Use of intermittent pneumatic compression in the treatment of venous ulcers

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Venous ulcers affect up to 1% of the population. This review provides the hemodynamic, hematologic and clinical effects of intermittent pneumatic compression (IPC) in the treatment of venous ulcers. It presents the different IPCs and their application on venous disease. It points out that a large randomized study on IPC versus standard four-layer compression in the treatment of venous ulcers is needed. The cost–effectiveness of IPC in the treatment of venous ulcers should also be assessed.

Keywords: healing, intermittent pneumatic compression, sequential compression device, venous ulcer

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The combined prevalence of active and healed ulcers is approximately 1% [1,2]. The majority of venous ulcers will heal with elevation of the leg above the heart level and application of the appropriate amount of external pressure. The question is when? And can we speed up the process?

Could IPC be the solution?

In a review paper based on 24 randomized controlled trials, Fletcher and colleagues summarized the treatment of venous ulcers in the five following points [3]:

- Compression treatment increases the healing of ulcers compared with no compression;
- High compression is more effective than low compression but should only be used in the absence of significant arterial disease;
- No clear differences in the effectiveness of different types of compression systems have been shown;
- Intermittent pneumatic compression (IPC) appears to be a useful adjunct to bandaging;
- Rather than advocate one particular system, the increased use of any correctly applied high compression system should be promoted.

The IPC devices consist of an inflatable boot and a pneumatic pump that fills the boot with compressed air. The boot is intermittently inflated and deflated, with cycle times and pressures that vary between devices. The review of the literature presented below provides hemodynamic, hematologic and clinical information from studies already conducted.

Hemodynamic & other effects of pneumatic compression devices

Hemodynamic effects

Pneumatic compression devices increase venous velocities in the popliteal and femoral vein, decrease venous stasis and increase arterial flow. The degree of the hemodynamic effect depends upon the segments of the leg that are compressed, the amount and timing of the compression and the position of the leg. In patients with peripheral arterial occlusive disease (PAOD), it increases the walking distance by increasing the ankle brachial pressure index and the skin perfusion [4]. By decreasing venous stasis it is effective in deep vein thrombosis (DVT) prophylaxis [5].

A study in 1949 looked at the effect of compression (20–35 mmHG) on flow velocity on 20 patients by using inflatable leggings, elastic stockings and bandages [6]. They studied the patients with fluoroscopy, serial venograms, foot-to-tongue circulation times and limb venous circulation times. They found that the IPC increased the velocity of venous flow in both the superficial and deep veins.

In a study on six normal volunteers and six post-thrombotic patients, they used five IPC devices for a 3-h session once weekly for 5 weeks and they measured the peak velocity (cm/s) [7]. They concluded that:

- Post-thrombotic patients have lower baseline velocity and significantly reduced velocity response to compression
- There was no difference between single chamber and sequential devices
- There was no difference between below-knee devices in the normal volunteers
- Thigh-length compression generates higher common femoral vein velocity than below-knee compression

In the same group, they evaluated the venous velocity response of three high-pressure, rapid-inflation pneumatic compression (PC) devices versus two low-pressure, slow-inflation PCs in 22 legs of healthy volunteers and 11 legs of C_{4-6} patients. They concluded that patients with post-thrombotic venous disease have a compromised hemodynamic response to all IPC devices. However, high-pressure, rapid-inflation PCs may offer additional protection from thrombotic complications on the basis of an improved hemodynamic response, both in healthy volunteers and post-thrombotic patients [8].

Whitelaw and colleagues analyzed the blood-flow velocity of five healthy volunteers with six different IPC devices and compared it to that of active and passive foot dorsiflexion [9]. They found that average peak venous velocity increased more than 200% on dorsiflexion of the ankle and a similar result was achieved by devices enabling compression of the lateral and medial aspect of the calf. Foot compression produced the smallest increase in venous velocity.

Similar results were reported in another study on ten total knee replacement patients. They compared peak venous velocity in both the superficial and deep venous systems on active dorsal to plantar flexion and seven different IPC devices. While all the devices augmented venous volume, the greatest effect was seen with those incorporating calf compression [10].

