EFFECT OF LOW-DOSE HEPARIN AND DIHYDROERGOTAMINE ON FREQUENCY OF POSTOPERATIVE DEEP-VEIN THROMBOSIS IN PATIENTS UNDERGOING POST-TRAUMATIC HIP SURGERY

Gordon Lahnborg

From the Department of Surgery, Serafimerlasaretet, Karolinska Institutet, Stockholm, Sweden

(Submitted for publication December 6, 1979)

Abstract. The effect of low doses of heparin (5000 units of sodium heparin every 12 hours for 10 days) and dihydroergotamine (DHE) (0.5 mg at the same intervals as heparin) on the incidence of deep-vein thrombosis (D.V.T.) in the legs was studied on 210 patients undergoing nailing of a fractured neck of the femur. The patients were allocated randomly to receive heparin (70 patients) or heparin + dihydroergotamine (71 patients) or saline (69 patients, acting as controls). D.V.T. developed in 15 patients in the heparin group, in 12 patients in the heparin + DHE group and in 28 patients in the control group. There is a significant difference between the two groups receiving heparin on the one hand and the control group on the other. DHE does not seem to reduce the incidence of D.V.T. any further in this group of patients.

PATIENTS AND METHODS

210 consecutive patients admitted for nailing of a fractured neck of the femur were included in this study. The patients were allocated randomly to receive heparin + placebo (70 patients), heparin + dihydroergotamine (71 patients) and, as a third group acting as controls (69 patients), only placebo + placebo. The patients had no history of venous thrombosis or pulmonary embolism during two years before the trial. No patient was receiving oral anticoagulants for a previous thromboembolism. When D.V.T. was diagnosed, most of the patients received therapeutic doses of heparin. No patients were excluded from entering the trial.

Sodium heparin (Kabi Vitrum AB, Stockholm, Sweden) was given at a dosage of 5000 units (10000 units/ml) subcutaneously into the thigh every 12 hours for 10 days, starting 2-3 hours before the operation. Dihydroergotamine (Oristanorm®, Sandoz AB, Sweden) was given at a dosage of 0.5 mg (1 mg/ml) subcutaneously into the thigh at the same intervals as heparin.

As placebo, 0.5 ml of 0.85% saline was given in the same way and at the same intervals as heparin.

The number of injections given were carefully controlled and monitored on special formulas by a registered nurse managing this trial.

Informed consent was obtained.

Diagnosis of D.V.T.

D.V.T. was diagnosed by the method of Flanc et al. (1968) using the 125I-fibrinogen technique. Each patient received 100 μCi 125I-fibrinogen (Radiochemical Centre, Amersham) intravenously on entering the hospital. The patient was usually operated upon on the following day. The thyroid had been blocked by 100 mg potassium iodide, given orally 3-5 hours before the injection of 125I-fibrinogen and then daily for the next 10 days.

Scanning was performed over both legs at nine different points with a Pittman 233 isotope-localisation monitor. The legs were scanned preoperatively and then daily for 10 postoperative days.
Table I. The effect of heparin and dihydroergotamine on D.V.T. in patients undergoing nailing of a fractured neck of the femur

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>12</td>
<td>15</td>
<td>28</td>
<td>24</td>
</tr>
<tr>
<td>No</td>
<td>58</td>
<td>56</td>
<td>41</td>
<td>38</td>
</tr>
</tbody>
</table>

The fibrinogen injection was repeated if the count-rate was low.

RESULTS

Of the 210 patients who entered the trial, 72 were males and 138 females. The mean age was 77 (range 39–97) years. There were no significant differences between the groups in sex distribution, age, operated leg (right leg 97 patients, left leg 113), or duration of the operation (mean 122 min, range 60–240 min).

193 patients were nailed according to von Bahr or Thornton. 164 patients had spinal or epidural anesthesia, 38 patients had general anesthesia and 8 patients a combination of general and spinal anesthesia. Blood loss was below 500 ml in 191 patients, with no significant differences between the three groups.

Concerning injections not given they were less than 3% and equally distributed in the three groups of patients. Mainly because of transferring to other hospitals before all injections were given 5 patients in the group given heparin + DHE, 3 patients in the group receiving only heparin and 4 patients in the control group could only participate during 4–6 days of the stipulated period of 10 days. These patients were not excluded from the trials as the distribution in the three different groups was similar.

Incidence of D.V.T.

D.V.T. developed in 12 patients in the group given heparin + DHE, in 15 in the group receiving heparin + placebo and in 28 in the control group. There is a significant difference ($p<0.005$, $\chi^2$-test) in the occurrence of D.V.T. between the patients given heparin + placebo and heparin + DHE on one hand and those acting as controls on the other. Pulmonary embolism, diagnosed clinically, developed in three patients, two of them treated with heparin + placebo and one given heparin + DHE. Two other patients given heparin + DHE died both from cardiac failure (Table I).

Local haematoma at the injection site developed in 49 patients given heparin + DHE and in 52 receiving heparin + placebo. There were no haematoma in the placebo group.

DISCUSSION

The results of the present study indicate that low-dose heparin prophylaxis is effective in preventing D.V.T. in patients undergoing nailing of a fractured neck of the femur. However, a combination of heparin and dihydroergotamine does not seem to reduce the incidence of D.V.T. further in this group of patients. This contrasts with other investigations, where a combination of the two drugs did decrease the number of postoperative D.V.T. (Sagar et al., 1976). Unlike the present trial, those studies were performed on patients undergoing elective surgery, when it is known that most D.V.T. develop on the day of the operation. This is logical, as all trauma activates the coagulation mechanisms (Lahnborg & Bergström, 1975). One can therefore assume that, on entering the present trial, perhaps some of the patients might already have D.V.T. that was not detectable with the $^{131}$-fibrinogen method as the trauma had already happened.

One reason for the ineffectiveness of DHE might be the lack of influence on a vessel filled with thrombi, as it has been demonstrated that 0.7 mg of DHE, when administered to healthy volunteers, markedly constricted the capacitance vessels or capillary filtration rate (Mellander & Nordenfelt, 1969). It has also been reported that 0.5 mg of DHE produced maximum vasoconstriction, the resistance of the vessels was only slightly affected (Lange, 1972) and the same dosage increased the velocity of the venous blood-flow in the legs by up to 20% (Ricke, 1971). These effects of DHE on the vessels would, at least theoretically, prevent the development of D.V.T.

It has been suggested that DHE also would potentiate the pharmacokinetics of heparin (Buttermann et al., 1977). This runs counter to a recent study, where no such effect could be found (Beermann & Lahnborg, 1979).

Another influence on the development of D.V.T. in con-

Acta Chir Scand 146
Effect of low-dose heparin

ACKNOWLEDGEMENTS

The author wishes to acknowledge the excellent technical assistance of Mrs Margaretha Lindell, reg. nurse.

REFERENCES


Lahnborg, G. & Schildt, B. The incidence of deep vein thrombosis following lower limb surgery in the bloodless field under external analgesia. (To be publ.)


Sagar, S., Stamatakis, J. D., Higgins, A. F., Nairn, D., Mattei, F. H., Thomas, D. O. & Kakkar, V. V. 1976.
