

The Incidence of Venous Thrombosis in the Lower Limbs Following Elective Gallbladder Surgery

A Study with the ¹²⁵I-Fibrinogen Test

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ABSTRACT

The frequency of postoperative venous thrombosis and the prophylactic effect of dextran 40 and 70 were studied in 90 otherwise healthy patients undergoing cholecystectomy. The ¹²⁵I-fibrinogen test was employed as the diagnostic method. The frequency of thrombosis was very low (1.1 %) compared with other investigations on patients undergoing elective general surgery. Thus nothing can be concluded about the prophylactic effect of dextran from this series, but it can be presumed that this type of patient does not need routine prophylaxis against deep venous thrombosis.

INTRODUCTION

In previous studies using phlebography or the ¹²⁵I-fibrinogen test as diagnostic methods, we have found dextran 70 to be as good as (8, 11) or even better than dicoumarol (9) as a prophylactic agent against post-traumatic venous thrombosis in patients with hip fractures. These patients belong to a "high risk" group as far as venous thrombosis is concerned.

The ¹²⁵I-fibrinogen test has been shown to be a simple and reliable diagnostic method, which makes it possible to establish the frequency of venous thrombosis in the lower limbs in different patient groups, and to study the effects of different therapeutic and prophylactic regimens.

After general surgery the incidence of postoperative venous thrombosis has been found to be relatively high. Thus Kakkar (23) found a frequency of 27.8% among patients undergoing elective surgery, and Becker & Schampi (6) found it to be 21.7% in women over 50 years of age undergoing cholecystectomy and 50% in men undergoing trans-vesical prostatectomy for hyperplasia of the prostate.

This investigation was set up to study some aspects of the frequency of thrombosis and the effects of dextran prophylaxis in a group of patients, where the literature gives a frequency of thrombosis

of 15–20%, i.e. what could be called a "low risk" group. The aims were

1. to study the frequency of postoperative thrombosis in the venous system of the lower limbs after cholecystectomy, the ¹²⁵I-fibrinogen test being used for detection of thrombosis,

2. to study the thrombosis prophylactic effect of dextran, and to determine the value of routine prophylaxis in these patients.

3. to make a comparison between dextran 40 and dextran 70 as thrombosis prophylactic agents.

MATERIAL AND METHODS

Ninety patients were randomized into three equal groups. These were a control group, a group given dextran 40, and a group given dextran 70. Patients with known heart disease or malignancy were not included. One patient in the control group was later excluded because of severe hypotension treated by dextran 70 during the operation. From Table I it can be seen that the groups are closely comparable as far as sex ratio, age, weight, operation time and the listed factors predisposing to venous thrombosis are concerned.

Method for thrombosis prophylaxis

Prophylaxis was given as follows:

500 ml physiological electrolyte solution (Ringerdex®, Pharmacia AB, Uppsala, Sweden) or 500 ml dextran 40 (Rheomacrodex®, Pharmacia AB) or 500 ml dextran 70 (Macrodex®, Pharmacia AB) during the operation.

500 ml during the first 4 postoperative hours.

500 ml on the first postoperative day (given over 4 hours). The first infusion was started after the induction of anaesthesia to minimize the risk of reported anaphylactoid complications (4).

Method for thrombosis diagnosis

The ¹²⁵I-fibrinogen test as developed by Atkins & Hawkins (3) was used. In summary it was performed thus: 3 ml sodium iodide was injected intravenously at the time of admission to block the uptake of free radioiodine by the thyroid gland, and then 200 mg potassium iodide were given perorally every day for 3 weeks. About 8 hours after the injection of sodium iodide 50–100 μ Ci of ¹²⁵I-labelled

Table I. The comparability between the three groups

The groups do not differ in the factors shown in the table. Mean and S.D.

