Prophylaxis for deep vein thrombosis with aspirin or low molecular weight dextran in Korean patients undergoing total hip replacement

A randomized controlled trial

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Accepted: 25 February 1997

Summary. 150 Korean patients undergoing primary uncemented total hip replacement were randomized into 3 treatment groups for deep vein thrombosis (DVT) prophylaxis. Group A(50) were controls; Group B(50) received aspirin 1.2 g daily in 3 divided doses from 2 days before, to 14 days after surgery; Group C(50), received low molecular weight dextran 500 ml, infused intravenously at 50 ml/hour during surgery, and on each of the following 2 days. Contrast venograms were performed prior to surgery and 7–10 days after. The incidence of DVT was 20% in the control group, 12% in the aspirin group ($p < 0.1$ vs control), and 6% in the dextran group ($p < 0.05$ vs control). In patients developing DVT, the ratio of proximal to distal thrombi was increased in the control group as compared to treated groups (4:1 in the control group vs 1.5:1 in the treated groups). Both aspirin and dextran were well tolerated. Obesity ($p < 0.05$) and long-term administration of steroids ($p < 0.05$) were risk factors for deep vein thrombosis which reached statistical significance in the control group. Intraoperative venograms performed on 10 patients, showed that hip flexion (mean 40.4°) plus adduction (mean 11.5°) plus internal rotation (mean 81.5°), resulted in severe twisting or kinking of the femoral vein with stagnation of blood flow. Low molecular weight dextran significantly reduce the incidence of deep venous thrombosis and aspirin, though less effective, had a similar effect.

Internal rotation of the hip joint should be minimized during operation in order to limit stagnation of blood flow in the femoral vein.

Résumé. 150 patients coréens opérés pour un remplacement total de hanche non-cimentée ont été triés au hasard en 3 groupes de traitement de prophylaxie de la thrombose. Le groupe A(50): groupe de contrôle. Le groupe B a reçu 1.2 g d'aspirine par jour en 3 doses à compter de 2 jours avant l'opération jusqu'à 14 jours après celle-ci. Le groupe C(50) a reçu des petites molécules de dextrane 500 ml par injection intraveineuse de 50 ml/heure pendant l'intervention et durant les 2 jours suivants. Une phlébographie de contrôle a été réalisée avant l'intervention et 7–10 jours après celle-ci. Le taux de thrombose veineuse profonde (TVP) était de 20% dans le groupe du contrôle, 12% dans le groupe «aspirine» ($p < 0.1$ contre contrôle) et 6% dans le groupe de «dextrane» ($p < 0.05$ contre contrôle). Parmi les patients développant une TVP, le ratio proximal/distal était cliniquement augmenté dans le groupe du contrôle comparé avec les groupes traités (4:1 dans le groupe du contrôle contre 1.5:1 dans les groupes traités). L'aspirine et la dextrane ont bien été tolérées. L'obésité ($p < 0.05$) et l'administration à long-terme de stéroïde étaient des facteurs de risque pour la TVP avec une signification statistique dans le groupe du contrôle. Les phlébographies per-opératoires faites chez 10 patients ont montré que la flexion (moyenne 40.4°) plus l'adduction (moyenne 11.5°) plus la rotation interne (moyenne 81.5°) se sont traduites par une grave torsion de la veine fémorale accompagné d'une stagnation circulatoire. Les petites molécules

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Table 1. Age and Sex distribution

Age	Control		Aspirin		Dextran		Total
	M	F	M	F	M	F	
21–30	2	1	1	0	2	1	7
31–40	4	0	5	1	7	1	18
41–50	8	1	8	2	6	1	26
51–60	15	3	13	2	14	2	49
61–70	10	3	10	5	10	2	40
71–80	1	1	1	1	1	2	7
81–	1	0	0	1	0	1	3
Total	41	9	38	12	40	10	150

les de dextrane réduisent significativement le taux de thrombose veineuse chez les patients coréens qui ont subi une intervention chirurgicale de remplacement de la hanche et l'aspirine, quoique moins efficace, réduit aussi le taux de TVP. Pour limiter la stagnation de la circulation du sang dans la veine fémorale pendant l'intervention chirurgicale, la rotation interne de la hanche doit être minimisée.

