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Prevention of Postoperative Deep-Vein Thrombosis by Low-Dose Heparin in Open Prostatectomy

M. Vandendris[1], M. Kutnowski[2], B. Futeral[2], X. Gianakopoulos[1], M. Kraytman[2] and W. Gregoir[1]

[1]Department of Urology and [2]Department of Medicine, Brugmann University Hospital, Brussels, Belgium

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Summary. A double-blind trial was designed to investigate the efficacy of low-dose heparin in preventing deep-vein thrombosis (DVT) after open prostatectomy. The diagnosis of DVT was established by the ^{125}I-fibrinogen test. The incidence of DVT was 39.4% in the control group (33 patients) and 9.7% in the heparin group (31 patients) ($p < 0.01$). These results suggest that low-dose heparin effectively prevents DVT after open prostatectomy.

Key words: Low-dose heparin, Deep-vein thrombosis prophylaxis, ^{125}I-fibrinogen test, Open prostatectomy.

Patients undergoing open prostatectomy constitute a particularly high-risk population with respect to deep-vein thrombosis (DVT) and pulmonary embolism. DVT after open prostatectomy is associated with clinical signs in about 6% of the cases (1, 9). However phlebographic and isotopic investigations have demonstrated the inadequacy of the clinical diagnosis of DVT (3, 11). The ^{125}I-labelled fibrinogen test has showed an incidence of isotopic DVT of about 50% after open prostatectomy (4, 13, 15). Release of tissue thromboplastin into the circulation during prostatic enucleation, as well as postoperative changes in platelet adhesiveness and fibrinolytic activity, seem to play an important role in the pathogenesis of DVT (6, 18). Fatal lung embolus has been reported to range from 0.6% to 5.8% in open prostatectomy and may be considered as the most common cause of death (5, 7, 8, 9).

Subcutaneous low-dose heparin has been shown to reduce the postoperative incidence of DVT and fatal pulmonary embolism in general surgery, as well as in urological patients (2, 7, 9, 10, 12, 14, 16, 19). However, the efficacy of low-dose heparin in patients undergoing open prostatectomy has been questionned (17, 18). In this paper, we record the results of a double-blind trial specifically designed to check the value of the drug in this operation.

MATERIALS AND METHODS

All the patients entered in the trial were admitted to hospital for an open prostatectomy. The operation was performed under general anaesthesia and required at least 7 days of hospital stay. Transcapsular prostatectomy was used in most of the cases and occasionally it was associated with another operation at the same time. Patients with thyroïd disease, recent venous thrombosis or lower limb amputation were excluded from the study. Patients taking anticoagulants or antiaggregating drugs were also rejected.

A list of allocations was prepared randomising patients to a placebo or heparin group. The allocations were sealed in numbered envelopes. The allocation of the patient in the heparin or in the placebo group was unknown until the end of the trial. Ampoules of identical appearance contained either 0.2 ml calcium heparin (5000 U) or 0.2 ml distilled water. The first subcutaneous injection was given 2 h before operation and then every 8 h for 6 days.

The ^{125}I-labelled fibrinogen method was used to detect postoperative DVT (11). During the postoperative period, all patients underwent physiotherapy with passive and active exercices for the legs. Patients with varicose veins wore elastic stockings during and after operation. No patient received intravenous dextran.

Quick-time and cephalin-kaolin time were determined preoperatively, as well as 3 and 5

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days after operation. In case of haemorrhage, more detailed tests were carried out. Notice was taken of operative and postoperative blood-loss, blood transfusion volume, as well as haemoglobin before and 7 days after operation. An investigator, who was unaware of the results of the fibrinogen test, examined the patients daily in the postoperative period for clinical signs of DVT or pulmonary embolism.

RESULTS

The study included 64 patients, 31 in the "heparin" group and 33 in the "placebo" group. The average age was 72.2 years in the heparin group and 70.0 years in the control group. The 2 groups were well-matched for weight and other factors possibly influencing the incidence of DVT, as well as for associated operations (Tables 1 and 2). The average postoperative stay in both groups of patients was almost identical (Table 1). Injections of heparin or placebo were stopped for postoperative bleeding in 2 patients in the heparin group and in 1 patient in the control group.

Three patients in the heparin group (9.7%) had a positive fibrinogen test. In the placebo group, this test detected a DVT in 13 patients (39.4%). The difference between the 2 groups is statistically significant ($p < 0.01$, Fisher's exact test). Deep vein thromboses occuring in the heparin group were less extensive and appeared later after the operation than in the placebo group (Table 3). Amont the patients developing a DVT, 2 patients of the heparin group had a malignant disease compared with only 1 in the control group.

In both groups, coagulation tests were normal and no significant difference was observed in the volume of peroperative blood loss and/or blood transfused, or in the average decrease of haemoglobin 7 days after operation (Table 4).

Clinical examination disclosed signs of DVT in five patients; only 2 of these had a positive fibrinogen test. No obvious clinical signs suggesting pulmonary embolism were observed in patients in either group.

DISCUSSION

The incidence of DVT is very high after open prostatectomy (13, 15). Accordingly there has been interest recently in the prophylactic use of low-dose heparin in this operation. This form of prophylaxis prevents blood hypercoagulability without altering the usual coagulation tests and thereby inducing possible haemorrhage associated with classical doses of this anticoagulant (17). In our study, low-dose heparin was effective in preventing DVT after open prostatectomy.