| | Control | Dextran 40 | Dextran 70 |
|--|----------------------|----------------------|----------------------|
| Female/male ratio | 2.0 | 2.8 | 1.3 |
| Age (years) | 56.6±11.0 (37-74) | 55.3±13.4 (30-82) | 51.8±13.6 (30-74) |
| Weight (kg) | 71.8±13.9 | 69.4±11.5 | 68.0±10.5 |
| Operation time (min.) | 117.7±35.0 | 123.8±47.0 | 131.6±46.8 |
| Factors predisposing to venous thrombosis: | | | |
| fracture of the leg | 2 | 3 | 3 |
| varicose veins | 16 | 12 | 16 |
| previous thrombosis | 0 | 1 | 1 |

fibrinogen from hepatitis-free blood donors were given intravenously. Radioactive uptake was measured over the heart and at eight points on each leg preoperatively, immediately after the operation, on postoperative days 1, 2, 3 and 4, and then on every second day until discharge. The radioactivity was measured with a mobile scintillometer containing a sodium iodide crystal, a photoamplifier and round brass collimator 8 cm in diameter, connected to an impulse calculator with a clock.

In a methodological study we found that a 15% increase in uptake activity, compared with the adjacent points for two or more succeeding investigations, was a reliable criterion for the diagnosis of thrombosis when checked by phlebography (7). In the present study we used this criterion, as well as that suggested by Becker (5), i.e. a 10% increase in uptake which increases further the following day. We also studied the frequency of the so-called primary pathological pattern, which means an uptake maximum at one of the points seen preoperatively (5).

RESULTS

The results are summarized in Table II. Only one patient in the whole series (one in the dextran 40 group) developed venous thrombosis, according to the criteria which we earlier found reliable (7). If the

criteria put forward by Becker (5) are used, the frequency is somewhat higher, i.e. 4 in the control group, 1 in the dextran 70 group and 2 in the dextran 40 group. The reduction in the dextran groups is not significant ($p > 0.1$). All the increases in uptake were situated at points 6 or 7, that is distally in the calf, and the mean age of the patients with increased uptakes was 58.1 years. The frequency of primary pathological patterns in the sample of patients was 10%, but none of these 9 people developed a thrombosis. The primary pathological pattern was bilateral in one of the patients, and 3 of them had varicose veins within its area. The mean age of these 9 patients was 61.4 years. One patient in the dextran 40 group developed a haematoma at the site of subcutaneous premedication on the thigh, and developed increased radioactive uptake in this area (point 2). The patient excluded from the control group because of severe hypotension treated with dextran developed bilateral thromboses with very high uptakes (point 6). Phlebography was performed on the right leg and verified this diagnosis. The diagnostic and prophylactic procedures were undertaken without any complications.

Table II. Frequency of increased radioactive uptake and primary pathological patterns in the lower limbs in otherwise healthy patients undergoing cholecystectomy

| | Number of patients | | | Number of patients with a primary pathological pattern |
|------------|--------------------|-----------------------------------|-------------------------------------|--|
| | Total | With increased radioactive uptake | | |
| | | 15% two days | 10% and a higher value the next day | |
| Control | 30 | 0 | 4 | 6 |
| Dextran 40 | 30 | 1 | 2 | 0 |
| Dextran 70 | 30 | 0 | 1 | 3 |

Table III. Review of frequencies of postoperative venous thrombosis from the literature

The patients have undergone elective surgery, have no prophylaxis against deep vein thrombosis and the ^{125}I -fibrinogen test has been used for the diagnosis

