THROMBOSIS RESEARCH 15; 611-616

0049-3848/79/0815-0611 $02.00/0

PREVENTION OF VENOUS THROMBOSIS BY INTERMITTENT SEQUENTIAL CALF COMPRESSION IN PATIENTS WITH INTRACRANIAL DISEASE

Alexander G.G. Turpie, Terry Delmore, Jack Hirsh, Russell Hull, Edward Genton, Cheryl Hiscoe and Michael Gent.
McMaster University, Department of Medicine, Hamilton General Hospital, Hamilton, Ontario, Canada.

(Received 5.3.1979; in revised form 20.3.1979. Accepted by Editor E.W. Salzman)

ABSTRACT

Intermittent sequential pneumatic compression of the calf was evaluated for the prevention of venous thrombosis in a prospective randomized study of 199 patients with intracranial disease. Sequential calf compression was applied for a maximum of 14 days and reduced the frequency of venous thrombosis from 20.8% in 96 control patients to 7.8% in 103 patients given prophylaxis, p=0.01. Sequential calf compression also reduced the frequency of proximal vein thrombosis from 8.3% in control patients to 2.9% in patients given prophylaxis, p=0.09. Calf compression was well tolerated by patients and is recommended as a practical form of prophylaxis in these patients.

INTRODUCTION

Venous thromboembolism is a common cause of morbidity and mortality following neurosurgical procedures and in patients with paralysis from stroke. Conventional treatment of venous thromboembolism with anticoagulants, while effective, exposes patients to the risk of bleeding which could be critical in this group. Therefore, it is particularly important to develop effective means of prophylaxis for these patients. Low-dose heparin prophylaxis has been reported to be effective in one study in neurosurgical patients (1) but is not ideal because even a minor increase in the risk of operative or post-operative bleeding at the site of surgery is unacceptable. Intermittent pneumatic compression, a method which prevents venous stasis by rhythmically emptying the calf veins of blood, has also been shown to be an effective form of prophylaxis against venous thrombosis in this patient group (2,3).

We have previously reported that intermittent pneumatic compression using inflatable plastic boots is effective in reducing the frequency of venous thrombosis in patients who have neurosurgical procedures and in

patients with stroke (2). In that study, intermittent calf compression, which was started immediately after operation in patients treated surgically, reduced the frequency of venous thrombosis during the five days that the boots were worn, but there was a relatively high frequency of late thrombosis, negating their early benefit, when the boots were removed. It is possible, therefore, that calf compression delayed rather than prevented venous thrombosis in the patients who remained at risk. This study was a controlled randomized evaluation in hospitalized patients with intracranial disease of the feasibility and effectiveness of pneumatic calf compression for 14 days.

METHODS

Study Population

All patients 16 years of age or over admitted to the Regional Centre for Clinical Neurosciences at the Hamilton General Hospital were eligible for entry into the study. Patients were excluded from the study and not randomized if they had a history of allergy to iodine, if they had peripheral vascular disease, if they had suffered multiple trauma, or if they were admitted for observation after head injury and likely to be discharged from hospital within 24 hours.

Randomization into control or pneumatic cuff treatment was by sealed envelopes, and the patients were stratified into four diagnostic groups; stroke, subarachnoid haemorrhage, brain or spinal tumour, and head or spinal injury.

Pneumatic Calf Compression

Intermittent sequential pneumatic compression was applied to the calves using inflatable knee-length plastic cuffs with four compartments which were inflated sequentially from the ankle to the knee (Gaymar Industries, Inc., Buffalo, New York). There was a five second inflation time for each compartment, and the whole cuff remained inflated for a further five seconds and was then rapidly deflated. The relaxation phase of the cycle was maintained for 60 seconds. The pressure was applied to the cuffs using portable electrically driven pumps which were calibrated to deliver a pressure of 50 mmHg. to each compartment. These cuff pressures and cycle times were selected after plethysmographic studies in normal controls and hospital volunteers had demonstrated that they produced optimal calf emptying and refilling with each cycle.

