VenaPro™ White Paper

A LOOK AT VENOUS STASIS ULCERS AND TREATMENT WITH THE VENAPRO™ INTERMITTENT PNEUMATIC COMPRESSION DEVICE

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The VenaPro™ is an ultra-portable intermittent pneumatic compression device. This paper discusses its use in treating venous stasis ulcers, bringing portability to the well-established and effective treatment of intermittent compression.

Venous stasis ulcerations (VSU) are fairly ubiquitous in our society with a frequency around 1-2% in the general population.[1-3] The prevalence of such ulcerations is higher in developed industrialized countries than in underdeveloped countries. Risk factors include age, sex, family history, obesity, pregnancy, phlebitis and previous leg injury.[4] The overall prognosis of VSUs is poor, because delayed healing and recurrent ulcerations are very common. The socioeconomic impact of VSUs is dramatic because of the impaired ability to engage in social and occupational activities, reducing the quality of life and imposing financial distress as well. Estimates are of $2-3 billion annually for the cost of treating such wounds. The *sin qua non* of VSUs are continual venous hypertension of the lower extremities.[5] The normal vasculature and venous return of the legs depends on the patency of vessels containing a series of one-way valves, and the calf muscles serving as the so-called "blood-pump". During normal ambulation blood that enters the lower extremity venous system must travel against gravity and other pressures to return to the central circulation. The venous system of the leg consists of the superficial, deep, and perforating veins. The superficial venous plexus lies between the skin and the muscle fascia of the calf. The deep system lies below the fascia within the muscle itself, and the perforating system connects the two. With each contraction of the calf, blood is forcefully returned by means of the blood pump, to the heart. Of supreme importance are the perforating vessels which contain one-way bicuspid valves that prevent any blood returning to the superficial system, which, when damaged, would allow venous reflux resulting in elevated venous pressure with all its sequelae. What follow is a series of pathophysiological changes that are both complex and not fully understood. Currently it is thought that when the valves leak or are damaged it allows reflux of blood backward to the dermal circulation. This increased hydrostatic pressure then results in venous distention and varicose veins. This by itself can result in venous pooling and subsequent

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venous thrombosis, with its own significant morbidity. These large vessel problems directly contribute to microvascular changes, such as dilation and elongation of capillary beds, thickening of basement membranes with increased collagen and elastic fibers, endothelial damage with widening inter-endothelial spaces, and increased peri-capillary edema.[5-7] This increased pressure within the capillary pushes fluid, growth factors and other proteins, and white and red blood cells into the interstitial space. These changes also directly affect the skin with deposition of hemosiderin, an iron-containing protein, which causes hyperpigmentation and discoloration. These changes cause chemical reactions, probably oxidation or glycosylation of hemosiderin, that then contribute to eczematous changes in the skin with breakdown and a hardening of the subdermal fat—termed lipodermatosclerosis.[8,9] Because of the aforementioned reactions, there is increased risk of cellulitis, leg ulcerations, and delayed wound healing.

The treatment of VSU disease consists of conservative and interventional therapy. In this paper we will discuss mainly conservative treatment. For ulcerations of the lower leg caused by venous stasis disease, conventional treatment has been compression. Simply counteracting the increased hydrostatic pressure in the vein is the underlying treatment of venous stasis. The treatment of the ulcerations themselves has spawned an enormous wound care industry that produces literally hundreds of products, each claiming to hold the holy grail of wound repair. These products include hydrogels, hydrocolloids, a variety of silver impregnated dressings, iodinated pastes, growth factor gels and even bioengineered skin replacements. The cost of these products ranges from moderately to outrageously expensive, considering that treatment of VSUs is simply reversal of the underlying pathology by compression. Outcomes of compression therapy, however, has been disappointing. VSUs can last from weeks to a lifetime depending on a menagerie of co-morbidities and other factors. Large meta-analysis studies have shown that cases of VSUs heal 35%-55% of the time taking an average of at least 24 weeks.[10] The types of compression used in therapy are: Unna wraps, compression stockings, non-paste multiple layer wrap systems, and intermittent pneumatic compression. All of these systems have

