Effects of intermittent compression treatment on skin perfusion and oxygenation in lower legs with venous ulcers

P. J. Kolari and K. Pekanmäki

Leg ulceration constitutes a major problem among the elderly people. Some ulcers do not heal at all, and others have high recurrence rate [19]. Numerous methods have been introduced to assess venous disorders and to predict the healing of ulcers. These methods include direct measurement of venous pressure, skin fluorescence [20], radionuclide angiogram [2], skin perfusion pressure by an isotope washout technique [8, 14], and venography. However, the need for an atraumatic method is well recognized, and it is especially needed for patients with leg ulceration. Recently, the use of transcutaneous oxygen tension [5] and photoplethysmography have been suggested to screen for venous insufficiency [1, 28].

Laser Doppler flowmetry (LDF) is a new technique to measure microvascular blood flow [12, 22]. It has been applied widely in measurements of cutaneous blood flow. Recently, LDF has been applied to measure distal blood pressures, and it has proved to be more sensitive than strain-gauge method in low blood flow pressure range [3, 9]. Skin perfusion pressure has been measured using photoplethysmography [13, 18], and the strain-gauge technique has been used to measure finger venous opening pressure [27].

Intermittent pneumatic compression (IPC) treatment has been used to treat lymphoedema and to prevent formation of deep vein thrombosis [6, 17]. IPC has also applied to treat persistent leg ulcers [7, 11]. A reduction of oedema by any regimen may be correlated with an improved rate of healing. However, the mechanism of the effect of IPC on the healing of ulcers has remained uncertain [23].

The aim of present study was to evaluate the short-term effects of IPC treatment on the haemodynamics in legs with post-thrombotic ulcers. LDF was used to measure skin perfusion pressure (SPP) and venous opening pressure in the skin (SVOP) before and after IPC treatment. Comparisons were made with the changes in transcutaneous oxygen tension following IPC treatment.

Material and methods

Subjects

Measurement of SPP and SVOP was first tested among the group of eight healthy control male subjects with no evidence of peripheral vascular diseases. Their mean age was 35 (range 28-42) years. The study group comprised eight patients suffering from recurrent or persistent post-thrombotic leg ulcers. Five of the patients were females and three males. Their mean age was 66 (range 45-83) years. All had a previous history of deep venous thrombosis 2-20 years ago, verified by venography.

Pressure measurements

The arm blood pressure was measured by the Korotkoff method. The mean arm blood pressure (MAP) was calculated as the diastolic pressure plus one-third of the pulse pressure.

The LDF was measured using a Periflux® (Perimed Kh, Stockholm, Sweden) flowmeter on the anterolateral part of the calf approximately 10 cm distal to the knee joint [11]. During the measurement the skin circulation was assured by a cuff 12 cm wide, placed on the maximum girth of the affected leg. Light from an 2 mW HeNe laser was directed to the skin by an
optical fiber probe via a plastic disc fixed to the cuff, thereby compressing the probe to the skin surface equal to the cuff pressure. Laser light penetrates the outermost skin layers with an effective penetration depth (1/e) of about 0.8 mm [16]. A frequency cut-off level of 4 kHz and time-averaging of 1.5 s were used. The measurement system closely resembled those used by Holstein et al. [13], or Lax and Tooher [18].

From the recordings SPP and SVOP were evaluated (Fig. 1). During quick manual inflation of the cuff, the LDF value decreases sharply. The cuff is then slowly deflated, at a rate of about 2-3 mmHg s⁻¹. At certain point the LDF begins to increase, and the external pressure at the onset of this deflation, i.e., the minimal external pressure sufficient to keep skin vessels closed, was designated as the SPP. The SVOP was determined as the cuff pressure when the LDF begins to decrease. Distal blood pressure (SBP) in the legs can be measured by placing the LDF probe distal to the occluding cuff (Fig. 1) [1].

