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Oral anticoagulants and dextran for prevention of venous thrombosis in orthopaedics

A hundred and fifty-two patients who were to undergo major orthopaedic surgery were divided into two groups in order to study the value of dextrans administered as adjuvants to oral anticoagulants in the prevention of deep venous thrombosis.

The control group had oral anticoagulants only from the evening before the day of operation, aimed at the 15 per cent thrombotest level. The dextran group had peroperative and postoperative dextran infusions as well. Radionuclide venography was used for thrombosis detection.

The dextran group had a lower incidence of thrombosis, but more haemorrhagic problems. The incidence of thrombosis was high in both groups.

Bart A. Swierstra, Frank J. van Oosterhout, Bert Ausema[1], Willem H. Bakker[1], Willem B. van der Pompe[2] & Hubert J. A. Schouten[3]

Departments of Orthopaedic Surgery and [1]Nuclear Medicine, University Hospital Rotterdam – Dijkzigt, Dr Molewaterplein 40, NL-3015 GD Rotterdam, The Netherlands, [2]Department of Nuclear Medicine, Rotterdam Radiotherapeutic Institute, and [3]Institute of Biostatistics Erasmus University, Rotterdam, The Netherlands

We have been using oral anticoagulants to prevent deep venous thrombosis after orthopaedic surgery for years. We start on the evening before the day of operation and aim at a thrombotest of 15 per cent. However, a pilot study with the aid of radionuclide venography (Swierstra 1980, unpublished data) has revealed that the thrombosis rate was 35 per cent. Since this thrombosis rate could be expected to decrease if *peroperative* protection were improved, we decided to study the effects of adding dextran infusions to our original protocol.

Patients and methods

The study concerned consecutive patients admitted for total hip or total knee replacement, osteotomy of the hip or knee, or operation on the vertebral column. All operations were performed under general anaesthesia. Patients with contraindications to oral anticoagulants or dextran were excluded, as were patients already under anticoagulant therapy on admission.

In the end, 152 patients were divided at random into the control group and the dextran group (Table 1). The groups were matched for age, weight, height, presence or absence of rheumatoid arthritis and factors predisposing to thrombosis, as well as for duration of general anaesthesia, operation and tourniquet ischaemia.

Blood loss was estimated peroperatively in suction jars and gauzes and postoperatively in drains, and from the amount of blood transfused. The presence of wound haematomas was recorded.

Venous thrombosis was diagnosed on the basis of radionuclide venography, using Technetium-99M macroaggregates of albumin, performed approximately 1 week after the operation. The venograms were assessed independently by four observers and regarded as positive if three or four similar positive assessments were made.

Oral anticoagulants were continued for 3 months when thrombosis was diagnosed; otherwise, they were discontinued on discharge from hospital.

The Mantel-Haenszel, Yates-Cochran and Mann-Whitney tests were used in statistical analysis, and

Table 1. Thrombosis prophylaxis regimens

Control group

Day −1 = day before operation : 4 mg acenocoumarol.

Day 0 = day of operation : 4 mg acenocoumarol.

Days 1 through 5 : acenocoumarol doses based on daily thrombotest, aiming at 15 per cent.

Day 6 etc. : acenocoumarol as required in view of thrombotest, where necessary.

Dextran group

1) Acenocoumarol as in group A.
2) In addition:

Day 0 : 500 ml dextran 40 during operation after inducing anaesthesia.
500 ml dextran 40 after operation in recovery room.

Day 1 : 500 ml dextran 40 in the ward.

All doses of anticoagulants were determined by the same investigator.
Acenocoumarol = SintromMitis®; Dextran 40 = Rheomacrodex®.

the coefficient kappa was determined as a measure of the degree of agreement between two observers.

Results

There was a significant difference in the incidence of deep venous thrombosis with 34/81 in the control group and 21/71 in the dextran group (Table 2). The distribution of thrombosis over the calf and more proximal levels was the same in both groups: calf vein thrombosis was 1.5 times as frequent as more proximal thrombosis.

The blood loss during operation was 1088 ± 998 ml in the control group and 1225 ± 863 ml in the dextran group; after operation, it was 472 ± 412 ml and 599 ± 501 ml, respectively (no significant differences).

In the control group, 70 of the 81 patients received 253 units of blood, and in the dextran group 67 of the 71 patients received 275 units of blood. In the control group there were eight and in the dextran group there were 17 haematomas. Both differences were significant.

No clinically manifest pulmonary embolism was diagnosed in the course of the study. One patient with a negative venogram was later readmitted with pulmonary embolism and a venogram which had turned positive.

Allergic reactions to dextran were not observed. The level of anticoagulation as reflected by the thrombotest percentage was comparable in the two groups: during the first 2 postoperative weeks the thrombotest percentage was less than 15 in 41 per cent, and less

Table 2. Incidence of thrombosis following major orthopaedic surgery

Type of operation	Control group		Dextran group	
	Total	Thrombosis	Total	Thrombosis
Total hip replacement	49	20	35	11
Corrective osteotomy of the hip	14	3	14	2
Total knee replacement	7	4	7	1
Corrective osteotomy of the knee	10	6	6	2
Vertebral column operation	1	1	4	3
Others (removal of infected prosthesis)			5	2
	81	34	71	21

The control group had oral anticoagulants only. The dextran group had per- and postoperative dextran infusions as well. The difference in thrombosis incidence was significant just ($P_1 = 0.05$)

than 20 in 65 per cent of all performed thrombotests.

Interobserver agreement in assessment of the radionuclide venograms was good, with the kappa values ranging from 0.78 to 0.89.

Discussion

Our results confirm the value of dextran for thrombosis prophylaxis in orthopaedics (Steinmann et al. 1975). However, administration of dextrans as adjuvants to oral anticoagulants was associated with more haemorrhagic problems; more blood transfusions were required and more wound haematomas were observed. The per- and postoperative blood losses showed a tendency to be greater in the dextran group, without reaching significance. The thrombosis rates in both groups were high. Harris et al. (1974), using roentgen phlebography, demonstrated thrombosis in 31 per cent of cases of total hip replacement in which warfarin was given from the day before operation. The results of coumarin prophylaxis in hip fracture surgery show a similar incidence of thrombosis (Sturm & Gruber 1974). With the combined use of dextran and warfarin after femoral neck fractures, Korvald et al. (1973) found a thrombosis rate of 10 per cent at roentgen phlebography 2–3 weeks after operation. This low incidence may partly be explained by the late phlebographies, as indicated by their 30 per cent thrombosis rate observed by immediate postoperative ^{125}I-fibrinogen scanning.

Our relatively high thrombotest level of 15 per cent was chosen for fear of "overshoots" causing haemorrhages after joint replacements. Even though the daily dose of oral anticoagulants was always determined by the same investigator, not all patients had permanent thrombotest levels of 15 per cent. A similar situation has been reported by other investigators (Bergquist et al. 1972, Korvald et al. 1973, Morris & Mitchell 1976).

The good interobserver agreement in this study, added to the good correlation with roentgen contrast phlebography (Hayt et al. 1977), confirms our conviction that radionuclide venography is a reliable diagnostic aid.

The combination of two prophylactic measures, each affecting the mechanism of haemostasis, was associated with more haemorrhagic problems and since still one out of every three patients developed thrombosis, we are continuing our search for better preventive measures.

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