Mechanical prophylaxis of deep-vein thrombosis after total hip replacement

A RANDOMISED CLINICAL TRIAL

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Routine prophylaxis for venous thromboembolic disease after total hip replacement (THR) is recommended. Pneumatic compression with foot pumps seems to provide an alternative to chemical agents. However, the overall number of patients investigated in randomised clinical trials has been too small to draw evidence-based conclusions. This randomised clinical trial was carried out to compare the effectiveness and safety of mechanical *versus* chemical prophylaxis of DVT in patients after THR.

Inclusion criteria were osteoarthritis of the hip and age less than 80 years. Exclusion criteria included a history of thromboembolic disease, heart disease, and bleeding diatheses. There were 216 consecutive patients considered for inclusion in the trial who were randomised either for management with the A-V Impulse System foot pump. We excluded 16 patients who did not tolerate continuous use of the foot pump or with low-molecular-weight heparin (LMWH). Patients were monitored for DVT using serial duplex sonography at 3, 10 and 45 days after surgery.

DVT was detected in three of 100 patients in the foot-pump group and with six of 100 patients in the LMWH group ($p < 0.05$). The mean post-operative drainage was 259 ml in the foot-pump group and 328 ml in the LMWH group ($p < 0.05$). Patients in the foot-pump group had less swelling of the thigh (10 mm compared with 15 mm; $p < 0.05$). One patient developed heparin-induced thrombocytopenia. This study confirms the effectiveness and safety of mechanical prophylaxis of DVT in THR. Some patients cannot tolerate the foot pump.

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Although a number of chemical agents have been shown to reduce the risk of thromboembolic disease, there is no clear preference for prophylaxis in total hip replacement (THR).[1,2] A surgeon's choice is generally determined by weighing the risk of thromboembolic disease against the risk of side-effects due to the prophylaxis itself, such as bleeding. The most common reason cited for not using chemical prophylaxis is uncertainty regarding the safest and most effective agent.[3] However, pneumatic compression with foot pumps seems to provide the best balance of effectiveness and safety, but the overall number of patients investigated in randomised clinical trials is too small to draw evidence-based conclusions regarding the mechanical prophylaxis of deep venous thrombosis (DVT).[4,5]

This randomised clinical trial has been carried out to compare the effectiveness and safety of pneumatic compression with foot pumps *versus* low-molecular-weight heparin (LMWH) for prophylaxis against DVT.

Patients and Methods

The study was approved by the local ethical committee. Randomisation was performed using sealed envelopes containing a slip indicating the allocation, which had been derived from a computer-generated sequence.[6] No restriction was applied to the assignment of the interventions which were concealed until the time of surgery. All patients presenting to one hospital with osteoarthritis of the hip for uncemented total hip arthroplasty were considered for inclusion in the study. The criteria for exclusion were age less than 18 years and more than 80 years, refusal of consent, long-term anticoagulation treatment for pre-existing cardiac or cerebrovascular disease, an active malignant tumour, gastrointestinal ulceration, previous bleeding diatheses, and superficial wounds or painful joints in the feet. In order to standardise treatment all operations were undertaken or directly supervised by one surgeon (RPP) using a direct lateral approach to the hip joint. General anaesthesia was used in all patients. Blood loss was replaced with pre-

Table I. Patient demographics

	Foot-pump group (100 patients)	LMWH group (100 patients)	Level of significance
Gender (F/M)	70/30	68/32	p = 0.89
Age (years)	57.3 ± 12	58.1 ± 11	p = 0.70
Body mass index (kg/m^2)	27.8 ± 3.2	28.1 ± 2.9	p = 0.41
Duration of operation (minutes)	69 ± 10	65 ± 11	p = 0.53
Intra-operative estimated blood loss (ml)	680 ± 124	720 ± 143	p = 0.19
Duration of hospitalisation (days)	12 ± 2	13 ± 1.5	p = 0.66