**Compression treatment**

A new Ventispress® device, model 14 (Ventispress Ltd, Lahti, Finland) was used [15]. This system consists of a multicompartamental double-walled, rubberized textile boot, an electronic control unit with an air compressor, and magnetic valves. This compression device produces both a sequential and graded compression on the leg. The chambers of the boot are successively filled with air from the toes to kneecap; pressure first increases rhythmically on the ankle, then a pressure-wave moves dampering proximally. A compression pressure of 50 mmHg was used. The inflation time was set at 12 s, and the deflation time at 18 s [21]. Thus two complete pressure cycles occurred every minute. A treatment time of 60 min was used.

Skin oxygen tension was measured near the edge of the leg ulcer, using Kontron MicroGas 7640 monitor (Kontron Instruments Ltd., Zurich, Switzerland), before and after the compression treatment. The probe temperature was set at 44 °C, and a stabilization time of 13 min was used. All measurements were carried out with the patients in the recumbent position during a single occasion of the IPC treatment period, and results are expressed as the mean of two measurements.

**Data analysis**

All data are expressed as medians and ranges, and were analyzed by the Student’s t-test for paired samples and by the Wilcoxon rank sum test for unpaired samples.

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**Fig. 1:** Perfusion pressure and distal blood pressure measurement using laser-Doppler flowmetry. Skin perfusion pressure (SPP), venous opening pressure (SVOP), and systolic blood pressure (SBP) of a control subject.
Results

Figure 1 shows an illustrated example curves of the LDF in perfusion pressure and distal blood pressure measurements. In perfusion pressure curve the LDF first decreases during cuff inflation. At a cuff pressure of approximately 105 mmHg the LDF begins to increase. This pressure is defined to be the SPP. At a pressure of about 45 mmHg, the LDF again begins to decrease to the base level. This point in LDF is defined to be the SVOP. In measurement of distal blood pressure, the first increase in the LDF is seen at a pressure of about 140 mmHg. The peak LDF is recorded at a pressure of 100 mmHg, which corresponds to the measured SPP value. At a cuff pressure of about 45 mmHg, a marked increase in the LDF is observed; the pressure onset is equal to SVOP.

The mean arm blood pressure of the patients was 113 (range 90–128) mmHg. Before the IPC treatment the SPP was 105 (range 71–135) mmHg, and it increased slightly to value of 111 mmHg (range 99–134; p < 0.05). The SPP values did not correlate with the mean arm blood pressures. The SPP of the controls was 114 (range 99–130) mmHg.

The patients’ venous opening pressure before the IPC treatment was 19 (range 7–39) mmHg, and the SVOP was 41 (range 6–68) mmHg following the IPC treatment (Fig. 2). The SVOP increased significantly in all patients (p < 0.001). In the controls the SVOP was 55 (range 31–67) mmHg, which was significantly higher than the patients’ pre- or post-treatment SVOP.

Before the IPC treatment, the oxygen tension (TPO$_2$) was 24 (range 5–59) mmHg, and after the IPC treatment it increased significantly to 43 (range 17–83) mmHg (p < 0.005). The changes of the SVOP had a linear correlation with those of the TPO$_2$ (r = 0.810; Fig. 1).

Discussion

In this study laser Doppler flowmetry was used to measure cutaneous blood flow pressures. The LDF measures integrated velocity of the blood flow in the outermost skin tissue. The LDF flow velocity is shown to be partly dependent on the level of arterial inflow, but also depends on the prevailing pressure-flow and pressure-volume relation in the cutaneous vascular bed [24]. A venous occlusion pressure of 50 mmHg has been
found to affect the LDF recordings markedly (Fig. 4).

Skin perfusion pressure as measured using the isotope washout technique or photoplethysmography has been shown to be valuable in assessments of the severity of arterial occlusive disease and in assessments of healing arterial ulcers and amputations [16]. In this study there was only minor difference in the SPP between the controls and the patients before their IPC treatment. The SPP results confirmed that the patients did not suffer from peripheral arterial disease.

Ulceration is known to be due to tissue hypoxia, but the mechanism which leads to ulceration is probably multifactorial. It has been hypothesized that high ambulatory venous pressure allows large molecules, such as fibrinogen, to leak into the interstitial fluid where fibrinogen polymerizes to form an insoluble layer of fibrin [4]. The fibrin would be deposited around the capillary, thus forming a barrier to the diffusion of oxygen and other nutrients, a situation which would lead to cell death and ulceration. In addition, because of increased interstitial fluid volume and venous stasis, the perfusion pressure is inadequate to maintain a normal oxygen tension. It has also been shown that microangiopathy in patients with severe chronic venous insufficiency leads to decreased TcPO₂ [10].