Sequential calf compression was started in the prophylaxis group in the immediate postoperative period in patients undergoing craniotomy and within 24 hours of admission to hospital in non-operated patients. Prophylaxis was continued for a maximum of 14 days and terminated earlier only if the patient was discharged from hospital or was fully ambulant. The patients in the control group did not wear elastic stockings and received routine physiotherapy. All patients were evaluated daily for documentation of compliance.

Diagnosis of Venous Thrombosis

Patients were screened with ^{125}Iodine-labelled fibrinogen leg scanning and impedance plethysmography to diagnose venous thrombosis (4).

One hundred μCi of ^{125}Iodine-labelled fibrinogen was injected intravenously at the time of admission to the study in patients who had subarachnoid haemorrhage or subdural haematomas, and in the immediate postoperative period in patients who had elective craniotomy. Leg scanning was carried out on all patients for a maximum of 14 days, unless they were discharged earlier.

Impedance plethysmography (IPG) was carried out using the pressurized cuff technique (5), preoperatively and on days 3, 5, 7, 10 and 14 postoperatively. In medically treated patients, IPG was done within 24 hours of admission to hospital and repeated on day 3, 5, 7, 10 and 14.

The criteria for the diagnosis of venous thrombosis by leg scan and IPG have previously been described (4). Whenever possible, ascending venography was carried out to confirm a positive screening test using established criteria for the venographic diagnosis of acute deep vein thrombosis (6).

However, since venography could not be performed on all patients, the criteria used for the diagnosis of venous thrombosis was either a positive leg scan or an abnormal IPG which had previously been normal. Clinical follow-up was continued after the formal period of study, and their status documented by clinic, hospital or telephone assessment at 3-4 months.

RESULTS

Two hundred and eighteen eligible patients were randomized into the study, 106 were in the control group and 112 were in the prophylaxis group. Nineteen patients were excluded from the trial following randomization, 10 were in the cuff group and 9 were in the control group. The reasons for withdrawal from the study were not different between the control and prophylaxis groups and these included transfer to other hospitals, discharge from hospital or death of patients prior to their commencing venous thrombosis surveillance.

The age, sex, diagnostic groups and number of patients treated by craniotomy or by medical management were similar in the control and prophylaxis groups (Table 1). There was a slight imbalance in the male/female ratio between the control and prophylaxis groups and this was not statistically significant ($p=0.08$).

The cuffs were well tolerated and were not associated with any complications.

Frequency of Venous Thrombosis

Eight patients in the prophylaxis group (7.8%) and 20 patients in the control group (20.8%) developed deep vein thrombosis (Table 2). This difference was significant ($p=0.01$). Six of 8 patients in the prophylaxis group had the diagnosis confirmed by venography, and the other 2 patients who did not have venography had the diagnosis made by a positive leg scan. Eleven of 20 patients in the control group with venous thrombosis had the diagnosis confirmed by venography. Of the remainder, the diagnosis was made by leg scanning in 7 patients, by both leg scanning and IPG in one, and by IPG in one patient who subsequently died of an autopsy-proven pulmonary embolus. There were no false positive screening tests in the patients who had venography.

TABLE 1
Comparison of Control and Prophylaxis Groups: Number, Age, Sex, Diagnostic and Management Groups

	Control	Prophylaxis
Number	96	103
Age (years)		
Mean	48.7	52.2
Range	16 - 83	16 - 90
Sex		
Male	64	55
Female	32	48
Diagnostic Groups		
Stroke	19	21
S/A Haemorrhage	27	27
Brain Tumour	26	25
Head Injury	24	30
Management Groups		
Operated	64	65
Non-operated	32	38

TABLE 2
Venous Thrombosis (VT) in Control and Prophylaxis Groups

	VT	No VT	%
Prophylaxis	8	95	7.8
Control	20	76	20.8

$p = 0.01$

The frequency of proximal vein thrombosis in both groups was analyzed separately. Eight of 96 patients (8.3%) in the control group and 3 of 103 patients (2.9%) in the prophylaxis group developed proximal vein thrombosis. This difference is not statistically significant ($p=0.09$) but is consistent with the hypothesis that pneumatic compression had an effect on the frequency of proximal vein thrombosis. The diagnosis of proximal vein thrombosis was confirmed by venography in 2 patients in the cuff treated group and in 4 patients in the control group. The diagnosis of proximal vein thrombosis was made by IPG and leg scan in one patient in the prophylaxis group who did not have venography and in the 4 patients in the control group who did not have venography, by leg scan in 2, by both IPG and leg scan in 1, and by IPG only in 1.

