



## Review Article

## A review on grafting new ways in the management of chronic leg ulcers on an outpatient basis

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### Abstract

Chronic leg ulcer is a common condition leading to clinical concern. Accurate diagnosis and planning treatment are essential components of good management of wellbeing of the patient. Venous and arterial disorders comprise major aetiology of ulceration. Diabetes, hypertension, metabolic disorders, vasculitis and skin cancer are all uncommon causes of leg ulcers. Compression bandaging at a level adequate for their vascular state is beneficial to almost all individuals with ulcerated legs. This can be accomplished in patients with venous ulcers using a variety of bandaging techniques. Multilayer bandaging is a very cost-effective option especially if it is applied in community-based leg ulcer clinics. Oral medication treatment for venous and arterial disease has had unsatisfactory results. In ulcers that do not respond to compression therapy, local dressings are critical. The type of dressing chosen is decided by the type of ulcer and the patient's tolerance of the dressing. Few newer methods of dressing can be tried based of the affordability of the patient. A mention about methods such as PRP and split thickness skin grafting which can be done in OPD basis and are very effective options.

**Keywords:** Chronic ulcer, Venous ulcer, Neuropathic ulcer

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### 1. Introduction

Ulcer is defined as a wound caused due to break in the continuity of skin or mucosa with a slow healing tendency and heals by scarring.<sup>1</sup> Chronic leg ulcers are called so when there is a defect in the leg for a period of more than 6 weeks and shows no tendency to heal for a period of more than or equal to 3 months or not healed completely even after 12 months of time.

#### 1.1. Population dispersion pattern

There is increase in the incidence and prevalence with the increase in age. Prevalence of chronic leg ulcers is about 1.5 to 3/1000 people among adults which increases to 20/1000 people among elderly (more than 80 years of age). In about 10.5 per 1000 people, acute wounds were more common.

#### 1.2. Types

##### 1.2.1. Venous ulcer

It is commonly seen in chronic illness of the venous system. It most commonly presents with an irregular shape, mostly located on the gaiter area of the leg. Medial malleolus is most common location of these ulcers. Skin surrounding the ulcer can be eczematous, purpuric and hyperpigmented. Lipodermatosclerosis, ivory white coloured atrophic stellar scars may be seen, with surrounding telangiectasias (atrophie blanche) especially over the distal aspect of the leg. It is generally associated with varicosity. It is a painful condition which increases as the day passes and reduces with limb elevation.<sup>2</sup>

##### 1.2.2. Arterial ulcer

Arterial ulcers occur due to insufficient blood supply. Atherosclerotic disease and thromboembolism causing cutaneous infarction are the most common arterial causes of

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ulceration. It commonly presents with intermittent claudication. On elevating the limb, there is increase in the pain and in hanging position there is relief of symptoms.

### 1.2.3. Neuropathic ulcer

The most common causes are Hansen's, diabetes and alcoholic neuropathies. Symptoms appear prior to the establishment of the ulcer. Fissuring of the skin in plantar region as a consequence of thick and dry skin may be noted due to involvement of autonomic nerves. Decrease in sensations such as touch, pain, proprioception are commonly seen on involvement of motor nerves.

### 1.3. Other types

Diabetic ulcer, Martorell's hypertensive ulcer and Pressure ulcer

### 1.4. Management

Ideally patients with chronic leg ulcers should be managed by a coordinated approach. Primary goal is to determine the underlying pathophysiology behind the ulcer based on which appropriate treatment options can be provided to the patient.

It should include a detailed history, examination, investigations and various treatments options. Leg ulcers can be successfully managed by developing a treatment plan and sticking to it as the ulcer comes down in size.<sup>3</sup>

### 1.5. History taking

Thorough history taking and examination of the patient is the initial step to diagnose a leg ulcer. History includes general health condition, social and occupational background, past and present history of diseases. Current status of the skin, vessels, size and shape of the limb and status of the ulcer has to be considered. It's critical to figure out how long the ulcer has been there and whether it's a new or recurring occurrence. Patients' mobility should also be inquired about.

