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Efficacy of fixed minidose warfarin prophylaxis in total hip replacement

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Abstract

***Objective*—To determine whether a small fixed perioperative dose of warfarin would prevent deep vein thrombosis after total hip replacement.**

***Design*—Prospective, randomised, double blind placebo controlled trial.**

***Setting*—Winford Orthopaedic Hospital, Bristol.**

***Subjects*—148 patients having primary total hip replacement.**

***Intervention*—Warfarin 1 mg given daily for one week before and three weeks after surgery.**

***Main outcome measure*—Deep vein thrombosis diagnosed by the iodine-125 labelled fibrinogen uptake method.**

***Results*—Deep vein thrombosis occurred in 25 (34%) of the patients given warfarin and 19 (26%) of the controls (difference 8%; 95% confidence interval −6·8% to 22·8%).**

***Conclusion*—Fixed minidose warfarin does not prevent deep vein thrombosis after total hip replacement.**

Introduction

The incidence of thromboembolism is particularly high after total hip replacement. Deep vein thrombosis occurs in up to 70% of patients.[1] The incidence of the postphlebitic limb syndrome complicating thrombosis after hip replacement is unknown but may be as high as 51%, which occurs after long bone fractures.[2] Subclinical pulmonary emboli occur in up to 23% of patients,[3] and 1-2% of patients die of pulmonary embolism.[4]

Many prophylactic regimens have been described but none have proved ideal and there is no consensus on the most suitable prophylaxis.[5] Several studies found that low dose heparin was effective,[6,7] but Sikorski *et al* suggested that this regimen may only delay the onset of thromboembolic complications, describing a rebound surge in thromboembolism once heparin was stopped.[8] Other studies found low dose heparin to be ineffective.[9,10] Conventional full dose anticoagulation begun before surgery is highly effective in preventing thromboembolism[11] but has never been widely accepted because of the risks.[4]

A recent report of the success of fixed minidose warfarin in gynaecological patients[12] prompted us to test its efficacy after total hip replacement. The advantages of this simple regimen were that there were no haemorrhagic complications; prescription was by a daily fixed dose; and prophylaxis was continued after discharge from hospital, covering the period when 60% of fatal pulmonary emboli are likely to occur.[11]

Patients and methods

The study was modelled on projected estimations from the report of Poller *et al.*[12] We were seeking to detect a reduction in deep vein thrombosis from 50% to 20%. For the power of the study $(1-\beta)$ to reach 90% we required 75 patients in each group.

One hundred and forty eight patients who were having primary total hip replacement were randomly allocated to either the treatment group or the control group. The treatment group received 1 mg warfarin daily for one week before and three weeks after surgery. The control group received placebo for the same period. Randomisation was achieved by the use of random number tables by the hospital pharmacy, which prepared the tablets in foil packets. Thus neither the patients nor the investigators were aware of which group the patient was in. Prothrombin time, activated partial thromboplastin time, platelet count, and haemoglobin concentration were assessed at two weeks and at 24 hours preoperatively and 48 hours postoperatively. Patients were excluded if there was a history of thromboembolism or a medical contraindication to warfarin. Smoking history was not recorded. All patients gave fully informed consent.

All the hip arthroplasties were performed in the lateral decubitus position by either the posterior or direct lateral approach. Patients received a standardised general anaesthetic. Wounds were closed with subcuticular suture. Two 6 mm suction drains were used. Intraoperative blood loss was estimated and postoperative drainage and the volume of blood transfused were recorded.

Diagnosis of deep vein thrombosis—All patients were screened for deep vein thrombosis by the iodine-125 labelled fibrinogen uptake method.[10,13] The thyroid was protected by oral potassium iodide (100 mg daily). Each patient received 3·7 MBq (100 μCi) ^{125}I-fibrinogen on the morning after surgery. Daily scanning of radioactivity at nine points[13] on both legs[10] was performed either until discharge or until two weeks postoperatively. Deep vein thrombosis was diagnosed in the calf or popliteal veins when the ^{125}I-fibrinogen count was raised by at least 20% over one or more points and this increase persisted over two consecutive days. Any suspected thrombosis in the femoral vein was further investigated by phlebography as postoperative haematoma may cause a false positive increase in radioactivity in that region. Patients with thrombosis in the popliteal vein or more proximally received full anticoagulant treatment.

