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Prevention of Postoperative Deep-Vein Thrombosis by Low-Dose Heparin in Urological Surgery

A Double-Blind, Randomised Study

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Summary. The efficacy of low-dose heparin in preventing deep-vein thrombosis (D. V. T.) after urological surgery was investigated in a double-blind trial.
Thromboses were detected by the ^{125}I-labelled fibrinogen technique. The incidence of D. V. T. was 36% in the control group (25 patients) and 9% in the treated group (22 patients) ($p < 0.05$). Contrary to the current opinion this form of prophylaxis was effective following open prostatectomy.

Key words: Subcutaneous low-dose heparin - Deep-vein thrombosis prophylaxis - ^{125}I-fibrinogen test.

The introduction of the ^{125}I-labelled fibrinogen test has permitted the detection of an important percentage of postoperative deep-vein thromboses which are not clinically apparent (2, 7). The incidence of deep-vein thromboses (D. V. T.) after urological surgery is between 50 and 60% (8, 9).

Recent trials have demonstrated the effectiveness of low-dose heparin regimens in the prevention of postoperative D. V. T. (3, 6, 8). Low doses of subcutaneous heparin significantly increase the inhibition of the activated factor X, one of the main thrombogenic factors, by an α_2-globulin known as antithrombin III (11). Small quantities of the drug prevent blood hypercoagulability without altering the usual coagulation tests, thus avoiding the risk of haemorrhage which is encountered with classical doses of heparin.

There has been interest recently in the prophylactic use of low-dose heparin in urological patients and encouraging results have been reported (1, 4, 10, 13). Our purpose was to check the value of low-dose heparin prophylaxis in urological surgery by a double-blind trial.

MATERIAL AND METHODS

All the patients entered in the trial were aged 40 years or over and had been admitted to the hospital for a major urological operation; i. e. an operation performed under general anaesthesia, lasting more than half an hour and requiring at least 7 days of postoperative hospital care. Patients with thyroid disease, recent venous thrombosis or lower limb amputation were excluded from the study. Patients having emergency surgery, taking anticoagulants or antiaggregating drugs were also rejected.

Ampoules of identical appearance containing either 0.2 ml calcium heparin (5000 U), or 0.2 ml distilled water were assigned to every patient by randomisation. The allocation of the patients into the "heparin" or the "placebo" group was unknown until the end of the trial. The first subcutaneous injection was given 2 hours before operation and then every 8 hours for 6 days.

The ^{125}I-labelled fibrinogen method was used to detect postoperative D. V. T. (5).

During the postoperative period, all patients underwent physiotherapy with passive and active exercises for the legs. Patients with varicose veins wore elastic stockings during and after operation. No patient received intravenous dextran.

Coagulation tests (Quick time and cephalin-kaolin time) were determined preoperatively as well as 3 and 5 days after operation. In cases of haemorrhage, more detailed tests were carried out.

Table 1. Sex, weight, and age in heparin and placebo group

	Heparin group	Placebo group
Sex		
M	19	18
F	3	7
Average weight (kg)	65.0	65.3
Average age (yr)	70.5	60.7

Table 2. Factors possibly influencing the incidence of D. V. T.

	Heparin group	Placebo group
Previous myocardial infarction	6	1
Chronic bronchitis	5	1
Malignant disease	3	2
Diabetes mellitus	1	1
Previous leg fracture	2	0
Previous D. V. T.	1	1
Varicose veins	6	7
Healed varicose ulcer	0	1

Table 3. Types of operation

	Heparin group	Placebo group
Open prostatectomy	16	12
Nephrectomy	2	5
Ureterotomy	2	3
Pyelotomy	1	1
Pyeloplasty	-	1
Partial cystectomy	-	1
Vesicourethral suspension	-	2
Urethroplasty	1	-

Table 4. D. V. T. diagnosed by ^{125}I-fibrinogen test

	Heparin group n = 22	Placebo group n = 25
Number of patients with isotopic D. V. T.	2	9
Bilateral D. V. T.	1	3
Total number of D. V. T.	3	12
D. V. T. involving the whole limb	0	5
Time of onset of D. V. T. after operation		
before 3rd day	0	10
after 3rd day	3	2

Table 5. Haemorrhagic complications

	Heparin group	Placebo group
Operative blood-loss	-	1
Postoperative wound haematoma	1	2
Postoperative blood-loss	1	1

Notice was taken of operative and post-operative blood-loss, blood transfusion volume as well as haemoglobin value before and 7 days after operation. The presence of haematoma was similarly noted.

RESULTS

The "heparin" group included 22 patients and the "placebo" group 25 patients. The distribution according to sex, weight, and age is shown in Table 1. It must be noted that the average age was 10 years higher in the heparin treated group, which accounts for the higher incidence of previous myocardial infarction and chronic bronchitis in this group (Table 2). The two groups were well-matched for the other factors possibly influencing the incidence of D. V. T. and for the type of operation (Table 3).

No obvious clinical sign suggesting D. V. T. or pulmonary embolism was observed. Using the radioactive fibrinogen test, D. V. T. was detected in 2 patients (9%) of the "heparin" group and in 9 patients (36%) of the "placebo" group. The difference between the 2 groups is statistically significant ($0.01 < p < 0.05$). Table 4 shows that D. V. T's in the group of untreated patients were more extensive and occurred earlier. Among the patients developing a D. V. T., 2 patients of the "heparin" group had malignant disease compared with only one in the control group.

Of the 28 patients who underwent prostatectomy, 5 out of 12 (42%) in the control group developed D.V.T. The incidence in the treatment group was only 1 out of 16 (6%) (p: 0.03, Fisher's exact test).

In the heparin group, no significant increase in operative or postoperative bleeding was experienced and coagulation tests did not reveal any alteration in blood coagulation (Table 5). In both groups, no significant difference was observed in the volume of blood transfused or the average decrease in haemoglobin 7 days after operation.

DISCUSSION

In our study low-dose heparin decreased the frequency of D. V. T. in patients 40 years of age or over who were subjected to urological surgery. This was particularly significant since the mean age was 10 years greater in the "heparin" group, constituting an additional predisposing risk. Two patients of this group who developed a D. V. T. had malignant disease which is also known to be a risk factor. Our data also showed that the appearance of D. V. T. was delayed and the extent diminished in the low-dose heparin group.

The efficacy of heparin prophylaxis in patients undergoing open prostatectomy has been questioned (11, 12). However, our results show a statistically significant decrease in the incidence of D. V. T. with this operation when low-dose heparin is used. It would be useful to confirm the effectiveness of low-dose heparin in preventing D. V. T. following open prostatectomy with a study involving larger numbers of patients.

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