Prevention of venous thrombosis with minidose warfarin after joint replacement

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Without prophylaxis 5-10% of patients having elective hip replacement develop clinically important venous thrombosis and about 5% develop symptomatic embolism, which is fatal in up to 0.5%.¹ Effective preventive methods exist, but many orthopaedic surgeons do not use them systematically because they tend to be complex, cumbersome, dangerous, or not generally available.¹ Minidose warfarin (a fixed dose of 1 mg warfarin a day) is simple, seems to be safe, prevents leg vein thrombosis after elective gynaecological surgery,² and prevents subclavian vein thrombosis after central venous line insertion.³ We report a pilot study of its use in elective major joint replacement.

Patients, methods, and results

Forty five patients having elective hip replacement (35 patients) or knee replacement (10) completed the study. Thirty four were excluded because of previous thromboembolism, allergy to contrast medium, aspirin treatment, a potential drug interaction, refusal of consent by patient or surgeon, mild von Willebrand's disease, or insufficient notice of surgery. Venography failed in five patients.

Warfarin (1 mg/day) was given for a mean of 20 (SD 3) days (range 8 to 28 days) before surgery and continued until bilateral ascending venography seven to 10 days after operation. The trial protocol was approved by the relevant clinical investigation committees. Omitting an actively treated control group was justified ethically on the grounds that no prophylaxis was routinely used by orthopaedic surgeons at either hospital, whereas thrombosis detected by routine

venography could then be treated to prevent extension and embolism.

Results

Patients had a mean age of 70 (SD 9) years (range 52-94 years) and a mean weight of 72 (SD 15) kg (range 44-119 kg); 31 (89%) hip replacements and three of 10 knee replacements were done under general anaesthesia; 20 (57%) hips were replaced with cemented prostheses and 24 (69%) replacements were done with a lateral approach. The prothrombin ratio (international normalised ratio) was normal on the day of surgery (one patient with a ratio of 1.7 on the day before surgery remained in the trial after the ratio fell below 1.5 after vitamin K was given), increased slightly on day 3 but fell on day 7. Surgical and postoperative bleeding were not excessive. The rate of venous thrombosis was 40% after hip replacement and 70% after knee replacement (table).

Discussion

Our trial was a relatively unambitious pilot study, methodologically handicapped by its lack of randomised controls. Nevertheless, our findings strongly suggest that minidose warfarin cannot be recommended prophylactically in patients having elective major joint replacement.

We chose a cohort study because routine venography after hip replacement discloses a stable rate of thrombosis of about 50% in untreated patients,¹ giving us confidence that a pilot study would quickly indicate if a randomised trial would be worth while. In the event, the rate after minidose warfarin was similar to that in previous controls having hip or knee replacement (table).^{1,4,5} There was perhaps a trend towards a lower rate of venous thrombosis in the calf, but the rate in proximal veins remained unchanged. In addition, although 95% confidence intervals for the observed rates of thrombosis remained wide, their lower limits (table) suggest that any prophylactic effect of minidose warfarin that might be demonstrable with a much larger randomised study is unlikely to be impressive.

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Venous thrombosis at routine venography 7-10 days after total hip or knee replacement (95% confidence intervals calculated for observed proportions)

Site of thrombosis	Present study (n=45)		Historical controls Flinders Medical Centre* (n=115)	
	No (%)	95% Confidence interval	No (%)	95% Confidence interval
<i>Total hip replacement (n=35)</i>				
Calf	9 (26)	12.5 to 43%	58 (50)	40 to 60%
Proximal	11 (31)	17 to 49%	38 (33)	25 to 43%
Total	14 (40)	24 to 58%	70 (61)	52 to 71%
<i>Total knee replacement (n=10)</i>				
Calf	7 (70)	35 to 93%		
Proximal	3 (30)	7 to 65%		
Total	7 (70)	35 to 93%		

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