Smith et al. 1972, Kakkar et al. 1972, Nicolaides et al. 1972, Gallus et al. 1973, Ballard et al. 1973 and Strand et al. 1975).

The efficacy, however, in patients with proximal femoral fractures is disputed. Morris & Mitchell (1977) and Galasco et al. (1976) found a reduction in the frequency of deep-vein thrombosis, while Kakkar et al. (1972) in a small series of patients were unable to do so. We consequently decided to evaluate the effect of low dosage heparin in a controlled, randomised, double blind study.

## PATIENTS AND METHODS

From January the 3rd 1977 until January the 18th 1979 a total of 130 patients with proximal femoral fractures entered the trial.

Excluded from the study were the following categories of patients:

1. Patients under 20 years of age.
2. Patients with coagulation disorders.
3. Patients with a previous history of deep-vein thrombosis or pulmonary embolism.
4. Patients with an active malignant disease.
5. Patients receiving oral anticoagulants or heparin.
6. Patients receiving salicylates.
7. Pregnant women.
8. Patients admitted later than 6 hours after fracture.

We chose a sequential trial (Armitage 1960) and the patients were thus randomly allocated to either the heparin or the placebo group in matched pairs. The patients received 5000 units of heparin or placebo three times a day for 14 days, i.e. until mobilisation. The injections were given deep subcutaneously in the abdominal wall, the first injection being given as soon as the patients were admitted to the hospital.

0001-6470/81/010077-04 $02.50/0


*Figure 1. Age distribution of the patients.*

The age distribution is shown in Figure 1. The average age was 73 years (females 76, males 65 years); 97 patients were female, 33 male.

The detection of deep venous thrombosis was done according to Kakker et al. (1970). Human fibrinogen labelled with 110 μCi $I_{125}$ was administered intravenously upon admission. Measurements were made daily using the portable isotope localization monitor 235 (Pitman).

The measurements were made at four places along the medial margin of the tibia and at two places on the medial aspect of the thigh. No measurements were made in the vicinity of the fracture. The precordial count was adjusted to 100 per cent and the subsequent counts on the legs were expressed as a percentage of the precordial count. An increase of 20 per cent or more compared to the same point on the opposite leg or the neighbouring points on the same leg was considered a positive sign of thrombosis. This rise in the count should be present for more than 24 hours. This method of detecting venous thrombi is very reliable (Morris & Mitchell 1977). If deep venous thrombosis was detected the patient was treated in the usual way with active heparin and oral anticoagulants.

The results of the $I_{125}$ fibrinogen scans were sent to a doctor totally independent of the investigation, and he then entered the preferences in the sequential diagram.

## RESULTS

Of the 65 patients receiving heparin 15 developed deep-vein thrombosis, while in the 65 patients receiving placebo 28 cases of deep-vein thrombosis were detected. In two instances thrombosis occurred in both the matched patients; thus the number of preferences was reduced to 39. Figure 2 shows the sequential diagram after closing the study. This shows that the 0-hypothesis cannot be rejected, and that consequently no difference in the frequency of deep-vein thrombosis is demonstrated. A total of 21 deaths occurred within 6 months after the fracture, 15 in the heparin group and 6 in the placebo group. Only two patients died within the first 14 days, both from pulmonary embolism. One patient had been given placebo, the other heparin. The remaining 19 patients were all above 75 years and died of miscellaneous diseases mainly in nursing homes.

An average of 1.02 units of blood (0–6) was given in the heparin group, while the same figures in the placebo group were 0.85 units (0–4). This difference is not statistically significant.

## DISCUSSION

The high frequency of deep-vein thrombosis and pulmonary embolism in patients with fractures of the proximal femur raises a demand for a suitable, effective, and risk-free method of prevention. Prophylactic oral anticoagulation lowers the incidence of thrombosis but carries a high complication rate (Salzman et al. 1966). The addition of dextran 70 has been tried by Korvald et al. (1973) with the same result. Low-dose heparin prophylaxis introduced by Sharnoff in 1966

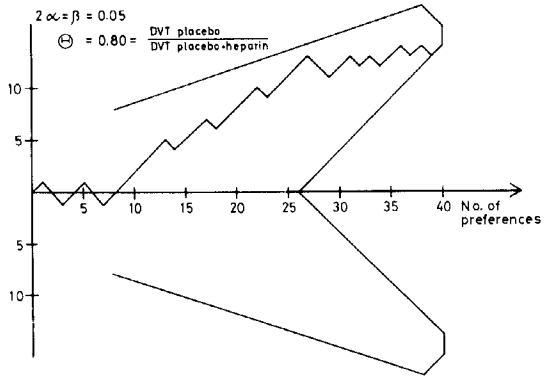


*Figure 2. Sequential diagram after closing the trial. An entry of / was made when thrombosis occurred in the placebo-treated patient with no thrombosis in the matched heparin-treated patient. An entry of \ was made when the opposite condition occurred.*

seemed to meet with the requirement of a very low complication rate. The effectiveness of this prophylaxis has later on been investigated by many authors in a variety of surgical patients, and all reported a significant decrease in deep-vein thrombosis (Kakkar et al. 1971, Gordon Smith et al. 1972, Kakkar et al. 1972, Nicolaides et al. 1972, Gallus et al. 1973, Ballard et al. 1973, and Strand et al. 1975). The patients treated were mainly patients undergoing elective surgery for abdominal or gynaecological conditions. Kakkar in his 1972-report found no effect in 50 patients with fracture of the neck of the femur and attributed this to the possibility that their clotting mechanisms had already been activated. In patients requiring total hip replacement no effect has been shown on either the frequency of pulmonary embolism (Williams et al. 1978) or deep-vein thrombosis (Hampson et al. 1974 and Evarts & Alfidi 1973). In patients with hip fractures Morris & Mitchell (1977) found some reduction in the frequency of venous thrombosis, but the reduction did not achieve statistical significance.

Galasco et al. (1976) found a significant reduction in deep-vein thrombosis based on clinical signs supplemented by phlebography, but the study excluded men, and was not designed as a double blind trial.

Normally heparin is administered as 5000 units every 12 hours. We chose 5000 units every 8 hours as there is some indication that patients with fractures require more heparin to acheive the same effect (Gallus et al. 1973, Kakkar et al. 1972). Sharnoff (1973) recommends that the first dose of heparin should be given as early as possible after the fracture and we have adopted this principle by restricting the admission of the patients to the trial to 6 hours after the fracture.

In spite of this we could not demonstrate the effect of low-dose heparin on deep-vein thrombosis in patients with proximal femoral fractures. We believe that this is due to coagulation mechanisms already having been activated (Gormsen et al. 1974) and feel that other ways of preventing deep-vein thrombosis should be investigated in these high-risk patients as a real prophylactic administration of heparin, i.e. before the fracture, is not possible.

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