### 1.6. Examination

Examination of the legs has to be done for presence of symptoms of venous hypertension such as varicosity of veins. Peripheral pulses should be palpated. Range of movement of knee, hip and ankle should be evaluated to rule out peripheral neuropathy. Sensations should be tested.

The number, location, size, floor, base and skin in the surrounding area has to be examined during the ulcer inspection. Tenderness, oedema, warmth, erythema, hardening, darkening, dryness and scarring, cyanosis and capillary refill time should all be checked in the skin surrounding the ulcer.<sup>3</sup>

### 1.7. Investigations

1. Routine investigations: complete blood picture, blood sugars, lipid profile, renal function analysis and liver function analysis
2. Imaging studies: X-ray, CT and MRI of the foot.
3. The Ankle Brachial Index (ABI):
- 4.

Assessed in cases with coexistence of arterial diseases such as decreased or absence of peripheral pulses. It is calculated by measurement of pressure at ankle in dorsalis pedis or posterior tibial artery and pressure at brachial artery with the help of doppler.

ABI<0.8 indicates arterial insufficiency

0.5–0.8 indicates moderate arterial insufficiency

ABI≤0.5 indicated referral to vascular surgeon

1. Duplex venous mapping: It is a non-invasive test for assessment of superficial, deep and perforating venous system<sup>4</sup>
2. Ulcer biopsy to rule out malignancy
3. Bacterial swabs if signs of infection are present

## 2. Treatment

### 2.1. Venous Ulcers

1. General measures
  - a. Lifestyle modification
  - b. Exercise of calf muscles to improve haemodynamics.<sup>5</sup>
  - c. Legs should be kept raised while sitting, with the legs propped up on a cushion or pillow to keep the legs above the heart. This is necessary to keep blood flowing out of the leg and avoid pooling.
2. Ulcer management
  - a. Cleaning and debridement: According to NICE guidelines for surgical site infections, "necrotic debris or slough within a wound margin acts as a medium for bacterial development and should therefore be eliminated by debridement."<sup>6</sup>
  - b. Dressings: Different types of dressings were studied for its effectivity in healing the wound. In 42 trials, non-adherent dressings were compared against hydrocolloid dressings (792 patients), alginate dressings (60 patients), foams (42 patients) and hydrogels (151 patients). There was no evidence to support that one dressing type was better than another when used under sufficient multilayer bandaging.<sup>7</sup> Venous ulcers of the leg are better healed when simple non-adherent dressings are used.

### 2.2. Types of dressings

1. Traditional and cheap: Honey, Gauze, Plaster, Films
2. Newer and expensive: Hydrogels, Hydrocolloids, Alginates, Foams, Silver, Collagen
  - a. *Honey*: Mechanism of action of honey in the healing of ulcer is by rehydration of wound bed, promoting autolytic debridement and antimicrobial action. The drawback of this type of dressing is that it causes

