Management of venous leg ulcers

Abstract

The management of leg ulcers has proven to be a tremendous burden on patients, healthcare practitioners and healthcare resources. The refractory nature of venous ulcers affects the quality of life and work productivity of those persons afflicted. This, in combination with the high costs of long-term therapy, makes venous ulceration a major health problem. The majority of lower limb ulcers are associated with venous disease (80%), but other causes or contributing factors include arterial disease, neuropathy (often due to diabetes), pressure (immobility, obesity), vasculitis, trauma, infections and cutaneous neoplasia. Very little information is available with regards to the estimated cost of the management of venous ulcers in South Africa. The cost of venous leg ulcers is estimated to be $1 billion per year in the United States, and the average cost for one patient over a lifetime exceeds $40 000. In the United Kingdom this cost is estimated at more than £400 000 000 a year. Proper diagnosis and adequate management are vital when caring for patients with venous leg ulcers to promote faster healing and prevent recurrences. By standardising the treatment of patients with venous leg ulcers, the patients could be treated more efficiently and the total cost of treatment, could be reduced.

Introduction

Most venous leg ulcers could be healed if patients were admitted to hospital or clinics for continuous leg elevation and wound care under appropriate supervision. This once popular approach is now considered impractical, due to the general shortage of hospital beds, the high cost of inpatient care and the need to maintain mobility and independence in the elderly population. Furthermore, these venous ulcers often recur when the patient returns home and resumes a lifestyle in which most of the day is spent with the legs in dependency.

Outpatient systems of care that maintain mobility and avoid the complications of bed rest are more cost effective and appropriate. Outpatient and community based care also maintain independence, as well as quality of life.

Care for patients with leg ulcers has improved in the past two decades as research based approaches have been adopted. Hospital based outpatient woundcare clinics and private woundcare clinics are now available in the larger centres. By utilising appropriate compression bandaging, these woundcare specialists have dramatically improved healing rates and reduced costs, but close supervision is essential if standards are to be maintained. This is where the woundcare specialist and the various surgical subspecialties all make their contribution.

Causes of venous ulceration

The pathophysiology of venous ulceration is contentious and detailed consideration of the microcirculatory changes leading to tissue necrosis is beyond the scope of this paper. However, management of venous ulceration must be based on an understanding of the causes of the ambulatory venous hypertension that is ultimately responsible for both the symptoms of chronic venous insufficiency and venous ulceration. Ambulatory venous hypertension is an abnormally sustained elevation of the venous pressure upon ambulation. Chronic venous insufficiency has been widely assumed to be due to deep venous obstruction or incompetence, and the term “post-phlebitic limb” has been used, even though approximately 70% of people with venous ulcers have no history of deep vein thrombosis. Venous ulceration is clearly associated with age and younger patients with severe chronic venous insufficiency may avoid ulceration by virtue of their mobility, which maintains function of the calf muscle pump. Whether the final mechanism in ulceration is a fibrin cuff, leukocyte trapping or chronic inflammation due to a repetitive ischaemia reperfusion injury, the treatment for venous ulceration is based almost entirely on avoiding sustained venous hypertension. Venous hypertension is usually caused by a combination of factors, of which venous disease, obesity and immobility are perhaps the most important; many factors develop with increasing age.

Sustained venous hypertension results in oedema within the dependent lower limb, which increases the distance over which metabolites and nutrients must diffuse from the microcirculation to tissue cells. The tissues around the ankle become ischemic during dependency, with reperfusion on walking or elevation. This chronic reperfusion injury results in an inflammatory process with further oedema, tissue fibrosis and formation of a cuff of extracellular matrix proteins around capillaries. These changes result in the features of chronic venous insufficiency, which include aching, heaviness of the legs, lipodermatosclerosis, hyperpigmentation (haemosiderin), swelling, eczema, itching and ultimately ulceration.
Treatment is based on preventing sustained venous hypertension and reducing its effects by compression bandaging to reduce venous stasis and tissue oedema.

**Diagnosis and investigation**

Management must start with a full history and examination to identify risk factors such as age, gender, cardiovascular disease, body mass index, mobility, arthritis, diabetes and a history of leg injury or deep vein thrombosis. Leg ulceration can be defined as any chronic ulcer on the lower leg but excluding those on the forefoot or toes.

Several risk factors for the development of venous ulcers have been identified. Up to 50% of patients with chronic venous insufficiency have a history of leg injury. Obesity, phlebitis, family history of varicose veins, type of employment and lifestyle (activities that require long hours of standing or sitting), deep venous thrombosis, and previous surgery for varicose veins have also been considered important risk factors for venous ulcerations.

Patients with venous ulcers often report swelling and aching of the legs, often worse at the end of the day, which may be exacerbated by dependency and improved by leg elevation. A history of ulcer recurrence, particularly at the same location, is characteristic. Recent publications have challenged the assumption that venous ulcers are not painful; as many as three quarters of patients with venous ulcers report pain that adversely affects their quality of life.