In another study on 12 legs of $C_{4–5}$ EAP patients who used graduated elastic compression (GEC; 30–40 mmHg) and foot impulse technology (FIT – the act one device) 2 h per day for 3 months, they studied the patients with air-plethysmography (APG) and recorded the clinical score before and at 1, 2 and 3 months [11]. The clinical score improvement for edema and pain was $p < 0.05$ and $p < 0.04$, respectively. On APG, there was reduction of the residual volume fraction ($p < 0.05$). The venous volume and venous filling index (VFI) reduction was nonsignificant.

Other investigators measured the flow velocity on 12 healthy volunteers with duplex at the femoral vein at the supine, semi-recumbent and sitting position, with two devices [12]. The sequential compression device (SCD) sequel compression (11”compress–60”deflation) versus the SCD response compression (11”compress-?deflation). They found that the response refilling time was 24–60” (41” in sitting), which is considerably longer than that measured in the supine and semi-recumbent positions. The total volume of blood expelled per hour in the response increased by 76% in supine, 59% in the semi-recumbent and 21% in the sitting position.

From the same department in another study, they used APG and duplex scan for femoral vein flow velocity in the supine, semi-recumbent and sitting position on ten post-thrombotic patients and ten patients with varicose veins [13]. They used the SCD sequel compression (11”compress–60”deflation) versus the SCD response compression (11”compress-?deflation). They found:

- Inverse association between post-compression refill time and VFI
- Shorter refill time in patients with advanced venous disease
- By achieving more frequent cycles, the SCD response is more effective

In a third study, they compared the SCD EXPRESS™ compression system versus the VenaFlow® (rapid inflation device) on 12 normal volunteers [14]. They observed at the femoral vein flow velocity and volume using duplex scan in the semi-recumbent position. With both devices, the venous flow velocity increased by 3.8-times from baseline ($p < 0.001$). However, VenaFlow had a shorter refill time ($p < 0.001$), that is, there was incomplete vein evacuation. By sensing the refill time, the express device also resulted in more compression cycles over time.

In our study, the total volume flow (TVF) and the peak systolic velocity (PSV) were obtained at the popliteal vein with ultrasound on 20 legs with venous ulcers [15]. Measurements were performed without bandage, with four-layer bandage and following the application of the SCD EXPRESS compression system on top of the four-layer bandage. We found that both TVF and PSV increased slightly with the addition of the four-layer bandage. However, with the addition of the SCD system these parameters increased threefold.

All the studies mentioned demonstrate the hemodynamic improvement that IPC provides. The increase of venous velocities, in the popliteal and femoral vein, the decrease of venous stasis and increase of arterial flow should promote healing.

Salvian and colleagues, who measured velocity changes in the common femoral vein using three different IPC devices concluded that correct cuff application was critical, suggesting that some of the failures of IPC may have resulted from improper cuff placement [16].

Malanin and colleagues, in an attempt to clarify the pathophysiology of hemodynamics in legs with venous ulcers, investigated the effect of a single IPC treatment on eight venous ulcer patients and ten normal [17]. They found that it raised the peripheral resistance in the arteries of legs with ulcer and laser Doppler flux of the skin more in ulcer legs than in healthy legs ($p = 0.046$ and $p = 0.034$, respectively). Their findings suggest that removal of edema causes redistribution of skin blood flow in the legs with ulcers, favoring the superficial capillary perfusion and could explain why IPC promotes the healing of ulcers.

Hematologic & other effects of IPC

Venous ulcers, like other wounds, have low oxygen tension and, if the tension is lower than 20 mmHg, the ulcers are unable to heal. However, studies on the effect of IPC on oxygen tension gave contradictory results [18–21].

Intermittent flow associated with IPC upregulates endothelial cell fibrinolytic potential [7,22,23] and influences factors altering vasomotor degradation activity [22]. In addition, Jacobs and colleagues found that IPC induces prompt but short-lived alterations in fibrinolytic function [24]. More specifically, IPC induces significant increases in fibrin products, fibrinogen degradation products and tissue plasminogen activator–plasminogen activator inhibitor-1 complex (tPA–PAI-1) and decreases in euglobulin lysis time and PAI-1, all of which quickly reverted to baseline on termination of compression. This last finding would suggest that instead of applying it for one long session, IPC might be more beneficial if used more times each day.