Introduction

Previous studies suggest that deep venous thrombosis (DVT) is less frequent in Asia than in Western countries [7]. We have undertaken a study to establish the incidence of DVT in Korean patients undergoing uncemented hip replacement without prophylaxis, and to evaluate the efficacy of (i) low molecular weight dextran (ii) aspirin, in preventing DVT in such patients.

In addition, in a sub-group of patients, the impact of perioperative manipulation of the hip on blood flow in the femoral vein was studied.

Patients and methods

This study was performed at the Hanyang University Hospital, Korea between December 1990 and July 1994. The patients who were undergoing primary uncemented total hip replacement were all aged greater than 18 years and informed consent was obtained in every instance. We excluded those with a history of aspirin intolerance or who had ingested aspirin containing compounds or other antiplatelet agents within 14 days prior to surgery.

The age and sex distribution of the 150 patients in the study is shown in Table 1. The preoperative diagnoses are listed in Table 2; the majority (70%) of the patients had avascular necrosis of the femoral head. The general condition of those in the three groups was comparable.

Table 2. Diagnosis

Preop. diagnosis	Control (%)	Aspirin (%)	Dextran (%)	Total (%)
Avascular necrosis	37 (74)	34 (68)	35 (70)	106 (70.8)
Sequelae of hip fracture	7 (14)	9 (18)	9 (18)	25 (16.7)
Osteoarthritis	2 (4)	3 (6)	2 (4)	7 (4.7)
Dysplastic hip	2 (4)	1 (2)	1 (2)	4 (2.6)
Sequelae of hip dislocation	1 (2)	2 (4)	1 (2)	4 (2.6)
Quiescent tuberculosis	1 (2)	1 (2)	2 (4)	4 (2.6)
Total	50	50	50	150 (100)

Every patient was operated upon under general anesthesia by one of the authors (Y.H.K.) using a modified Gibson approach. Two Haemovac drains were placed in the wound and removed 2 days after insertion. Crutch walking was permitted when discomfort could be tolerated.

Aspirin, 1.2 g daily in 3 divided doses, was supplied as 100 mg buffered or enteric coated tablets ("Aspirin", Bayer Korea), starting 48 hours before the operation and finishing 14 days after. Low molecular weight dextran ("Rheomacrodex" 500 cc) was infused intravenously at a rate of 50 cc/h perioperatively, and continued during the following 2 days.

Patients were randomly allocated to a control group, an aspirin group, and a low molecular weight (LMW) dextran group, with 50 in each.

All had contrast venography of the affected limb 3 days before operation, and 7–10 days after. The criteria for diagnosis of deep venous thrombosis were an intraluminal filling defect, non-filling of a vein, or abrupt termination of a vein.

An intraoperative venogram of the operated limb was performed on 10 patients. With the patient in the lateral position and the hip joint dislocated posteriorly, 20 cc of contrast media (Ultravist) was twice injected into a pedal vein. The velocity of venous flow was assessed following the first injection, and the impact of flexion, adduction, and internal rotation of the femur on the flow in the femoral vein assessed following the second injection. The velocity of venous flow was calculated on a basis of the distance from the pedal injection site to the inferior pubic ramus on the affected side (cm) divided by the time (s) taken for the contrast medium to reach the inferior pubic ramus. The primary endpoint was the presence or absence of deep venous thrombosis in the affected lower limb as revealed by venography.

Statistical analysis was undertaken using the chi-square test.

Results

None of the preoperative venograms showed evidence of DVT.