The effects of IPC treatment can be explained by the fact that a decrease in the venous tone of the skin increases the perfusion pressure and increases the arterial inflow which, in turn, augments tissue oxygenation. The IPC treatment also reduces the interstitial fluid volume, which benefits oxygen diffusion. We found that the changes in the SVOP and the TcPO₂ correlated significantly. Some previous studies have found marked improvement in arterial or venous leg ulcers treated with IPC [7, 11]. We have also found that the IPC treatment accelerates the healing of persistent or recurrent post-thrombotic leg ulcers [26].

We suggest that SVOP in the skin and TcPO₂ are useful in assessing the severity of venous ulceration. These methods are simple, noninvasive, and fast compared with the technique of measuring the SPP with radioisotopes. However, evaluation of the SVOP from the flow recordings is not always simple. In addition, uneven compression of the LDF probe to the skin surface can cause errors in the SVOP, especially at low SVOP stages. Such errors can be avoided by using combined hand-held flow-pressure transducers [18]. Using a laser Doppler flowmeter instead of the conventional photoplethysmograph allows the distinction of different flow phases during cuff deflation as the LDF indicates changes in flow velocity compared with changes in blood volume (Figs. 1, 4). The LDF flowmeter used here also includes a photoplethysmograph, which can be used to measure photoplethysmograph recovery time [1, 28].
The IPC treatment was given by a multicompartment boot device which produces a graded and sequential pressure wave on the lower leg. Such waves are considered to be more effective in increasing peripheral venous flow than pure uniform compression [15, 17, 21]. Our results suggest that IPC may be a valuable treatment method, especially for leg ulcers accompanied with oedema. In this study only the short-term effects of IPC were studied. Further studies are needed to determine out how long the effects of IPC last as well as proper treatment schedules.

Acknowledgement: The study is part of the project on indicators and treatments with intermittent pneumatic compression supported by the Finnish National Fund for Research and Development. The intermittent compression device was provided for the study by Ventipress Ltd.

Summary

The short-term effects of intermittent pneumatic compression on skin perfusion pressure (SPP) and venous opening pressure (SVOP) in legs as measured by the laser Doppler technique were studied. The study group comprised eight patients with post-thrombotic ulcers. Their mean age was 66 (range 48-83) years. The SPP and SVOP were measured before and after 60 min sequential intermittent compression treatment at the pressure of 50 mmHg. The control group consisted of eight healthy subjects with no evidence of peripheral vascular disease. Their mean age was 38 (range 28-52) years. In the control group the median SPP was 115 (range 99-130) mmHg, and the SVOP was 55 (range 51-67) mmHg. In the study group the pre-treatment SPP was 105 (range 71-135) mmHg, and the SVOP was 19 (range 7-39) mmHg. After the IPC treatment the SPP was 111 (range 99-134) mmHg, and the SVOP significantly increased to 41 (range 16-64) mmHg (p < 0.001). The SVOP increased in all patients. The changes in venous opening pressure following compression treatment correlated with the changes in transcutaneous oxygen tension (r = 0.81, p < 0.01).

Zusammenfassung

Die Kurzzeit-Effekte der intermittierenden pneumatischen Kompression auf den Haut-Perfusionsdruck und auf den venösen Öffnungsdruck wurden mit der Laser-Doppler-Technik gemessen. Die Untersuchung erfolgte bei 8 Patienten mit postthrombotischen Ulcera. Das mittlere Alter betrug 66 Jahre (48-83 Jahre). Die beiden Parameter wurden vor und nach 60 minütiger sequentieller intermittierender Kompression mit einem Druck von 50 mmHg bestimmt. Als Kontrolle dienten 8 gesunde Probanden mit einem mittleren Alter von 38 Jahren (28-52 Jahre). In der Kontrollgruppe betrugen die beiden Parameter vor der Messung im Mittel 114 (99-120) mmHg bzw. 55 (51-67) mmHg, in der Untersuchungsgruppe 115 (71-135) mmHg bzw. 19 (7-39) mmHg. Nach Behandlung war der Haut-Perfusionsdruck in der Untersuchungsgruppe 111 (99-114) mmHg, der venöse Öffnungsdruck stieg signifikant auf 41 (16-64) mmHg. Dieser letzte Parameter stieg bei allen Patienten an. Die Veränderungen des venösen Öffnungsdruckes nach Kompressionsbehandlung korrelierten mit den Veränderungen der transcutanen Sauerstoff-Druckwerten.