Role of nitric oxide

Nitric oxide (NO) is an endothelium-derived relaxing factor [25]. The IPC increases intravascular flow and shear stress, resulting in increased production of NO. Nikolovska and colleagues established the hypothesis that venous stasis in the microcirculation reduces the rate of shear stress on the endothelial cells, effectively resulting in a decrease in cellular levels of NO, a key event of enhanced adhesion molecule expression and subsequent massive neutrophil activation, causing trophic changes [26]. NO causes venodilatation by inhibiting smooth muscle cell contractions, platelet aggregation, platelet and monocyte adhesion to endothelial surfaces and smooth muscle cell proliferation, as well as stimulating platelet disaggregation [25].

Table 1. IPC versus FIT (A-V impulse system or Foot Impulse Technology).

	IPC	FIT
Inflation period	11–60”	0.4”x1–3”
Compression cycles	60”	20”
Pressure	30–50	100–200 mm Hg

A-V: Arterio-venous; FIT: Foot impulse techonology; IPC: Intermittent pneumatic compression.

Different pneumatic compression devices & their clinical applications.

In 1983, Gardner and Fox used serial venography to demonstrate the existence of a physiologic venous pumping mechanism in the plantar surface of the foot that emptied rapidly when weight-bearing flattened the plantar arch [27]. Blood from the plantar venous plexus was transmitted upward through the deep venous system, resulting in increased venous outflow. Their work led to the development of the arterio-venous (A-V) impulse system otherwise known as FIT.

Andrews and colleagues used an A-V impulse system and on altering its parameters, they used duplex scanning to measure the velocity and blood flow in the superficial femoral and popliteal veins [28]. They found that foot compression of 50, 125 and 200 mmHg significantly increased the maximum venous blood flow ($p < 0.001$). In addition, reducing the frequency of compression from six to three cycles every minute significantly increased the peak flow ($p < 0.001$). They concluded that increased blood flow is best achieved with high-pressure lower-frequency foot compression.

In a study using IPC with an optimal pressure of 40 mmHg, they measured the femoral vein flow with an electromagnetic flow meter [29]. An IPC with a fast rate of 3 s inflation and 20 s deflation with a frequency of three every minute was compared with an IPC with a continuous inflation-deflation cycle of 2 min. The former generated an enhanced net volume flow, peak flow and flow amplitude.

Although IPC and FIT have similar hemodynamic effects on venous flow and velocity, their settings are quite different. It is important to make this distinction as the two devices have different clinical applications (Table 1). The IPC devices have a much longer inflation period (11–60 s) at lower pressures (30–50 mmHg), with compression cycles every 60 s. These are suitable for augmentation of venous return. Conversely, the A-V impulse system begins with a rapid pressure rise in the first 0.4 s, which is then held for either a 1-s (short) or 3-s (normal) total pressure impulse, every 20 s and at adjustable pressure settings (100 or 200 mmHg) [30]. These are suitable to enhance arterial inflow and have been used for PAOD [4] and for reduction of post-revascularization edema [31].

The clinical studies on IPC & healing of venous ulcers

In 1981, Hazarika and Wright conducted a study involving 21 patients who were treated with compression bandages and IPC (Table 2) [32].

Table 2. Summary of clinical studies on compression and the effect of addition of IPC.