- drawing type of pain due to osmotic effect. These are available in the name of Veeba Honey mustard dressing, Hellmann's Honey and mustard dressing.
- b. *Alginates*: Alginate is biocompatible, non-toxic, and has good mucoadhesive qualities. The inability of alginate-based polymers to undergo efficient and quick enzymatic breakdown in mammals is their principal limitation. Alginates are also extremely hydrophilic, which makes it difficult for them to interact with skin proteins. Calcium alginate-based dressings are known for their ability to absorb wound exudates efficiently, allowing for easier debridement and faster wound healing. It is available as Algisite M, Sorbsan, Seasorb in the market.
  - c. *Foams*: Foam-type dressings have been created as a substitute for hydrocolloid-type dressings in wounds with a moderate to high draining rate.<sup>8</sup> They are extremely absorbent, protective and conformable to the surfaces of the body. They're also simple to work with and may be tailored to the size of the wound. These dressings can be placed on the wound for a period of one week due to their absorbency and protecting properties. These are available by the name of 3M Tegaderm silicon foam dressing, Aquacel foam dressing and so on.
  - d. *Hydrocolloids*: The fluids in the wound are absorbed when these dressings come in touch with wound exudate.<sup>9</sup> They are semi-permeable to oxygen and water as well. However, there may be increase in chance of infection of the wound and amplification of necrotic tissue autolysis when hydrocolloid dressings are used and hence they are avoided in severely infected wounds. These are available in the market as 3M Tegaderm HP pad, Hydrocolloids Hydrofiber aquacel Ag dressing.
  - e. *Hydrogels*: These systems are made up of one or mixture of hydrated polymers in the form of a gel that hold at least 20% of their weight in retained water and are mostly employed to keep wounds wet. These materials are commonly referred to as superabsorbents if the proportion of water exceeds 95%. Hydrogels, like hydrocolloid dressings, can promote autolytic debridement of necrotic tissues and are often better at drying wounds with little exudates.<sup>10</sup> They cannot be used in wounds with excessive exudate as it might promote wound maceration.<sup>11</sup> It is available as Amerigel dressing, Plurogel dressing.
  - f. *Iodine*: It has a antimicrobial property, indicated in low to high exudating wounds. It can be used in wounds which are critically infected or wounds showing clinical signs of infection. These are called by the name Iodosorb cadexomer dressings in the market.
  - g. *Activated charcoal*: Its main function is odour absorption. Its use is mainly in malodorous wounds. It is avoided on necrotic tissues. These dressings are available in the market as Actisorb Charcoal dressing.
  - h. *Silver*: Its antimicrobial property is the reason for its use in ulcer management, It is preferred in critically colonised wounds and those which show signs of infection clinically. Its absorption is increased on combined it with foam and alginates. In some cases it can cause discolouration of the wound. It is contraindicated in patients with known sensitivity. It is by the name of Medline Silvasorb gel, Aquacel Ag in the market.
  - i. *Films*: These wound dressings are commonly used because they are transparent, resilient, conformable, easy to handle, adhesive, affordable, semi-permeable to oxygen and water vapour, and often resistant to liquid and bacterial contamination.<sup>9</sup> Film-type dressings have one major drawback: they should only be used for wounds with modest exudates, such as protective dressings in superficial pressure wounds. It can be left for 4–5 days before being replaced.<sup>11</sup> It is available as 3M Tegaderm film dressing, Cardinal health film dressing.
  - j. *Collagen*: Collagen is the most abundant protein in the extracellular matrix found in human tissues (e.g. skin, bone, cartilage, tendon and ligaments). It provides tissue matrices with strength and integrity, accounting for 25% of total protein body content. Collagens are biocompatible and have a high mechanical strength. Collagen's low inflammatory and cytotoxic reactions, as well as its biodegradability, are all appealing features.<sup>12</sup> As a result, and because collagen is a key component of human ECMs, it is frequently regarded as an ideal biomaterial for tissue engineering and wound dressing.<sup>13</sup> This is available as Hycol hydrolyzed collagen gel dressing and even powder dressings are available.

### 2.3. PRP dressings

#### 2.3.1. Principle

PRP is a concentrated plasma generated from centrifuged autologous blood that contains platelets, cytokines, and growth factors. Platelets initiate wound healing by secreting locally active growth factors that attract and encourage the division of undifferentiated cells at the damage site. By blocking cytokine release at the injury site, PRP may also help to reduce inflammation.

#### 2.3.2. Procedure

The double centrifuge system is a technique for making Platelet-Rich Plasma (PRP) that involves spinning entire blood twice to maximise platelet concentration. A PRP tube

or vacutainer containing anticoagulant is used for the 1st spin. The red blood cells are separated from the plasma, which contains the platelets, in the first spin. The cellular components in the plasma are concentrated much more in the second spin. (**Figure 1**) The appropriate concentration of platelets and growth factors is attained using a double centrifuge process.

In a study necrotic and diseased tissue was removed by debriding the ulcer initially. This is followed by extensive cleaning of ulcer with betadine solution. 2–3 mL of PRP was aliquoted from the 6 mL produced PRP solution for gel formation based on the wound size and area, while the remaining 3–4 mL was injected subcutaneously inside and around the periphery of the ulcer. On day 3 after therapy, the dressing was changed. Irrigation of wound with normal saline was done and infection was evaluated. After then, every week the dressing was changed and monitoring of patient was done for 24 weeks after therapy. All of the patients who were treated saw a considerable reduction in wound size.<sup>5</sup>

#### 2.4. PRF dressings

PRF, an autologous fibrin substance rich in platelets and leucocytes, is a significant development in regenerative medicine.