The patient should be examined both lying and standing to detect varicose veins. Hand held Doppler is essential to measure the ankle brachial pressure index to exclude arterial disease and assess superficial venous reflux.

Duplex-Doppler imaging is indicated for patients with recurrent or complicated varicose veins, short saphenous incompetence or suspected deep venous disease. Superficial venous incompetence is almost universal and is the predominant cause of venous hypertension in approximately half of limbs with venous ulcers, particularly in younger patients with good mobility.

Venous function in patients with mixed deep and superficial disease could be investigated by ambulatory venous pressure measurements. This involves cannulation of a foot vein and the use of tourniquets to occlude incompetent superficial veins to select those patients who may benefit from superficial venous surgery. The less invasive modality of photoplethysmography can also be used in this setting.

**Management of the ulcer**

Despite considerable research, little evidence of major benefits from modern interactive dressings has been published. An emphasis on education, training and further development of compression systems is needed to improve patient care and ulcer healing.

**Where should care be carried out?**

Patients with venous leg ulcers are best managed in the community for two reasons:

- Maintenance of independence and mobility is important in this elderly population
- The number of patients would overwhelm hospital services

However, direct access to appropriate specialised hospital services is essential for the investigation of underlying vascular disease and for microbiology, histopathology and dermatology. Rates of healing have been shown to be improved and cost to be reduced when a multidisciplinary, coordinated service using research based protocols is introduced.

Responsibility for patient care should not be removed from woundcare nurses; they should be provided with resources and training aimed at delivering an appropriate, high quality service in specialist woundcare clinics. Evidence from research in two large health authorities in the United Kingdom showed that standards could be maintained only with close supervision; when a leg ulcer service was continued without the direct involvement of a woundcare specialist, healing rates declined and costs increased.
The underlying causes need to be identified. Multiple pathologies are common, but patients with diabetes may have simple venous ulcers that are no more difficult to heal than in people without diabetes. As 80–85% of ulcers are associated with venous hypertension, compression remains the mainstay of treatment.

Dressing materials

Patients with leg ulcers are prone to contact sensitivity, particularly from wool, alcohols, topical antibiotics, cetylshearyl alcohols, parabens and rubber mixes, which are present in many dressings, ointments and creams. Many entirely inadequate studies have examined the role of different dressing materials; most have shown that modern “designer” dressing materials have no additional effect on wound healing over that achieved by simple low adherence dressings under multilayer compression bandaging. Palfreyman and co-authors concluded in their review that “there was no evidence of additional benefit associated with wound dressings other than simple dressings when used beneath compression. There was no evidence of difference in healing rates between other dressings but most studies are too small to allow us to rule out important differences. Inexpensive, simple non-adherent dressings should be used beneath compression therapy unless other factors, such as patient preference, take precedence”.

Compression treatment

Sustained graduated compression overcomes the effects of venous hypertension by reducing venous stasis and preventing or reducing tissue oedema. The pressure within the veins on standing is largely hydrostatic and the level of external pressure needed to counteract this decreases progressively up the leg. Compression treatment has been covered in a Cochrane review on the cost effectiveness of both bandaging and stockings in the treatment of venous ulceration. Twenty two trials were identified and consistently showed that compression encouraged healing of ulcers. More ulcers were healed at 12–15 weeks with high compression systems than with low compression systems. No significant difference was found between the effectiveness of different high compression systems, but more ulcers healed at 24 weeks with four layer bandages than with a single layer.

The most effective level of compression to overcome venous hypertension has been determined to be around 40 mmHg at the ankle. Correct application of bandages is essential to avoid pressure ulceration over bony prominences and along the anterior border of the tibia. To achieve this pressure in a range of limb diameters, bandaging regimens must be adjusted according to ankle circumference. The correct sizing of compression hosiery is just as important.

A review of the literature available on the role of intermittent pneumatic compression showed conflicting evidence about whether or not this modality can help heal venous leg ulcers. The authors suggested further trials.

As woundcare practices improve, more patients have their ulcers healed and are then at risk of recurrence; recurrence rates of 26% at one year and 31% at 18 months have been quoted. A Cochrane review on the role of compression in the prevention of recurrence identified few adequate trials, but concluded that recurrence may be lower with higher compressions.

Limb elevation

Limb dependency, immobility and oedema all contribute to venous hypertension. Limb elevation, with the feet preferably above the level of the heart, reduces oedema and enhances flow in the microcirculation, reducing trapping, sequestration, and activation of white cells – a necessary first step in the pathophysiology of ulceration. Leg elevation in hospital enhances healing.

Exercise

The importance of exercise has been confirmed with several studies. By increasing the muscular endurance, efficacy and power of the calf muscle, isotonic exercise improves its ejection ability and the global haemodynamic status in limbs with venous ulceration. The patient should be told to walk, cycle or swim. Ideally graduated pressure hosiery should be worn during exercise. In a less mobile individual dorsiflexion, plantar flexion and rotation exercises of the feet should be encouraged.