Bibliography

neous) of the life and limb. While measurement of the ankle blood pressure, a method widely used to identify AOD of the legs, is usually not possible in patients with lower leg ulcers, the systolic digital blood pressure (SDBP) proved to be a valuable prognostic parameter under these circumstances. Our figures of 10 out of 19 legs amputated with SDBP ≤ 30 mmHg are consistent with those of Holstein & Lassen (4) and suggest moreover that the SDBP interval of 30-60 mmHg constitutes the borderline zone. The prognosis of the ulcer on this interval as regards healing is doubtful but the risk of amputation seems to be small.

In a previous investigation (5), we measured the SDBP in legs classified by physical examination as status ulceratius. A wide range of pressures were found showing the coexistence of AOD in many cases. The present investigation shows that the combination of ischaemic leg pains and a short ulcer history is strongly successive of significant AOD. But it is difficult to discern by clinical examination, whether a given ulcer is non-healing or even deteriorating due to venous stasis, due to ischaemia or due to a combination. The poor outcome with SDBP ≤ 30 mmHg as found in the present study demonstrates that in such cases AOD is the dominating disease. In the study mentioned above (5), no correlation was found between the level of the distal blood pressure and the presence of ulceration. But once ulceration has developed in low pressure legs, a serious prognosis is suspected from the observations in the present study of a short ulcer history together with a high percentage of amputations within one year.

The classification according to the SDBP is also valuable in identifying high-risk patients as regards survival. In a recent study (6) the mortality rates for leg and ulcer patients were found to be twice as high as for the age-matched background population, primarily due to an increased mortality rate from ischaemic heart disease. The question arises whether the mortality figures in our study are related to the very condition of the ischaemic ulcer patient, suffering from ischaemic leg pains and immobilization.

The present study has influenced our program for patients with ulceration of the lower leg. When the digital blood pressure is below 30 mmHg, reconstructive arterial surgery is considered. In all other cases, conservative ulcer treatment is attempted, but surgical correlation of venous disease - or perhaps both venous and arterial disease - can be considered if this treatment is not effective.

ACKNOWLEDGEMENT
The authors wish to thank Mrs Marianne Hey for excellent practical assistance.

REFERENCES
all players went through a similar practice or game daily as well as one meal. At the end of the study, the maximum oxygen consumption of both groups improved from means of 45±6.7 ml/kg/min to 49.0±9.1 and 46.7±7.5 to 57.3±10.3 ml/kg/min at the time of exhaustion. There was a significant difference between the groups at r < 0.05. From this study, it seems that vitamin E has no beneficial effect in improving the oxygen transport system of active individuals.

T. WATT
J. R. ROMET
I. MCFARLANE
D. McGEE
C. ALLEN
R. C. GODDE

Department of Physiology,
University of Toronto,
Toronto, Ontario, Canada.

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VIRUSES IN GASTROENTERITIS

Sir,—We have lately described finding an arthritis in
doctorial epidermal cells 1 and stools 2 from children with
acute gastroenteritis in Melbourne, Australia. Reports have
since been published of the finding of similar particles in
stools from children with acute gastroenteritis in the United
Kingdom, 3 Singapore, 4 Canada, 5 and Rhodesia. 6

We have exceeded our search to Aboriginal children in
communities widely separated on the Australian continent.
The morbidity and mortality due to gastroenteritis in these
children is 10-15 times greater than in the White Australian
population. Specimens of diarrheal feces obtained 2-3
usually at the onset of acute gastroenteritis were processed
previously described. 7


Children in these Aboriginal communities are subject to
acute attacks of gastroenteritis throughout childhood,
usually starting soon after weaning. In this pilot study we
carried out diarrheal specimens obtained from children with
acute gastroenteritis who had no previous history of the
disease and from children with a recurrent attack of acute
gastroenteritis. No children in either group were fully
immunized against the hepatitis A virus.