The time of thrombosis development was evaluated, and tended to occur somewhat later in cuff treated patients. In the control group, 14 out of 20 patients developed venous thrombosis in the first week and the majority (9) occurred between the 5th and 7th day. Six patients developed thrombi in the

second week. In the cuff group, 3 of 8 patients developed thrombosis in the first week and 5 during the second week of the trial.

The occurrence of venous thrombosis based on whether the patients were treated medically or surgically is shown in Table 3. The benefit from prophylaxis was more evident in patients who had surgery.

TABLE 3
Venous Thrombosis (VT) in Operated and Non-Operated Patients: Control versus Prophylaxis

	Control			Prophylaxis		
	VT	No VT	%	VT	No VT	%
Operation	15	49	23.4	4	61	6.2
No Operation	5	27	15.6	4	34	10.5

In the cuff group, 4 of the 8 patients developed venous thrombosis while the cuffs were worn. Three of the other 4 patients wore the cuffs for only 2, 3 and 4 days and developed venous thrombosis, 3, 10 and 9 days, respectively, after the cuffs were discontinued. The last patient was randomized to the treatment group, but cuffs were not applied and venous thrombosis developed on the second day.

Late follow-up was obtained in 190 patients (95%) for a mean time of 3.8 months. Fifty-two patients died; and autopsy was performed in 28. During follow-up, 4 patients developed venous thromboembolism, including two from the prophylaxis group 5 and 9 days after the cuffs were removed and 2 patients from the control group on days 2 and 7 following the 14 day study period.

DISCUSSION

This study confirms previous reports indicating the high incidence of venous thrombosis in patients hospitalized with intracranial disease which persists during the period of immobilization. Also documented is that intermittent calf compression is a safe and effective method of prophylaxis for venous thrombosis in these patients. In addition, the data indicate that protection continues during even prolonged use of pneumatic cuffs and that presently available devices are practical and well tolerated by most patients as suggested by a recent report (3). Protection appears to be greatest in patients who have undergone craniotomy.

When patients require immobilization from intracranial disease, pneumatic cuff use appears to be a suitable and at present the preferable approach to prophylaxis during the first few weeks. If more prolonged prophylaxis is necessary, alternate methods may be possible after the risk of bleeding has subsided.

REFERENCES

1. CERRATO, D., ARIANO, C. and FIACCHINO, F. Deep vein thrombosis and low-dose heparin prophylaxis in neurosurgical patients. J. Neurosurg. 49, 378, 1978.

2. TURPIE, A.G.G., GALLUS, A.S., BEATTIE, W.S. and HIRSH, J. Prevention of venous thrombosis in patients with intracranial disease by intermittent pneumatic compression of the calf. Neurology 27, 435, 1977.

3. SKILLMAN, J.J., COLLINS, R.E.C., COE, N.P., GOLDSTEIN, B.S., SHAPIRO, R.M., ZERVAS, N.T., BETTMANN, M.A. and SALZMAN, E.W. Prevention of deep vein thrombosis in neurosurgical patients: A controlled, randomized trial of external pneumatic compression boots. Surgery 83, 354, 1978.

4. HULL, R., HIRSH, J., SACKETT, D.L., POWERS, P., TURPIE, A.G.G. and WALKER, I. Combined use of leg scanning and impedance plethysmography in suspected venous thrombosis. An alternative to venography. New Eng. J. Med. 296, 1497, 1977.

5. HULL, R., TAYLOR, D.W., HIRSH, J., SACKETT, D.L., POWERS, P., TURPIE, A.G.G. and WALKER, I. Impedance plethysmography: The relationship between venous filling and sensitivity and specificity for proximal vein thrombosis. Circulation 58, 898, 1978.

6. LEA THOMAS, M. Phlebography. Arch. Surg. 104, 145, 1972.