| | Type of operation | Age (years) | Thrombosis frequency (%) | Diagnostic criteria | No. of patients |
|-----------------------------------|---|-------------|--------------------------|---------------------|-----------------|
| Own material | Cholecystectomy | 54.6 | 1.1 | 15% | 90 |
| Atkins & Hawkins, 1968 (3) | Elective surgery | | 25 | Increasing uptakes | 20 |
| Flanc et al., 1968 (17) | Elective surgery | >40 | 35.4 | Phlebography | 65 |
| Negus et al., 1968 (32) | Major surgery | 62 | 34.4 | 15% | 93 |
| Lambie et al., 1970 <i>b</i> (26) | Major surgical and gynaecological op. | >40 | 44 | Phlebography | 111 |
| Milne et al., 1971 (29) | Major abdominal op. | >45 | 33 | 15% | 75 |
| Tsapogas et al., 1971 (40) | Major abdominal op. | 56.1 | 14 | 15% | 44 |
| Bonnar & Walsh, 1972 (10) | Hysterectomy | 46 | 10.7 | 20% | 140 |
| Gordon-Smith et al., 1972 (18) | Transvesical prostatectomy | >50 | 28 | 15% | 32 |
| Hills et al., 1972 (20) | General elective op. | 59 | 30 | 15% | 50 |
| Kakkar, 1972 <i>a</i> (23) | Elective surgery | >40 | 27.8 | 20% | 469 |
| | Prostatectomy | | 23.8 | 20% | 42 |
| | transvesical | | 50 | | 18 |
| | transurethral | | 4 | | 24 |
| | Gynaecology | >30 | 18.4 | 20% | 92 |
| Jackson, 1973 (21) | Tubal ligation | 30.8 | 4.5 | 20% | 44 |
| Becker & Schampi, 1973 (6) | Cholecystectomy | 64 | 21.7 | 10% | 23 |
| | Transvesical prostatectomy | 67 | 50 | 10% | 12 |
| Hassan et al., 1973 (19) | General surgery | >40 | 12 | 20% | 100 |
| Williams et al., 1973 (42) | Elective surgery | 63 | 12 | 20% | 75 |
| Dormandy & Edelman, 1973 (16) | Elective general and gynaecological surg. | >20 | 21.2 | Not given | 52 |

DISCUSSION

The frequency of thrombosis is very low in this series.

Different authors have used different criteria for the diagnosis of thrombosis with the ^{125}I -fibrinogen test. For example, 10% increase in uptake which increases over subsequent days (5), 15% increase in uptake or more for at least two succeeding days (12, 13, 20, 32, 41), 20% increase in uptake (23, 35, 43) or 30% increase in uptake (30). We found the 15% criterion to be valuable and in good agreement with the results from phlebography on patients with fracture of the femoral neck (7). If we use the criteria suggested by Becker (5), the frequency of thrombosis is more nearly what would be expected from earlier studies with the same age group and type of operation.

It is always difficult to compare differing groups of patients, but in Table III a review is given of the frequency of thrombosis in patients receiving no prophylaxis against it, and obtained by authors using the ^{125}I -fibrinogen test. There can be several expla-

nations for the differences shown in the table and for the low frequency found in our sample. Patient's age is such a factor, being rather low in this series. Cholecystectomy is an upper-abdominal operation and certainly carries less risk of thrombosis than operations in the lower part of the abdomen. Our patients were mobilized early, i.e. on the first post-operative morning, and we believe this to be a factor of great importance as it is known that stimulation of the calf muscles considerably improves flow in the venous system (33, 38), and several authors have shown the preventive effects of different kinds of calf muscle stimulation during operation (6, 13, 15, 33, 36, 37). Moreover we excluded from the study such high risk patients as those with heart disease or malignancy. It can be concluded that it is of great importance that diagnostic criteria and patient material are reported in detail if different investigations are to be comparable.

Another factor that must be taken into account when explaining the low frequency is that the ^{125}I -labelled fibrinogen could have been defective. This seems unlikely as the patient who was excluded

showed a very high uptake which was proved to correspond to a thrombus in the region by phlebography. In addition, high uptake was seen over a haematoma, and coagulability tests showed good clotting properties of the fibrinogen at intervals throughout the investigation.

Even when using the 10% criterion for diagnosis, all uptake maxima were seen in the distal part of the calf (points 6 and 7), and the clinical significance of such thrombi has recently been a matter of debate (24, 27, 28, 34, 39).

Ten percent of the patients exhibited increased radioactive uptakes even preoperatively, a pattern which Becker (5) called "primary pathological". We found a frequency which was only half that found by Becker, and the frequency of patients with varicose veins was also less in our material than in his.

For obvious reasons, no conclusions can be drawn from this investigation on the thrombosis prophylactic effect of dextrans or on the comparability of dextran 40 and dextran 70. One conclusion that seems reasonable is that otherwise healthy patients undergoing uncomplicated cholecystectomy do not need routinely given prophylactic treatment against deep vein thrombosis.

As far as dextran is concerned, there are now several published investigations showing a prophylactic effect against deep venous thrombosis and pulmonary embolism (1, 2, 6, 10, 14, 22), and showing that its effect is as good as that of anticoagulation (8, 9, 11, 25, 31).

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