Prevention of thromboembolism in total hip replacement

Aspirin versus dihydroergotamine-heparin

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In a prospective and controlled study, we compared the prophylactic effect of high-dose acetylsalicylic acid (ASA) and dihydroergotamine-heparin (DHEH) in 82 patients over 50 years of age undergoing total hip replacement. The patients were screened by pulmonary scan and ^{125}I fibrinogen uptake. Phlebography was done if the 125 I fibrinogen test was positive. According to our criteria, thromboembolism developed in 9 of 40 receiving ASA and in 5 of 42 patients receiving DHEH. The effect of ASA was limited to men; in 16 men on this therapy, none had thromboembolism versus 9 of 24 women. Twenty-two patients showed wound hematomas, but none needed surgical intervention.

Harris et al. (1977) in a study of 95 patients undergoing total hip replacement found that the protection against thromboembolism by acetylsalicylic acid (ASA) was effective, but limited to men. Low-dose heparin has been ineffective (Barber et al. 1977, Harris et al. 1974, Ritter & Hamilton 1975), but adding dihydroergotamine appears to improve efficacy (Kakkar 1978, Barrowcliffe et al. 1979).

To ascertain whether high doses of ASA has a prophylactic effect comparable to dihydroergotamine-heparin, we performed a prospective, randomized and controlled study on consecutive patients over the age of 50 years undergoing total hip replacement.

Patients and methods

Patients over 50 years of age undergoing total hip replacement were selected. The total number of arthroplasties was stated in advance, but of a planned 100 total hips, 82 remained to be studied. The criteria for exclusion were a history of myocardial infarction in the previous 6 months, severe cardiac insufficiency or angina pectoris at rest, severe hypertension, postthrombotic syndrome, disease of the thyroid or treatment with thyroid drugs, hypersensitivity to ASA or iodine, or a history of hemorrhagic diathesis.

Patients awaiting a hip arthroplasty were consecutively, at least 4 weeks before admission, clinically examined in the outpatient department. Eleven were excluded according to the criteria mentioned above. Informed consent was obtained from the patients. Patients were assigned randomly to treatment groups and stratified by sex. ASA and all ASA-containing compounds except for the study group were discontinued at least 4 weeks before admission to the hospital and were prohibited throughout the study.

The preoperative diagnosis was primary arthrosis in all the cases except 2 with secondary arthrosis and in 1 patient with rheumatoid arthritis.

All the patients underwent total hip replacement (Exeter) under intubation anesthesia using a posterolateral approach without osteotomy. All the patients were given the same type of peroperative infusion and none received plasma expanders. Immediately after the operation, the legs were bandaged with graded compression stockings (TED, Kendall Corp.) and this treatment

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continued until discharge. Postoperative management included physiotherapy and weight bearing on the first postoperative day. Six patients were excluded because of technical errors, such as 3 patients wrongly given plasma expanders, 2 due to misunderstanding among the staff, and 1 with a preoperative perfusion defect. One patient could not complete the study because of gastric intolerance for ASA. Eighty-two patients remained in the study – 42 in the DHEH group and 40 in the ASA group. There were no differences between the two groups regarding age, weight, and duration of operation (*t*-test).

The ASA prophylaxis started 24 h before operation with 1.5 g twice daily for 9 days (Premaspin, acid. acetylsalic. 0.5g Lääke/Farmos, Finland).

In the DHEH group a constant combination of dihydroergotamine-heparin was administered (Orstanorm with heparin, dihydroergotamine, mesyl 0.5 mg and sodium heparin 5,000 IU, Sandoz AB, Sweden). The prophylaxis began 2 hours before surgery, and the second injection was given on the same day, but not earlier than 6 hours after operation. Thereafter, DHEH was given every 12 h during the first 9 postoperative days. The injections were administered subcutaneously in the abdominal wall.

A radionuclide fibrinogen uptake test, lung perfusion scintigraphy, and a chest roentgenogram were done preoperatively on all the patients. Perfusion scintigraphy and a roentgenogram were repeated on the 9th postoperative day. A two-plane phlebography was performed when a positive scan occurred or clinical examination suggested thrombosis.

I-125 fibrinogen uptake test. Four MBq I-125 fibrinogen (Amersham) was injected intravenously and measurement performed with a 2-inch scintillation detector equipped with a 2-inch cylindrical collimator (Novo Trombograph). The iodine uptake of the thyroid gland was suppressed with a daily oral dose of 150 mg potassium iodine. Measurements were made in eight points over the inside of each leg expressed as percentage of the count rate over the heart. The first 17 patients received only one injection of fibrinogen. Because of bleeding a second dose was given 2 days after the operation to the remaining 65 patients. Evidence of deep venous thrombosis was assumed if a measurement deviated more than 20 per cent from its previous value and the deviations persisted in the next examination, which was performed on Days 1, 2, 5, 7, and 9 postoperatively.