Skin grafting

Split skin grafting is technically demanding and requires hospital admission. The discharge from the surface of venous ulcers tends to dislodge continuous sheets of split skin, leaving a choice between mesh and pinch skin grafting. Pinch skin grafts provide epithelial islands, from which epithelial growth may spread outwards as well as inwards from the ulcer margin.

Bioengineered skin products, including bilayered skin constructs and frozen human allogeneic epidermal cultures are being developed and may stimulate wound healing through the release of growth factors and cytokines. The numbers of patients recruited to such studies have been small, and most products are not yet widely available for clinical use. These new approaches have yet to be compared with pinch skin grafting, which is simple and inexpensive.

A recent Cochrane review concluded that there was evidence that tissue-engineered skin composed of two layers, used in conjunction with compression bandaging, increases the chance of healing. There was not enough evidence to recommend any other type of graft and suggested that further research is required.

Growth factors

Wound fluid from non-healing ulcers contained higher concentrations of pro-inflammatory cytokines, interleukin-1, interleukin-6 and...
tumour necrosis factor and had reduced proliferative responses compared with fluid from healing ulcers. Research on platelet derived growth factor, hepatocyte growth factor and human keratinocyte growth factor-2 has been published, but these studies were small and inconclusive.

Drug treatment
Antibiotics have little effect on ulcer healing but are needed for clinical infections with surrounding cellulitis.6 Pentoxifylline has been evaluated in clinical trials, but the largest placebo controlled, double-blind, randomised study included only 80 patients; 88% were healed by 12 months on pentoxifylline compared with 44% on placebo. A recent review concluded that pentoxifylline is an effective adjunct to compression bandaging for treating venous ulcers and may be effective in the absence of compression.10 Oxerutins failed to improve ulcer healing or influence recurrence. Fibrinolytic agents such as stanozolol have also been disappointing. Studies on prostaglandin E1 and micronised purified flavonoids were simply too small to influence clinical practice. Sulodexide is a profibrinolytic and antithrombotic drug that was evaluated in a clinical trial that recruited 94 patients and achieved healing rates at two months of 58%, compared with 36% in controls (p = 0.03). Aspirin has also been studied in a randomised trial and significantly improved healing, but only 20 patients were randomised.

In both the above studies, the healing rate achieved with drugs was no better than that achieved without drug treatment in community leg ulcer clinics.

Hyperbaric oxygen therapy was also reviewed as a possible treatment modality in chronic wounds. The authors concluded that hyperbaric oxygen therapy seems to reduce the number of major amputations in people with diabetes who have chronic foot ulcers, and may reduce the size of wounds caused by disease to the veins of the leg, but found no evidence to confirm or refute any effect on other wounds caused by lack of blood supply through the arteries or pressure ulcers.11

Venous surgery
Superficial venous surgery has been shown to improve ulcer healing in patients with only superficial venous incompetence. In patients with no deep reflux on duplex imaging, superficial venous surgery also reduced ulcer recurrence at three years from 44% to 26% in a non-randomised study. When superficial venous surgery was compared with compression alone in 87 patients with venous ulcers, surgery achieved complete healing at a mean of 31 days compared with 63 days with compression; recurrence rates at three years were 9% and 38%.

A recent randomised controlled trial investigated the long term results of compression therapy alone versus compression plus surgery in chronic venous ulceration (ESCHAR-trial) in 500 patients. The authors concluded that surgical correction of superficial venous reflux in addition to compression bandaging does not improve ulcer healing but reduces the recurrence of ulcers at four years and results in a greater proportion of ulcer free time.12

The role of surgery in mixed superficial and deep venous incompetence is less clear. In unselected patients with combined superficial and deep incompetence, superficial surgery without postoperative compression failed to improve venous hypertension or achieve ulcer healing. However, where the deep incompetence was limited or “segmental”, improvements in healing were achieved. Ambulatory venous pressures may help to identify patients who would benefit from surgery. Virtually no research has been done on prophylactic surgery to prevent ulceration in at-risk patients with superficial venous incompetence.

Alternative treatment modalities
Various other treatment modalities have been implemented in an attempt to treat venous ulcers. Based on the available literature the use of electromagnetic therapy,13 electrical stimulation,14 laser therapy,15 therapeutic ultrasound,16 topical negative pressure dressings17 and topical warming18 require further investigation. Due to the lack of evidence supporting these treatment modalities the application thereof would only be appropriate in the setting of a prospective randomised trial. The FDA has banned any research using ozone therapy due to its toxic potential in humans.

Future research
Research is currently focused on the role of superficial venous surgery and the use of cultured skin allografts. The level of compression needed to optimise healing should be explored. On a microvascular level, the wound healing process is thought to be directed by a variety of cell derived soluble factors, including cytokines (growth, regulatory, and chemotactic factors) and proteolytic enzymes (proteases); these will inevitably become future targets for specific treatments. In the South African setting we should determine the optimal cost-effective approach to treatment of patients with venous ulcers in our own environment. Ultimately, our focus should move from treating active ulcers to the prevention of ulceration by identifying at-risk populations. Prevention would undoubtedly be cheaper than cure and would also improve quality of life for patients with chronic venous hypertension at risk of ulceration.

References: