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The Incidence of Deep Vein Thrombosis in Prostatectomised Patients Following the Administration of the Fibrinolytic Inhibitor, Aminocaproic Acid (EACA)

J. Sinclair*, C. D. Forbes, C. R. M. Prentice, and R. Scott

Departments of Urology and Medicine, Royal Infirmary, Glasgow, U.K.

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Summary. Forty patients undergoing prostatectomy for benign prostatic hypertrophy were included in a double blind trial of epsilon aminocaproic acid, and the incidence of postoperative deep vein thrombosis determined, using the ^{125}I-fibrinogen technique. There was no significant difference between the groups, the overall incidence of abnormal scans being 50 per cent, but of the patients undergoing enucleative prostatectomy 68 per cent developed significant scan findings compared with 33 per cent following transurethral surgery.

Key Words: Prostatectomy - Deep vein thrombosis - Epsilon aminocaproic acid.

The use of the synthetic inhibitor of fibrinolytic activity, epsilon aminocaproic acid (EACA) to reduce blood loss following prostatectomy is well established (11, 13, 8, 14). It has been postulated that a dynamic equilibrium exists between coagulation and fibrinolysis and concern has been expressed over the theoretical risk of an increased incidence of post-operative deep vein thrombosis when such a fibrinolytic inhibitor is administered (15, 4).

To determine whether these fears were justified, a double blind randomised controlled trial was carried out using the ^{125}I-fibrinogen screening technique, to assess the incidence of calf vein thrombosis in patients receiving EACA and those receiving the placebo.

MATERIALS AND METHODS

Forty patients, all aged over 50 years, undergoing elective retro-pubic prostatectomy or transurethral resection of the prostate for benign prostatic hypertrophy were selected for the study and informed consent was obtained. All operations were carried out by R. S. or J. S. under general anaesthesia. Patients were randomly allocated to one of two groups and twenty patients received EACA (treated group) and the other twenty acted as controls. Coded ampoules and tablets were provided by the hospital pharmacy. EACA or placebo was administered by intravenous infusion at the time of induction of anaesthesia at a rate of 0.5 g. per hour for 12 hours, followed by oral dosage of 6 g twice per day for 10 days. The total dose given was 126 g.

Deep vein thrombosis was detected by the ^{125}I-fibrinogen technique (1). 100 μc of ^{125}I-fibrinogen (Radiochemical Centre, Amersham) was injected intravenously the day before operation after blocking the thyroid gland with potassium iodide. The lower limbs were scanned immediately pre-operatively and on the first, third, fifth, seventh and tenth post-operative days, using the Pitman Isotope Localisation Counter, model 235. The criteria for diagnosis of deep vein thrombosis, were as suggested by Kakkar et al. (7). Urine was inspected daily for clots, and all patients were examined daily for clinical signs of deep vein thrombosis with special reference to pitting oedema (16).

* Present address: Department of Surgery, Southern General Hospital, Glasgow.

Inhibition of fibrinolytic activity was measured in plasma by the urokinase sensitivity test (10).

RESULTS

The mean age of the treated group was 67 years and of the control group 70 years. Twenty of the 40 patients (50 per cent) had isotope evidence of deep vein thrombosis. Of these 11 had received EACA, and 9 were controls. There was no significant difference between the two groups. Ten of these 20 patients had bilateral abnormal scans but there was no correlation with administration of EACA, 5 having been controls. Seven patients had positive scans by the third post-operative day (3 were controls), a further 6 by the fifth day (3 were controls) and the final 7 by the seventh day (3 were controls).

Seventeen of the 20 patients with positive scans had abnormal physical signs suggestive of deep vein thrombosis, although in 11 this was minimal oedema. In addition to leg oedema, 3 patients had calf pain and tenderness and 3 patients had florid signs with obvious oedema, positive Homan's sign and raised leg temperature. These were evenly distributed among the patients given EACA and the controls.

Thirteen of 19 patients (68 per cent) who had retropubic prostatectomy, developed isotopic evidence of deep vein thrombosis which was bilateral in 6 cases whereas only 7 of 21 patients (33 per cent) in whom transurethral resections were carried out had positive scans of which 3 were bilateral. Only 1 of these 7 was detected after the fifth post-operative day, whereas 6 of the 13 patients with positive scans following enucleative prostatectomy had normal scans until the seventh day.

No attempt was made to estimate blood loss, but on average the patients given EACA had their urethral catheters in for 12 hours or less post-operatively. Two of the control patients required recatheterisation on account of persistent haematuria and a further control patient had a secondary haemorrhage. These 3 patients had all undergone retropubic prostatectomy and bleeding settled with conservative treatment.

When the drug code was broken it was confirmed that all patients taking the active drug had significant prolongation of the urokinase sensitivity test indicating adequate blood and urinary levels of fibrinolytic inhibition.

DISCUSSION

Despite fears that the large doses of EACA given to inhibit the urinary fibrinolytic enzyme urokinase might inhibit systemic fibrinolysis, and lead to intravascular thrombosis, various studies have now shown that there is no significant increase in the incidence of deep vein thrombosis in these patients, either on clinical grounds (2, 14) or using isolated phlebography two weeks after operation (4) or more satisfactorily using ^{125}I-fibrinogen (6). There would thus appear to be no contraindication to the routine use of fibrinolytic inhibitors in patients undergoing prostatectomy. Furthermore, there is no evidence that patients so treated, develop deep vein thrombosis either earlier, or on a more extensive scale than control patients.

Our results confirm these findings. Despite the administration of a larger dosage of EACA over a longer period (126 g over 10 days) than that given by Gordon-Smith et al. (a total of only 18 g. EACA covering only the peri-operative period) (6), we found no increased evidence of deep vein thrombosis. This is in keeping with the finding of Becker et al. (4) who had administered a longer course with an average dose of 148 g.

The high overall incidence (50 per cent) of deep vein thrombosis following prostatectomy in this series contrasts with that of Nicolaides et al. (12) who in a series of 50 patients found an incidence of only 24 per cent using the ^{125}I-fibrinogen test. These authors also commented on the low incidence of deep vein thrombosis (6.8 per cent) after transurethral resection as compared with 47.6 per cent after retropubic prostatectomy. Our figures of 33 per cent and 68 per cent respectively confirm this relative benefit of transurethral resection. These authors also point out that the duration of the retropubic operation, together with stasis occurring during operation and the presence of post-operative pain, all contribute to this high figure. Mayo et al. (9), however, demonstrated that the position adopted for transurethral resection was in fact less favourable if the legs are supported in the standard gutter leg supports, and as intra-operative factors may be more important than post-operative factors in the development of deep vein thrombosis, the position on the operating table should favour open prostatectomy. They also demonstrated the significant difference in incidence of deep vein thrombosis with 51 per cent after open prostatectomy and 10 per cent following transurethral resection. This figure of 51 per cent is similar to that for all major surgery (5). A lower incidence of deep vein thrombosis, 21 per cent, was described in a series of 243 transvesical prostatectomies submitted to ascending phlebography, but not to the ^{125}I-fibrinogen test (4), and an overall incidence of D. V. T. of 29 per cent in 62 patients submitted to retropubic prostatectomy and assessed by the latter test (6). The late onset of abnormal scans in our

series was noteworthy with 6 of the 13 patients undergoing open prostatectomy having normal scans on the fifth day. This contrasts with the findings of Gordon-Smith et al. (6), who found that 16 of their 18 cases had abnormal scans within 48 hours, the remaining 2 being positive after 4 days.

The low incidence of abnormal physical signs is in keeping with previous authors (5, 16) who found that less than 30 per cent of patients with positive scans had abnormal signs.

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R. Scott, M. B., F. R. C. S.
Urological Department
Royal Infirmary
Glasgow 64 OSF
U. K.