Lung perfusion scintigraphy. Lung perfusion scans were performed with a wide-angle gamma camera after the injection of 75 MBq 99-Tc-MAA (Solco). Four projections were recorded. All the patients included in the study had normal preoperative perfusion scans. A defect suspected of being pulmonary embolism was reported if it was verified in two projections when compared with the initial scan. The first scan was made before the fibrinogen uptake test and the second on the 9th day or when the study was interrupted after a positive phlebography and treatment for thromboembolism had to be instituted.

The *t*-test was used for comparisons of blood loss and the Fischer test for comparison of prophylactic effects within the groups.

Definitions. Deep vein thrombosis (DVT): positive uptake test combined with positive phlebography.

Pulmonary embolism (PE): a pulmonary scintigraphic defect comprising at least one segment.

Thromboembolic disease: Deep vein thrombosis or pulmonary embolism or both.

Results

By our criteria, thromboembolic disease developed in 9 of 40 patients receiving ASA and in 5 of 42 receiving DHEH (NS,Table 1). In the ASA

Table 1. Number of patients with positive fibrinogen uptake test combined with positive phlebography (DVT); pulmonary scintigraphy defects only (PE) and the number of patients with a positive fibrinogen uptake test, positive phlebography, and pulmonary scintigraphy defects (DVT+PE)

		Number of patients	DVT	PE	DVT+PE
ASA	Male	16	0	0	0
	Female	24	3	2	4
DHEH	Male	19	1	1	0
	Female	23	2	1	0
	Total	82	6	4	4

group, there were 6 patients, 4 of them men, with positive fibrinogen uptake, but with negative phlebography. In the DHEH group, these findings were confined to 3 women.

In the ASA group, none of the 16 men developed thromboembolic disease, but of 24 women, 3 developed deep vein thrombosis, 2 pulmonary defects, and 4 showed combined deep thrombosis and pulmonary defects ($P < 0.01$). In the DHEH group there was no difference between males and females.

All but three thrombi were located in the calf or popliteal areas; the remaining thrombic spread out both in the calf and in the femoral vein. Four of 10 patients with phlebography-verified deep thrombosis had moderate clinical symptoms. All of them were treated with heparin and warfarin. None of the patients developed fatal pulmonary embolism, and only 3 of 8 patients with pulmonary scintigraphic defects complained of pain in the chest and dyspnea. When the patients were examined after 6 weeks for any clinical signs of thrombosis or pulmonary symptoms, only 1 patient showed slight edema of the calf, and none had any new pulmonary complications.

None had major bleeding complications. Three patients in the DHEH group showed minor hematomas in the injection spots. Wound hematomas occurred in 9/40 patients in the ASA group and in 13/42 patients in the DHEH group. None of the hematomas required surgical intervention, and none caused delayed wound healing or infection. Four of the patients complained of slight subjective discomfort. In the ASA group, women had a somewhat larger blood loss and required more blood replacement than the men ($P < 0.01$, Table 2). There was no difference in intraoperative blood loss, total estimated blood loss, and total blood replacement between the ASA and the DHEH groups.

Two patients in the ASA group complained of vomiting, but could continue with the study. The mean hospitalization time was 14 days for the ASA group and 16 days for the DHEH group.

Table 2. Peroperative and postoperative blood loss (L) and compensation. Average (1 SD)

		Perop	Postop	Compensation units
ASA	Male	0.7 (0.3)	0.5 (0.4)	1.4 (1.1)
	Female	1.0 (0.6)	0.4 (0.2)	2.3 (1.1)
DHEH	Male	0.7 (0.3)	0.4 (0.2)	1.2 (1.0)
	Female	0.9 (0.4)	0.3 (0.2)	1.9 (1.3)

Discussion

The prevalence of nonfatal pulmonary emboli in both groups was comparable to other series (Harris et al. 1977). All the thrombi were diagnosed within 7 days, most within 3 days. The prompt initiation of systemic anticoagulation once thrombi were diagnosed may have contributed to the reduction of pulmonary embolism.

ASA and heparin are among the prophylactic agents that have been most extensively studied. Harris et al. (1977) found that the prevalence of thromboembolic disease was reduced by moderate doses of ASA (1.2 g daily), but, unexpectedly, this protection was limited to men. McKenna et al. (1980) found an incidence of deep thrombosis of 78 per cent in patients receiving 1 g of ASA a day, but only 8 per cent with a daily dosage of 4 g. Based on these studies, we gave our patients 3 g of ASA daily. Harris' study and ours indicated that the thromboprophylactic effect of ASA is limited to men. This difference in the response according to sex needs to be explored further.

Failure of low-dose heparin to reduce postoperative thromboembolism can be due to one of two factors; a massive stimulus of thrombosis, for example, a total hip replacement, or an abnormal clearance of heparin. By adding dihydroergotamine the efficacy appears to be improved (Kakkar 1978, Barrowcliffe et al. 1979). In our study the incidence of thromboembolism was low in both sexes. Even including patients with a positive fibrinogen uptake test but negative phlebography, the total incidence was only 19 per cent – a low figure compared with series of elective hip surgery without prophylaxis, where the frequency is reported to be on an average 59 per cent (Bergqvist et al. 1982). Early mobilization and treatment of the legs with graded stockings may have contributed to our low total incidence.

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