The values are given as the mean and SD

donated autologous blood and with blood salvaged intra-operatively using the Cell Saver (Haemonetics, Braintree, Massachusetts). The overall blood-loss was calculated with a validated method.[6] All patients received peri-operative chemical prophylaxis against thromboembolism. LMWH (Fraxiparin, Sanofi-Synthelabo, Paris, France) was administrated subcutaneously (dose adjusted according to body-weight, 0.2 to 0.6 ml; 0.1 ml = 950 IU of anti-Xa) 12 hours before operation. Following randomisation, patients either continued chemical prophylaxis after surgery, or used the A-V Impulse System foot pump (Orthofix Vascular Novamedix, Andover, UK). The foot pump slippers were fitted to both feet in the recovery room, and the machine was activated. Nurses were advised to activate the foot pump whenever the patient was not bearing weight. During rest a reverse Trendelenburg position (head-high, feet-low) was preferred to optimise the effect of the pump.[7] The pneumatic compression cycle was set at 20 seconds with a pressure of 130 mmHg applied for one second. All patients wore bilateral thigh-high anti-thromboembolic stockings. Physiotherapy with exercises for range of movement, and mobilisation with partial weight-bearing usually started on the second post-operative day. Partial weight-bearing continued for six weeks. Patients were free to discontinue treatment with the foot pump at any time. If use of the foot pump was stopped for more than four consecutive hours, the patient was excluded from the study and prophylaxis with LMWH was commenced. Compliance with the regime for the foot pump was measured with an internal meter which recorded the total number of hours that the device was activated. At discharge, patients were asked if they found the treatment with foot pump painful, comfortable, relaxing, or annoying. Patients in the LMWH group continued chemical prophylaxis until discharge. The primary outcome measure was the incidence of DVT as shown by serial bilateral duplex studies (Sonoline Elegra, Siemens, Erlangen, Germany) using a 5.0 and a 7.5 MHZ linear transducer pre-operatively and on post-operative days 3, 10, and 45.[3] The images were analyzed by an observer who was blinded with regard to the method of prophylaxis used. Reliability of duplex ultrasonography at our institution was assessed in a previous study.[8] Detection of a DVT warranted continuation with the foot pump and treatment with LMWH (dose adjusted according to body-weight, 0.6 to 1.2 ml). The secondary outcome measures were those related to adverse side effects. Swelling and bruising of the thigh and oozing of the wound were assessed and scored using published criteria.[9] Assessment of soft-tissue side-effects was not blinded. Post-operative bleeding events were monitored and classified as minor bleeding from the wound, major bleeding from the wound, or major bleeding not related to the wound.[8]

Statistical analysis. With use of a two-sided 95% confidence interval (95% CI), we determined that a randomised study with a sample size of 200 patients would have an 80% power to detect a 20% difference in the effectiveness of the two interventions for the prophylaxis of DVT. The continuous demographic data of the two groups of patients were analyzed with use of a two-tailed, unpaired Student's *t*-test. For rank-scaled data, median values were given with the interquartile range. Relative frequencies of unpaired samples were compared with use of Fisher's exact test. Unpaired groups of continuous data without assumption of normal distribution were compared with use of the Mann-Whitney U test. Two-sided p values of ≤0.05 were considered significant. Correction for multiple comparisons was done with the method of Hommel to control type-I error. All calculations were carried out with use of SPSS for Windows (version 9; SPSS, Chicago, Illinois).

Results

During the period of study 326 patients with osteoarthritis of the hip were admitted. Of 216 patients included in the study, 16 stopped using the foot pumps at a mean of five days (3 to 10) post-operatively. The reason for termination was sleep disturbance in 13, and discomfort around the ankle in three. No DVT was detected in this group. Table I gives the demographic details of the 200 randomised patients. There were no statistically significant differences between the two groups for any of these factors. None of the patients were lost to follow-up.

Venous thrombosis was detected during hospital stay in three of the 100 patients in the foot pump group and in six of the 100 in the LMWH group; this difference was significant ($p < 0.05$) (Table II). All three patients with the foot pump had a distal DVT. In the LMWH group, four had a distal DVT and two a proximal DVT. No DVT occurred in either group after discharge. The DVT was in the ipsilateral limb in all patients. The mean length of the thrombus was 15 cm (9 to 28) in the affected patients of the foot pump group and 12 cm (7 to 32) in the patients in the LMWH group. The difference between the groups was not signifi-

Table II. Detection of DVT by serial duplex ultrasonography

	Foot-pump group 100 patients	LMWH group 100 patients	Level of significance
Total DVT	3	6	$p < 0.05$
Detection at day 3	2	4	
Detection at day 10	1	2	
Detection at day 45			
Proximal DVT	-	2	$p < 0.05$
Distal DVT	3	4	$p = 0.11$
DVT involving entire limb	-	-	
DVT of contralateral limb	-	-	
Symptomatic DVT	1	1	
Resolution of DVT at day 45	2	3	
Pulmonary embolism	-	-	

Table III. Side effects

	Foot-pump group 100 patients	LMWH group 100 patients	Level of significance
Post-operative drainage (ml)	259 ± 14.6	328 ± 20.4	$p < 0.05$
Blood-loss index*	3.43	3.71	$p = 0.46$
Number of blood units transfused	2.3 ± 2.1	2.5 ± 1.7	$p = 0.77$
Swelling of thigh at day 3 (mm)†	17.4 ± 3.1	20.1 ± 3.6	$p < 0.05$
Swelling of thigh at day 10 (mm)†	10.1 ± 2.2	15.2 ± 3.4	$p < 0.05$
No bruising at day 3 (number of hips)	59	42	$p < 0.05$
No bruising at day 10 (number of hips)	78	50	$p < 0.05$
No oozing at day 3 (number of hips)	40	23	$p < 0.05$
No oozing at day 10 (number of hips)	95	75	$p < 0.05$
Minor bleeding from the wound	-	3	$p < 0.05$
Major bleeding from the wound	-	-	
Major bleeding not related to wound	-	-	
Heparin-induced thrombocytopenia	-	1	

The values are given as the mean and the standard deviation.

* Median values of blood-loss index = pre-operative level of haemoglobin − level of haemoglobin before discharge + number of units transfused, including predonated blood units.