The incidence of DVT following operation was 20% in the control group, 12% in the aspirin group and 6% in the LMW dextran group ($P < 0.05$ for LMW dextran vs control) (Table 3). The ratio of thromboproximal to the trifurcation of the popliteal vein to more distal clot was clinically higher in the control group (4:1) as compared to the aspirin and

Table 3. Patients with venograms

	Experimental group		
	Control (%)	Aspirin (%)	Dextran (%)
Positive venogram	10 (20)	6 (12)	3 (6)
Negative venogram	40	44	47
Overall incidence	10/50 (20)	6/50 (12)	3/50 (6)
Significance		$0.05 < P < 0.1$	$P < 0.05$
		$\chi^2 = 1.501$	$\chi^2 = 0.904$

LMW dextran groups (1.5:1). A total of 13 (68.4%) patients had evidence of thrombosis in more than one site (Table 4).

Obesity ($P < 0.05$) and long-term administration of steroids ($P < 0.05$) were statistically significant risk factors for deep vein thrombosis in the control group. Aspirin and dextran prophylaxis were effective in reducing the influence of these factors in the treated groups (Table 5).

Intraoperative phlebography performed on 10 patients revealed a wide variation in the velocity of venous flow (Table 6). (Mean velocity 6.89 cm/s, max = 15 cm/s, min = 3 cm/s). It was possible to completely interrupt blood flow in the

Table 4. Distribution of thrombi in patients with deep vein thrombosis

Site/group	Control	Aspirin	Dextran
Iliofemoral	8/10	1/3	1/2
Superficial femoral or profound femoral below S-F junction	2/10	1/3	1/2
Distal femoral	6/10	2/3	1/2
Popliteal	4/10	2/3	2/2
Major calf vein	3/10	3/3	2/2
Muscular branch	2/10	1/3	1/2

femoral vein in all patients (Fig. 1). Deep vein thrombosis developed in 2 of these patients, 1 in the control group and 1 in the aspirin group.

There were no major bleeding complications. Wound hematoma occurred in 1 member of the control group and 2 of the dextran group. There were no statistically significant differences in measured intraoperative blood loss, total blood loss or total blood replacement amongst the three groups. The quantity of wound-suction blood loss was 723 ± 122 ml in the control group, 698 ± 135 ml in the aspirin group, and 739 ± 102 ml in LMW dextran group; the differences were statistically insignificant.

Table 5. Risk factors influencing the incidence of deep vein thrombosis

Suspicious risk factors/group	Incidence of DVT (%)			Significant difference		
	Control	Aspirin	Dextran	Control	Aspirin	Dextran
Age						
60yrs below	4/31 (12.9)	2/32 (6.2)	1/34 (2.9)	$P > 0.1$	$P > 0.1$	$P > 0.1$
60yrs above	6/19 (31.5)	2/18 (11.1)	3/16 (18.7)			
Sex						
Male	7/43 (16.27)	3/38 (7.8)	3/40 (7.5)	$P > 0.1$	$P > 0.1$	$P > 0.1$
Female	3/7 (42.8)	1/12 (8.3)	1/10 (10.0)			
Op time						
2 h below	4/28 (14.2)	3/33 (9.1)	2/28 (7.1)	$P > 0.1$	$P > 0.1$	$P > 0.1$
2 h above	6/22 (27.2)	1/17 (5.8)	2/22 (9.1)			
Bleeding						
100 Occ below	1/11 (9)	1/16 (6.3)	2/24 (8.3)	$P > 0.1$	$P > 0.1$	$P > 0.1$
100 Occ above	9/39 (23)	3/34 (8.8)	2/26 (7.7)			
Obesity						
Yes	3/4 (75)	1/3 (33.3)	2/8 (25)	$P < 0.1$	$P > 0.1$	$P > 0.1$
No	2/46 (4.3)	3/47 (6.4)	3/42 (7.1)			
Alcohol abnae						
Present	2/12 (16.6)	1/13 (7.7)	2/19 (10.5)	$P > 0.1$	$P > 0.1$	$P > 0.1$
Absent	8/38 (21.5)	3/37 (8.1)	2/31 (6.5)			
Steroid medication						
Present	8/14 (57.1)	3/14 (21.4)	2/11 (18.2)	$P < 0.05$	$P > 0.1$	$P > 0.1$
Absent	2/36 (5.6)	1/36 (2.7)	2/39 (5.1)			
Diabetes mellitus						
Present	1/4 (25)	1/16 (6.3)	1/12 (8.3)	$P > 0.1$	$P > 0.1$	$P > 0.1$
Absent	9/46 (18.3)	3/34 (8.8)	3/38 (7.9)			
Mobilization						
Early	4/28 (14.2)	2/37 (5.4)	1/31 (3.2)	$P > 0.1$	$P > 0.1$	$P > 0.1$
Late	6/22 (27.2)	2/13 (15.4)	3/19 (15.8)			