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their advantages and disadvantages. Practitioners usually prefer to use the systems they were trained in during their residencies. For the past twenty years it has been known that compression wraps, even those that are currently being used in medicine today, do not provide adequate sustained, or for that matter, active compression.[11] This missing key element would still allow retrograde blood flow and blood settling in the leg with all its complications. Intermittent pneumatic compression (IPC), *actively* compresses the leg, mimicking the action of the so called leg blood pump and naturally returning blood to the central circulation. More importantly, it reduces venous hydrostatic pressure much more effectively than any wrap system.[14] The VenaPro™, a new form of IPC, is a tubeless and cordless device designed to allow safe ambulation during use. The VenaPro™ is a self-contained unit with a small battery powered microcomputer attached to the sleeve chamber that controls its inflation/deflation cycle. The battery can be recharged by simply plugging the device into any standard 110v electrical source. Having no tubes, the patient is free to ambulate without concern for the tripping hazard that they create. It has been known that IPC can reduce edema, be used prophylactically to prevent DVTs, increase blood flow into ischemic limbs, and even help to heal diabetic ulcerations. It is thought to do this by decreasing the venous pressure in the leg by accelerating blood exiting the leg and returning to the heart. This dramatically increases the vein/artery pressure gradient, rapidly emptying the arteries into the venous system thus increasing arterial blood flow into the leg.[6]

IPC affects the circulation through four mechanisms; 1. Hemodynamic, 2. fibrinolytic,

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3. tissue oxygen tension, and 4. effects on edema.[7,12] IPC reduces venous stasis and increases flow velocity in the deep veins. This results in optimal hemodynamic changes, such as decreased venous pressure and decreased interstitial edema. IPC increases venous volume return as well as venous velocity. This results in increased shear stress (increased flow friction against the arterial wall or endothelium). This mechanical stress on the endothelium generates well-known pro-fibrinolytic, vasodilatory, and anti-thrombotic cascades. The hematological benefits, such as changes in blood coagulation chemistry, can also be attributed to increased shear stress. This increases endothelial production of vasodilatory and anti-thrombotic substances such as; prostacyclin, endothelial-derived relaxing factor, platelet-derived growth factor, and tissue plasminogen activator.[13,14] IPC also reduces tPA, uPA, and PAI-1, (all proteins involved in clotting) through a series of complicated reactions that are still being investigated.[15] Lastly, when edema occurs it causes an increase in interstitial pressure, thus reducing blood perfusion and skin oxygenation, by compression of the microvasculature.[15,16] This can readily be reversed with IPC, it is done so by reducing interstitial edema with gentle compression, thus increasing blood flow and returning oxygenation to normal levels. Since the initial studies in 1981, evidence has been accumulating to support the use of IPC as therapy for VSUs. [17] This new modality effects the actual underlying pathophysiology of VSUs, by increasing venous return, reducing leg edema, increasing fibrinolysis, reducing intravascular coagulation, and improving skin oxygenation. Therefore it should not be surprising that well designed clinical trials show that using IPC with conventional wound care improves healing rates of ulcers. These observations have led to suggestions from the American College of Chest Physicians that IPC be used to speed healing of VSUs.

Once a mystery, the pathophysiology of venous stasis ulcers is beginning to slowly come into focus. This is due, in large part, to improved technology in molecular biology. This has allowed scientists to delve deeper in to the inner workings of cells as well as microcomputing components, which have now made fabrication of products like the VenaPro™ a reality.

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VenaPro™ is in an ideal position, being both cordless and tubeless, to markedly reduce the pain and suffering of patients with this disease and to ameliorate venous stasis wounds. Patients are no longer tethered to a machine for hours at a time creating an inconvenience that reduces the likelihood of compliance with the prescribed treatment. The freedom the VenaPro™ allows makes it possible for patients to do almost any activity while using the device without interference or tripping hazards created by cords and tubes. These improvements in pneumatic compression technology enhance the treatment regimen resulting in better patient compliance, more positive patient satisfaction, and improved healing times. The results are a reduction in infections, hospitalizations, and amputations. This would undoubtedly result in a decrease in overall treatment cost for this difficult to manage disease.

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