† Median of the differences of the thigh circumferences measured after the operation, compared with the pre-operative measurement (base-line). Swelling was assessed by measuring the circumference of the thigh 20 cm proximal to the patella.

Minor bleeding from the wound: bleeding at an injection site, epistaxis, or wound hematoma not requiring operative decompression. Major bleeding from the wound: wound hematoma requiring operative decompression. Major bleeding not related to the wound: gastrointestinal or intracerebral haemorrhage.

cant. Resolution of the DVT was observed at post-operative day 45 in six of the nine patients with positive findings on ultrasonography.

There were no differences between the two groups with regard to the transfusion requirements. However, the patients of the foot-pump group had less post-operative drainage, oozing, bruising, and swelling than those in the LMWH group (Table III). One patient in the LMWH group developed clinically asymptomatic heparin-induced thrombocytopenia (HIT-syndrome type 1) on the second post-operative day. Of the patients who had used the foot pump, 12 found it to be uncomfortable, 37 reported some difficulty with sleeping, 29 reported no discomfort and 22 found that the foot pump was relaxing. The internal compliance meter indicated that the foot pump had been used for a mean of 19.4 hours daily (15 to 21.5). The mean daily use of the three patients who had a DVT was 19.1 hours.

Discussion

Three independent randomised clinical trials have shown that mechanical prophylaxis with foot pumps in THR achieves equivalent if not superior results compared with chemical management. The side effects and haemorrhagic complications of anti-thrombotic agents make chemical management less desirable. These side effects are still a feature of new drugs such as pentasaccharide.[9,10,12] However, only 242 patients have been investigated in the three trials and the number is too small to draw evidence-based conclusions.

DVT was detected in three of 100 patients in the foot-pump group compared with six of 100 patients in the LMWH group ($p < 0.05$). No patient had clinical signs of pulmonary embolism (PE). The excellent results are probably related to the nearly constant use of the foot pumps by the patients, a factor for inclusion in the study. Other randomised clinical trials demonstrated higher rates of DVT in patients who were treated with intermittent foot compression. Warwick et al[9] reported a DVT rate of 18% in 136 patients managed with foot pumps after THR, Fordyce and Ling[11] reported a rate of 5% in 40 patients, and Santori et al[12] reported a DVT rate of 13.4% in 67 patients.

In the present study all patients received peri-operative prophylaxis with LMWH in order to prevent activation of the coagulation cascade induced by fat and bone marrow

embolisation which inevitably occurs during the operation.[8,13] This intervention may well explain the low rate of DVT observed in both groups of patients. It remains to be shown whether the pneumatic foot compression can also achieve a significant reduction of the PE rate. Asano et al[14] found a 21% incidence of PE using perfusion scintigraphy in 42 patients managed with foot pumps after hip joint surgery, and a 55% PE incidence in 20 control patients.

In the present study, DVT was investigated by serial duplex ultrasonography. This method has the advantage of being non-invasive, safe and repeatable. Nevertheless, much of the research on thromboembolism in orthopaedic surgery has been based on venography. Contrast venography is more sensitive than ultrasonography, but, since it is invasive, uncomfortable, and possible thrombogenic, repeated investigation using this technique is impractical. A single venogram can only measure prevalence, the rate at the moment when the test is carried out, rather than incidence and the total rate in the post-operative period.[15] Duplex ultrasonography is highly operator-dependent, with accuracy varying widely depending on the expertise and the experience of the observer. Thus, in a previous study performed by the same observer as in this trial we investigated the reliability of duplex ultrasonography for the detection of post-operative DVT at our institution.[8] On comparison with venography, duplex ultrasonography demonstrated 93% sensitivity, 98% specificity and 95.5% accuracy with regard to the overall detection of DVT.

The potential lack of side-effects with pneumatic compression has been regarded as a major advantage.[2,4] Patients in the foot-pump group had significantly less wound drainage, minor wound bleeding, bruising and oozing of the wound and swelling of the thigh when compared with patients in the LMWH group. This confirms findings of other randomised studies.[9,11,12]

Compliance and tolerance has been reported to be a problem with pneumatic compression systems.[16,17] Of 116 patients who were initially randomised to the foot-pump group, 16 discontinued its use before discharge. The main reason was disturbance of sleep at night due to the noise produced by the device. Warwick et al[9] reported a 3% rate of discontinuation in patients who wore the foot pumps for a mean of only 15 hours daily for seven days. In contrast, the foot pumps in the present study were used for a mean of 19.4 hours for 12 days. An improved pump unit driven pneumatically instead of using electrically has subsequently been developed. This has led to marked reduction of noise.

Consideration needs to be given to the cost of providing prophylaxis, and also the costs related to side-effects. Costs of chemical prophylaxis with LMWH in Europe may range, dependent on which product is used, between €35 and €50 per patient. Although in many countries the pump units are given in consignment without charge. The foot pads which are used by only a single patient are sold at an approximate cost of €80. The costs associated with the side effects of LMWH are unclear. As in this study, Warwick et al[9] also concluded that the foot pump is associated with fewer soft-tissue side-effects than LMWH. It was not possible to determine the increase in costs caused by the side-effects.

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