Table 1 shows the incidence of arthritis in children with
a history of gastroenteritis and in children without a
history of gastroenteritis.

Table 1

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<th>Age-Group</th>
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These results indicate that arthritis occurs as the
major cause of the initial attack of gastroenteritis in children in
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INTERMITTENT COMPRESSION: A NEW PRINCIPLE IN TREATMENT OF WOUNDS?

Sir,—Venous drainage is widely used in the postoperative care of surgical wounds and has proved very valuable. Apart from this innovation, however, methods of avoiding infection and with improved postoperative care, little fundamental progress has been made in accelerating the natural process of healing or replacing the postoperative discomfort. Recent experience with wound dressings which include intermittent compression of the traumatized area after extensive surgery for chronic venous insufficiency suggests that the natural process can be directly influenced. Because the subjective effects on wound healing and on postoperative pain and swelling achieved by this method have been so striking, I feel it right to make my observations known to others at an early stage in the development of this technique.

The application of intermittent compression was first proposed in 1965 for the prevention of thromboembolic complications in surgical patients on the ground that it keeps the large muscular veins of the foot and leg lower and contracted. 3 Since then studies with an intermittent compression legging (Flowtron-Aire Limited) have shown, in a double-blind controlled trial, that a considerable reduction in the incidence of postoperative deep-vein thrombosis can be achieved. 4 The work of Allenby et al. 5 suggests that the effect is not so much hemodynamic as metabolic. Clinical and experimental work with this system convinced me that intermittent compression affects mainly the inferior flow of water and solute between the capillary and interstitial spaces. As it is this exchange which is disturbed by trauma, I considered that an improvement in the early stages of wound healing might be expected to follow the use of intermittent compression. Since 1972 the Flowtron system has been applied to more than 200 patients to test this contention.

168 patients underwent radical surgery for late stages of chronic venous insufficiency and 53 patients had Kellet's operation for hallux valgus. Each had bilateral disease of approximately equal extent, and in each one leg was operated upon and the wounds were dressed by conventional methods. The response to these operations formed the controls which were compared to similar operations on the other leg. The leg was treated by intermittent compression for 8 hours preoperatively and subsequently for a further 8 hours during the first 4 postoperative days. The treatment was of approximately 2 hour's duration repeated four times on each arm.

In all the treated cases the subjective response was obvious. Pain was much reduced as was swelling and tenderness. Examination of the wounds showed a con-
DIMITERFORMAMID: A CAUSE OF
ACUTE PANCREATITIS?

SIR,—May I report some observations in workers exposed to dimethylformamide?

On Sept. 17, 1973, a man aged 27 was admitted to this hospital after exposure to dimethylformamide at work. He complained of upper abdominal pain radiating to the back, associated with nausea and vomiting. He had an erythematous rash of his hands and forearms, and epigastric tenderness. The blood-picture was normal, but the serum-ampulase level was 2400 i.e. per l. He improved with intravenous fluids and restriction of oral fluids. Cholecystography and intravenous cholangiogram were normal and there was no history of alcoholism. He has changed his job and remains symptom-free.

The factory records revealed admission to hospital of another man, aged 28, after accidental exposure to dimethylformamide. He complained of upper abdominal pain, nausea, and vomiting. He also had an erythematous rash of his hands and forearms, and tenderness in the epigastrium. Unfortunately serum-ampulase was not measured. Cholecystography and barium meal were again normal. On follow-up he had occasional epigastric discomfort after contact with dimethylformamide. Since changing his job he is symptom-free.

In view of these admissions, the other three workers at this factory were questioned and all confessed to intermittent gastro-intestinal symptoms, erythema of exposed parts, and purpura, especially after ingestion of alcohol. Serum-ampulase levels were measured before and after a shift and the levels were in the upper normal range.