Authors	n	Type of compression	Type of IPC	Result	Ref.
Hazarika *et al.*	21	Compression bandage	Flowtron Mk2 (A/C2002)	Subjective improvement	[32]
Dillon	17		The circulator boot system. An end-diastolic pneumatic compression boot	All patients improved or healed	[33]
Pekanmaki	8	Elastic bandage	Sequential and graded pressure IPC	Shortens ulcer healing time markedly ($P < 0.05$)	[34,35]
Smith *et al.*	45	GEC	SCD (Kendall)	Increased ulcer healing rate ($p < 0.05$)	[36]
Mulder and Reis	8	Elastic bandage and Unna Boot	SCD (Kendall)	Significant decrease in wound area over time ($P < 0.01$)	[38]
McCulloch *et al.*	22	Unna Boot	A single chamber IPC	Improved healing rate	[39]
Schuler *et al.*	53	Unna Boot	GEC/IPC (HomeRx, Kendall)	Equally effective in ulcer healing rates	[40]
Rowland	16	Compression bandage	IPC	Equally effective in ulcer healing rates	[41]
Kumar *et al.*	47	Four-layer bandage	IPC	Faster healing ($P < 0.05$)	[42]
Alpagut and Dayioglou	76	GEC	Flowtron plus AC2002 Huntleig Healthcare	IPC shortens mean treatment time and improves quality of life	[43]
Nikolovska *et al.*	104		Rapid versus slow IPC	Rapid IPC healed ulcers more rapidly ($P = 0.0002$) and in more patients ($P = 0.003$) than slow IPC	[44]

GEC: Graduated elastic compression; IPC: Intermittent pneumatic compression; SDC: Sequential compression device.

The authors concluded that chronic leg ulcers benefit from IPC and, even if complete healing is not achieved, in every case there is a definite, subjective improvement.

In 1986, Dillon reported his experience on treating 17 patients with difficult or refractory stasis dermatitis and ulcers [33]. He used an end-diastolic pneumatic compression boot and all patients improved or healed. He subsequently used periodic out patient boot treatment for maintenance of healing.

In an open clinical trial, eight patients suffering from persistent or recurrent venous ulcers were treated by an IPC producing sequential and graded pressure [34,35]. Compared with previous conservative treatment only, IPC together with conservative treatment was found to shorten the ulcer healing time markedly ($p < 0.05$).

It has also been shown that IPC plus GEC increased ulcer healing (ten out of 21 patients) more effectively than compression alone (one out of 24 patients), relative risk for healing 11.4, (95% confidence interval: 1.6 to 82) [36]. However, in view of the small size of this study, a Cochrane Review suggested that further trials are required to determine whether IPC increases the healing of venous leg ulcers [37].

Mulder and Reis studied the effect of the addition of IPC, for 3 h per day, on eight patients who did not respond to GEC and Unna Boot [38]. They found a significant decrease in wound area over time ($p < 0.01$). Only one patient healed completely after 120 days. However, after study termination, on follow-up of these patients, two of them who discontinued pump use had recurrent wounds that healed after returning to pump use.

McCulloch and colleagues, in their prospective study, treated 22 venous ulcer patients with local wound care and Unna Boot [39]. In addition, 12 of these patients received a single-chamber IPC twice weekly for 1 h each session. A mean healing rate of 0.08 cm^2 per day per control subject and 0.15 cm^2 per day for the IPC patients was reported, which was statistically significant.

Schuler and colleagues allocated 53 ulcer patients into two groups [40]. Unna Boot ($n = 25$) versus below knee GEC ($n = 28$), removed only while IPC was applied for 3-h daily. They found complete healing in 15 of 25 (60%) patients treated with the Unna Boot compared with 20 of 28 patients (71%) in the IPC group. They concluded that GEC plus IPC heals venous ulcers at least as well as does the Unna Boot.

Rowland and colleagues, in a crossover study on compression to IPC and vice-versa involving 16 patients (11 of which were assessable), found that both methods are equally effective in ulcer healing rates or control of edema [41]. However, the compression pump was reported as being easier and more comfortable to use than bandages.

Kumar and colleagues studied two groups of patients [42]. In the first, comprising 47 patients with active ulcers, they all had weekly four-layer bandaging and in addition, 22 had below-knee single-chamber IPC (90 s inflation and 90 s deflation) for 1 h twice daily at 60 mm Hg, for 4 months or until the ulcer has healed. They found that the rate of healing per day was significantly faster in the IPC-treated patients ($p < 0.05$). In the second group they studied 53 patients with recently healed venous ulcers, 30 of whom had weekly support hosiery and 23, in addition to the hosiery, used IPC as above. Although there were more recurrences in the IPC group, there was no statistical difference between the groups ($p > 0.05$).