##### 2.4.1. Principle

One of the more recent techniques is platelet-rich fibrin (PRF), which has vascular endothelial GF, fibroblast growth factor (GF), platelet-derived GF and angiopoietin that promotes wound healing. It creates a well-organized network where platelets and leucocytes are concentrated, which causes a prolonged release of several growth factors (GFs) and promotes wound healing.<sup>14</sup>

##### 2.4.2. Uses

It has been discovered that platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) are effective in treating diabetic foot ulcers, venous leg ulcers, scleroderma-related chronic ulcers and neuropathic ulcers. Recently, PRP and PRF have become more widely used to treat leprosy trophic ulcers.<sup>15</sup>

##### 2.4.3. Procedure

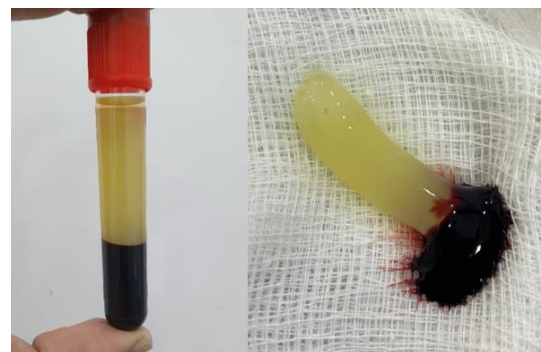
Following consent, 10 ml of the patient's own blood is collected into the vacutainer without the use of any anticoagulants, and it is then instantly centrifuged for 15 minutes at a speed of 3000 rpm to avoid blood coagulation. After 15 minutes, a fibrin gel forms in the centre of the vacutainer, sandwiched between the acellular plasma above and the red blood cells (RBCs) at the bottom. (**Figure 2**) After removing the adhering RBCs, the PRF obtained needs to be extracted with the aid of toothed forceps and applied to the ulcer. On average, 2.5 ml of clot are produced from 10 ml of whole blood.<sup>14</sup>

1. Topical antimicrobials and antiseptics: Use of topical antiseptics and antimicrobials for a long time is not recommended.
2. Skin grafting

It is a procedure in which a shaved piece of skin of varying thickness that is moved to a distant site and establishes a new blood supply once applied. Normal blade can be used to shave the skin. Transfer to a well-debrided, vascularized, and non-infected bed is required for graft 'take.' STSG (split-thickness skin grafting) is a procedure for covering and repairing regions of skin loss or defect. Large but not too deep skin ulcers, diabetic or traumatic wounds, and burns are all typical uses for it. STSG transplants the epidermis and some dermis from one place of the body to another. The donor site is the location where the normal skin will be removed like thighs, inner aspect of forearm, lower part of leg and upper arm. This can be done on a OPD basis and is a cost effective option. One such ulcer treated with Skin grafting is illustrated in **Figure 3**.



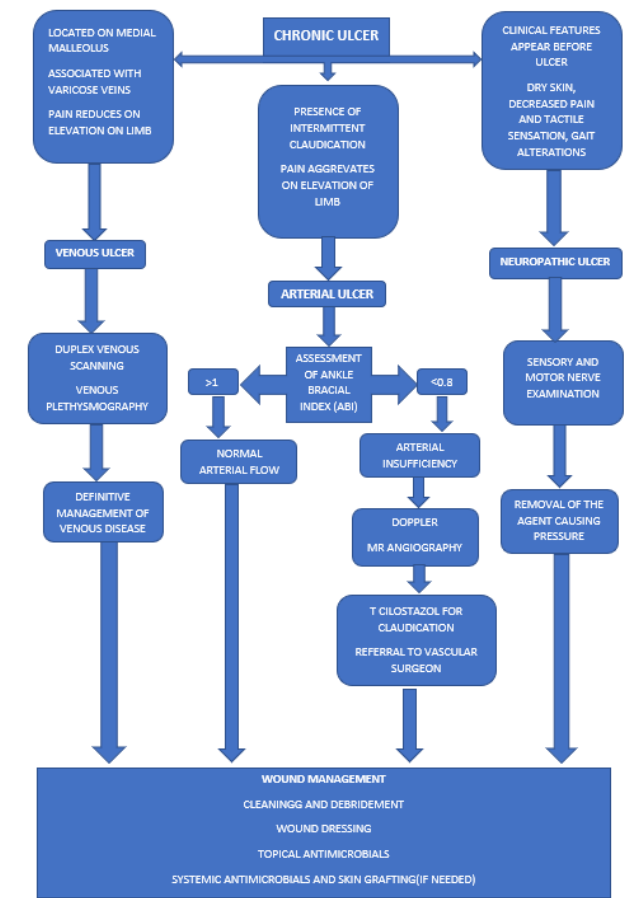
**Figure 1:** Shows platelet rich plasma obtained after performing double spin centrifugation