Table 1. Age, weight, postoperative hospital stay and associated operations in heparin and placebo group

	Heparin group	Placebo group
Number of patients	31	33
Average age (yrs)	72.2	70.0
Average weight (kg)	68.2	73.3
Postoperative hospital days	10.7	9.9
Associated operations		
- Bladder diverticulectomy	3	1
- Ureterotomy	2	-
- Herniorraphy	3	2
- Hydrocelectomy	-	3

Table 2. Factors possibly influencing the incidence of DVT

	Heparin group	Placebo group
Chronic bronchitis	10	7
Previous myocardial infarction	4	1
Previous leg fracture	4	4
Previous DVT	1	1
Varicose veins	10	11
Healed varicose ulcer	1	2

Table 3. DVT diagnosed by ^{125}I-fibrinogen scan

	Heparin group n = 31	Placebo group n = 33
Number of patients with isotopic DVT	3	13
Total number of DVT	3	17
Bilateral DVT	-	4
DVT involving the whole limb	1	2
Time of onset of DVT after operation		
- before 3rd day	1	12
- after 3rd day	2	5

Table 4. Haemorrhagic complications and average decrease in haemoglobin 7 days after operation

	Heparin group	Placebo group
Operative blood-loss	1[a]	1[a]
Postoperative blood-loss	3[a]	2[a]
Average decrease in haemoglobin (g %)	2.05	2.42

[a] Number of patients

In the heparin group, the frequency and the extent of the thromboses were statistically decreased and when they occurred their appearance was delayed.

A possible objection to the prophylactic use of low-dose heparin is the risk of haemorrhage. However, there was no significant difference in the mean transfusion requirements nor in the postoperative fall of haemoglobin between the 2 groups of our study. These results are in accordance with the findings of another study (9).

Prophylaxis with oral anticoagulants may present serious disadvantages: prolonged preoperative management for stabilisation of anticoagulation, risk of haemorrhage and limited short-term reversibility. Therefore, we believe that low-dose heparin is more appropriate and can be recommended in high-risk patients undergoing open prostatectomy.

REFERENCES

1. Aboulker, P., Benassayag, E., Draoui, D., Lassner, J.: Comparaison de deux procédés de prostatectomie. Cahiers d'Anesthésiologie 19, 653 (1971)
2. Aubert, J., Brisacier, P.: La prévention du risque thromboembolique en urologie par l'héparinate de calcium en sous-cutané. Journal d'Urologie et de Néphrologie 81, 175 (1973)
3. Becker, J., Borgström, S., Saltzmann, G. F.: Occurrence and cause of thrombosis following prostatectomy. A phlebographic investigation. Acta Radiologica Diagnosis 10, 513 (1970)
4. Collins, R. E., Klein, L. A., Skillman, J. J., Salzmann, E. W.: Thrombo-embolic problems in urologic surgery. Urologic Clinics of North America 3, 393 (1976)
5. Gormsen, J., Haxholdt, B.: The heparin tolerance test and thrombo-embolic incidence in surgery. Acta Chirurgica Scandinavica 120, 121 (1960)
6. Halverstadt, D. B., Albers, D. D., Krouvand, R. L., Rich, R.: Anticoagulation in urologic surgery. Urology 9, 617 (1977)
7. An International Multicentre Trial. Prevention of fatal postoperative pulmonary embolism by low doses of heparin. Lancet 2, 45 (1975)
8. Iversen, H. G., Larsen, J.: Prostatectomia transversicalis ad modum Freyer. Ugeskrift for Laeger 131, 593 (1969)
9. Jasper, W. S.: Anticoagulants in open prostatectomies. Journal of Urology 117, 72 (1977)
10. Kakkar, V. V., Field, E. S., Nicolaides, A. N., Flute, P. T.: Low doses of heparin in prevention of deep-vein thrombosis. Lancet 2, 669 (1971)
11. Kakkar, V. V., Nicolaides, A. N., Renney, J. T. G., Friend, J. R., Clarke, M. B.: ^{125}I-labelled fibrinogen test adapted for routine screening for deep-vein thrombosis. Lancet 1, 540 (1970)
12. Kutnowski, M., Vandendris, M., Steinberger, R., Kraytman, M.: Prevention of postoperative deep-vein thrombosis by low-dose heparin in urological surgery. Urological Research 5, 123 (1977)
13. Mayo, M. E., Habib, A. I. S., Browse, N. L.: The incidence of deep-vein thrombosis after prostatectomy. British Journal of Urology 43, 738 (1971)
14. Nicolaides, A. N., Dupont, P. A., Dessai, S., Lewis, J. D., Douglas, J. N., Dodsworth, H., Fourides, G., Luck, R. J., Jamieson, C. W.: Small doses of subcutaneous sodium heparin in preventing deep venous thrombosis after major surgery. Lancet 2, 890 (1972)
15. Nicolaides, A. N., Field, E. S., Kakkar, V. V., Yates-Bell, A. S., Taylor, S., Clarke, M. B.: Prostatectomy and deep-vein thrombosis. British Journal of Surgery 59, 487 (1972)
16. Seberi, O., Kummer, H., Zingg, E.: Controlled prevention of postoperative thrombosis in urological diseases with depot heparin. European Urology 1, 229 (1975)
17. Wessler, S.: Heparin as an antithrombic agent. Journal of the American Medical Association 236, 389 (1976)
18. Williams, H. T.: Prevention of postoperative deep-vein thrombosis with perioperative subcutaneous heparin. Lancet 2, 950 (1971)
19. Xerri, A., Deburge, J. P., Aubert, J., Weisberger, G.: Traitement prophylactique des complications thromboemboliques post-opératoires en urologie par l'héparinate de calcium sous-cutanée. Journal d'Urologie et de Néphrologie 80, 283 (1974)

Dr. M. Vandendris
Department of Urology
Brugmann University Hospital
4 Place Arth. Van Gehuchten
B-1020 Brussels
Belgium