Alpagut and Dayioglu used the Flowtron® IPC on 76 patients as an adjunct to GEC stockings and compared the results with the 159 patients who used only GEC [43]. In the GEC group, the healing of ulcers was 3 months (ranging 20 days to 5 months) while in the GEC plus IPC group the healing was 20 days (range 15–35 days). In addition, the return to active life was 25 days versus 7 days, respectively.

More recently in a clinical randomized trial on 104 venous ulcer patients using two types of IPC, it was shown that treatment with rapid IPC healed ulcers more rapidly ($p = 0.0002$) and in more patients ($p = 0.003$) than slow IPC [44].

All these clinical studies used different devices, methodology, patient population and follow-up, and although the majority of the results appear promising the number of patients involved and the time of follow-up are limited. Therefore, a prospective clinical study with an optimal IPC, including a large number of patients who are to be followed-up for adequate time is needed.

Advantages from the use of IPC in the treatment of venous ulcers

Should IPC prove to be clinically effective for venous ulcer treatment, the advantages are that it is compact, lightweight, some devices have battery power, and it provides the user with the ability of sequential, gradient and circumferential compression to each limb individually. In addition, the IPC can be applied at home, making the treatment flexible.

Prospective study: points to be taken into account for the protocol

There are no studies that directly compared single- with multiple-chamber devices [45]. However, compression with a single-chamber device in the prevention of venous stasis and post-operative DVT led to trapping of venous blood in the distal veins, while sequential gradient compression results in more complete emptying of the deep veins [5].

Nor are there studies on whether the effectiveness of the pump was dependent on types of treatment used concurrently with the pump [45]. However, in the guidelines for treatment studies on venous ulcer patients, it would be unethical to conduct treatment studies in patients with an exclusive venous ulcer without concomitant compression therapy that should be administered in a standardized form as the basic form of treatment [46].

The cost–effectiveness of IPC in the treatment of venous ulcer is another issue for consideration. Even if IPC proves effective, Dowson questions whether the cost would be forbidding for a wide use [47]. However, one has to take into account that delayed healing involves prolongation of current costs, including: patient transport, medical and nursing time, consumables, cultures, antibiotics and so on. The same was the case with the low molecular weight heparines when they first appeared on the horizon for the prevention and home treatment of DVT. Since then, many studies have proven their cost–effectiveness [48].

Conclusion & future perspective

Hemodynamic and hematological studies have demonstrated the effectiveness of IPC in the treatment of venous ulcers. There is evidence from clinical studies that IPC used in addition to standard compression might improve healing of venous ulcers. However, this evidence is limited. A clinical study of an adequate size on the effectiveness of IPC versus standard therapy in the treatment of venous ulcers in needed. The cost–effectiveness of such a study might change our future practice.

Executive summary
Intermittent pneumatic compression: is it an alternative treatment in the healing of venous ulcers?
• The majority of venous ulcers will heal with elevation of the leg above the heart level and application of the appropriate amount of external pressure. The questions are: – When will the ulcer heal? – Can we speed up the process? – Is intermittent pneumatic compression (IPC) the solution?
Differences in the settings & clinical applications of IPC & arterio-venous impulse system.
• IPC devices have a much longer inflation period, at lower pressures with compression cycles every 60 s. They are suitable for augmentation of venous return. • The sequential compression device EXPRESS™ compresses by sensing the refill time results in more compression cycles over time and appears to be the device of choice for a study on healing venous ulcers. • The arterio-venous (A-V) impulse system begins with a rapid pressure rise in the first 0.4 s that is then held for 1–3 s, at every 20 s, and has adjustable high-pressure settings. These are suitable to enhance arterial inflow.
Conclusion
• Hemodynamic and hematological studies have demonstrated the effectiveness of IPC in the treatment of venous ulcers. • From clinical studies, there is evidence that IPC used in addition to standard compression might improve venous ulcers' healing, however, this evidence is limited.
Future perspective
• A clinical study of an adequate size on the effectiveness of IPC versus standard therapy in the treatment of venous ulcers is needed. • The cost–effectiveness of such a study might change our future practice.

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