Wound complications—All wounds were inspected and scored clinically at one week. Wounds were judged to be clean, moist, or inflamed. Haematomas were sought with a real time ultrasound machine with a

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TABLE I—*Comparisons of fixed minidose warfarin and control groups. Except where stated otherwise figures are numbers (percentages) of patients*

	Fixed minidose warfarin group (n=74)	Control group (n=74)
Mean age (years) (range)	68 (41-86)	67 (38-86)
Men	56 (75·7)	48 (64·9)
Women	18 (24·3)	26 (35·1)
Mean obesity score*	3	3
Type of arthroplasty:		
Uncemented	10 (13·5)	11 (14·9)
Cemented	64 (86·5)	63 (85·1)
Mean operation time (min)	96	98
Diagnosis:		
Osteoarthritis	73 (98·6)	69 (93·2)
Rheumatoid arthritis	1 (1·4)	5 (6·8)
Varicose veins	18 (24·3)	14 (18·9)
Surgical approach:		
Posterior	39 (52·7)	31 (41·9)
Direct or anterolateral	35 (47·3)	43 (58·1)

*Calculated with weight and height tables: underweight=1; acceptable weight=2; overweight=3; obese=4.

TABLE II—*Blood loss and complications among patients in the two operated groups. Except where stated otherwise figures are numbers (percentages) of patients*

	Fixed minidose warfarin group (n=74)	Control group (n=74)
Mean blood loss (ml)	1388	1439
Mean units of blood transfused	2·5	2·5
Mean haemoglobin deficit (g/l)	15·0	13·0
Deep vein thrombosis:		
Present	25 (33·8)*	19 (25·7)*
Absent	49 (66·2)	55 (74·3)
Pulmonary embolism	5 (6·8)	3 (4·1)
Wound sepsis	0	1 (1·4)
Wound haematoma (>20 ml) detected by ultrasound	6 (8·1)	8 (10·8)
Mean No of fibrinogen scans	8·4	8·5
Femoral vein thrombosis confirmed by phlebography	6 (8·1)	5 (6·8)

*Difference in incidence 8·1% (95% confidence interval −6·8% to 22·8%).

5 MHz transducer.[14] A significant haematoma was judged to be one calculated to be more than 20 ml.

Follow up—All patients were reviewed six weeks after operation to ascertain whether any thromboembolic episodes had occurred since discharge.

Results

The treatment and control groups were comparable with respect to age, sex, obesity score, type of joint replacement, operative time, diagnosis, prevalence of varicose veins, and surgical approach (table I). Blood loss, transfused blood volume, haemoglobin deficit, and incidences of wound sepsis and haematoma were also similar (table II). Deep vein thrombosis was detected in 34% of patients (n=25) in the treatment group and 26% of patients (n=19) in the control group (difference 8%; 95% confidence interval −6·8% to 22·8%).

Discussion

The ^{125}I-fibrinogen technique was used in this trial to detect deep vein thrombosis because it offers a safe method of observing thromboembolic activity in the leg veins over a prolonged period. A modification of the original technique of Kakkar *et al*[13] was used as described by Hampson *et al*.[10] Because of its relative inaccuracy in the femoral vein segment any suggestion of an abnormal scan count in that segment was followed with a phlebogram before deep vein thrombosis was confirmed.

We found that a prophylactic regimen using 1 mg warfarin daily perioperatively had no effect on the incidence of fibrinogen positive scans in the leg veins of patients having total hip replacement. The overall rate of thrombosis was 30%, which was considerably lower than the collective mean incidence of 59% gleaned from 14 studies in the 1970s.[1] The difference may reflect the more modern practice of early mobilisation and shorter operating times.

The confusion on the issue of prophylaxis against deep vein thrombosis after total hip replacement is reflected by the current policy of prophylaxis used by British orthopaedic surgeons. Some 50·4% still take no routine prophylactic precautions for their patients and only 19·4% use anticoagulants.[5]

Our findings support the thesis that deep vein thrombosis after total hip replacement is more resistant to prevention than deep vein thrombosis after other types of surgery. We conclude that fixed minidose warfarin is unlikely to afford any useful prophylaxis against complications of thromboembolism in patients having total hip replacement and therefore that this regimen cannot be recommended for prophylaxis in these patients.

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Correction

Bone density in women receiving depot medroxyprogesterone acetate for contraception

In this paper by Cundy *et al* (6 July, p 13) figure 1 was incorrectly labelled. A correct version is given below.