Table 6. Intraoperative venography in 10 patients

Case	Sex/age	Time of dye flow from the dorsum of the foot to the hip (velocity of venous flow: cm/s)	Position of hip at kinked femoral vein			Postoperative 7 day venogram
			Flexion (degree)	Adduction (degree)	Int. rotation (degree)	
1	M/35	15 (5.3)	40	10	80	–
2	M/45	5 (15)	45	10	85	–
3	F/78	25 (3)	45	10	85	–
4	M/63	10 (7.5)	40	15	75	–
5	M/56	8 (9.4)	35	10	80	–
6	F/71	15 (4.7)	45	10	80	–
7	M/52	12 (6.7)	35	10	85	–
8	F/56	20 (4)	40	15	80	–
9	M/85	15 (5.3)	35	15	85	+
10	F/49	10 (8)	40	10	80	+
Mean		13.5 (6.9)	40.4	11.5	81.5	

Discussion

Venous thromboembolism is a well known complication of surgery of the hip joint [1, 6, 10, 12]. The reported incidence worldwide ranges from

35%–60% [2–5, 9, 11, 15, 16], with a 0.5–7% incidence of fatal pulmonary embolism [6, 14]. Our results cannot be compared directly with those from the Western world because of the difference

Fig. 1 a–d. The intraoperative venogram in a 49-year-old woman. **a** Normal flow of the media in the femoral vein at the neutral position of the hip joint. **b** Mild narrowing of the lumen of the femoral vein at 40 degrees of flexion of the hip joint. **c** Marked narrowing of the lumen of the femoral vein and stagnation of the contrast media at 40 degrees of flexion and 10 degrees of adduction of the hip joint. **d** Kink and complete occlusion of the femoral vein at 40 degrees of flexion, 10 degrees of adduction and 80 degrees of internal rotation of the hip joint

in variables of age and sex. Although the 20% incidence of DVT in our control group is lower than that reported in many Western studies, it is twice the incidence reported by Kim and Suh [7], and close to the 18% incidence noted by Yoo et al. in a similarly untreated group of 50 patients having elective hip replacements (personal communication). The rising incidence of DVT seen in all recent Asian studies, may reflect increasingly westernized life styles, notably diet.

In our study LMW dextran proved to be an effective and well tolerated prophylactic treatment. Aspirin, a potent antiplatelet agent, is not generally used for DVT prophylaxis, and several authors [8, 13, 16] have reported on its lack of efficacy in this context. Whilst the 12% incidence of DVT in our aspirin group did not reach statistical significance, it does suggest that aspirin prophylaxis might be of value and further studies on the possible use of aspirin for the prevention of DVT need to be undertaken.

Our intraoperative phlebography studies confirm those of Stamatakis et al. [17] who demonstrated that occlusion of the proximal portion of the femoral vein occurs during hip replacement. As venous stasis is implicated in thrombosis, manoeuvres of the hip joint which result in kinking of the femoral vein, notably internal rotation of the hip when flexed at 40 degrees, should be kept to a minimum.

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