Dimethylformamide is a solvent used to spin the polymer polyacrylonitrile for the preparation of synthetic fibre. It is absorbed through intact skin and on inhalation of dust or vapour.1 Animal experiments by Masseau2 have shown that liver damage is a consistent feature at necropsy but failed to show consistent changes in other organs. Toxicity seems to vary in different species. Occupational exposure is associated with gastrointestinal symptoms, but organ damage has not been reported.

From our own experience it seems that acute pancreatitis can also result after exposure to this chemical. I wonder whether others have encountered this situation in patients exposed to dimethylformamide.

S. Deka.

TUBERCULOSIS OF THE SPINE

SIR,—In your leader (July 20, p. 137) you make the unjustified assumption that "Properly prescribed and adequately controlled chemotherapy is all that is required for routine treatment of tuberculosis of the thoracic spine."

You base your observations on the three reports of the M.R.C. Working Party on Tuberculosis of the Spine. You ignore the fact that the conservatively treated patient in Busan and Masan were children and that the patients in Bulawayo were treated by a surgical procedure of questionable value—usually debriement. No one would doubt that the field trials conducted by the M.R.C. Working Party were of outstanding value, not only in terms of the results achieved as a standard for the treatment of the disease in underdeveloped countries, but also as an example of superbly planned field studies. However, the Working Party has persisted in maintaining an unbiased approach and only recently has stated that the trials in Hong Kong which incorporate radical surgery may well be the best possible treatment in technologically advanced countries.

The views expressed in your editorial appear to pre-emt this open-minded critical approach. The fact that the disease observed in this country affects a much older age-group, and is frequently modified by previous inadequate therapy, is tacitly ignored.

In the majority of the patients presenting in this country, including those with concomitant paraplegia, it is not easy to establish the diagnosis with any degree of accuracy, despite the availability of modern diagnostic methods. This can be more easily appreciated when it is realized that these patients are in the age-group in which other infectious and malignant disease are more frequently observed, diseases which mimic typical tuberculosis radiologically. Consequently, it is our practice to treat conservatively only those patients in whom the diagnosis can be accurately established on clinical grounds and in whom there is no risk of vertebral collapse and subsequent instability.

Apart from those patients with paraplegia the only patients who are submitted to surgery are those in whom the diagnosis is not established, in whom there is a question of drug resistance, or in whom there is evidence of vertebral collapse and spinal instability. A direct surgical approach to the lesion—debridement and grafting, coupled with decompression of the cord where this is indicated—facilitates correction of the deformity and restoration of spinal stability. In the short term, the obvious advantage to the patient are economic, in that he can rapidly return, almost invariably, to his original employment. In the long term, it would appear that correction of the deformity and sound bony fusion militates against late onset of paraplegia.

Royal National Orthopaedic Hospital,
St. Pancras,
Middlesex NW1.

J. W. JACKSON
H. R. KEMP

UNUSUAL TUBULAR STRUCTURES IN
BRAIN RETICULUM-CELL SARCOMA

SIR,—" Tubular structures" have been observed in a number of pathological as well as normal tissue. Thus far reported, they are either non-cellular, connected to the endoplasmic reticulum, approximately 25 mm. wide, and mostly found in endoplasmic reticulum of blood capillaries or parasmovirus nucleocapsid, approximately 18 mm. wide, and found in glial cells. We have observed tubular structures approximately 10-11 mm. wide in the cerebral white matter of a patient who died of reticulum-cell sarcoma supposed to have originated in the brain.

A 40-year-old male developed mild disturbance, anaemia, pyre-

cious, and intellectual decline over a period of 6 months and was admitted in a semicomatose state with decorticate posture. He died a month after admission. Necropsy was carried out 3 hours after death. No cell line could be established from the brain tissue subjected to necropsy. No hematopoietic, lymphoendothelial, or cysptic agents could be isolated from the material as far as Vero cells were used. These facts suggest

1. Kemp, H. R. S., Jackson, J. W., Jeremiah, J. D., Cook, J. J., and
Sey 1972, 258, 715.