**Figure 2:** Shows platelet rich fibrin obtained after performing centrifugation



**Figure 3:** Shows progressive healing of chronic leg ulcer post skin grafting



**Figure 4:** Management of chronic leg ulcers

2.5. Management of surrounding skin

General skin care around an ulcer is required to maintain integrity of the skin and prevent the incidence of recurring ulcers. To prevent maceration of surrounding skin, it should be treated with a bland emollient on a regular basis. There are latex-free compression bandages and stockings available which are used on a regular basis.

Main aim of compression therapy is to improve venous return while lowering venous hypertension. In a Cochrane evaluation evaluating the role of compression in the healing of venous leg ulcers, seven RCTs comparing compression versus no compression were found.<sup>16</sup> In four studies, compression therapy was compared to routine treatment by the general practitioner in specialist leg ulcer community

clinics. When compared to no compression, they all discovered that compression improved ulcer healing rates.

High pressure compression can harm the skin, especially in patients with a weakened vascular supply. Compression should be used in patients with an ABPI of less than 0.8 only under the supervision of a physician. Patients have identified pain, discomfort, and a lack of valid lifestyle guidance as the main culprit for non-compliance. Patients assigned to class 3 stockings had higher patient-reported compliance than those assigned to short stretch compression bandages, according to a systematic study.

2.6. Systemic therapy

2.6.1. Antibiotics

It helps in control of infection in the ulcer. It is used only if there is evidence of clinical infection.

2.6.2. Pentoxifylline

It is supposed to enhance blood flow of microcirculatory system, while the exact action by which it acts is unknown. In a systematic review, 11 randomised controlled trials (RCTs) comparing pentoxifylline to placebo or no treatment were discovered. Pentoxifylline (400 mg thrice daily) improved venous leg ulcer healing rates by 21% when used as an adjuvant to compression (RR 1.56, 95 percent CI 1.14 to 2.13), and by 23% when used alone when compression was not possible. The use of pentoxifylline to treat venous leg ulcers is an unapproved indication. Venous ulcers treatment with pentoxifylline at the dose of 400 mg thrice daily for six months duration should be considered.

2.6.3. Analgesics

Leg ulcers due to arterial cause or when associated with cellulitis or ulcers which are infected deeply are sometimes painful, necessitating the use of strong painkillers.

2.7. Arterial ulcers

Reduction of risk factors, which include quitting smoking, lowering blood lipids, and managing diabetes and hypertension with antiplatelet medication.

Cilostazol has a vasodilatory effect and hence used to treat intermittent claudication caused by peripheral vascular disease in its early stages. The recommended dosage is 100 mg two times a day, orally. It is generally well accepted; nevertheless, headache, diarrhoea, and palpitations are common side effects.<sup>2</sup>

2.8. Neuropathic ulcers

Prevention should be the first step in treatment. This comprises daily foot inspections, digit cleaning and drying, lubrication, massage of the foot, straight nail cutting, avoid to walk barefoot, removal of callus, and assessment of pulses and the presence of foot abnormalities. In patients who

already have neuropathy, a multidisciplinary approach is required. In order to eliminate pressure points, doctors should advocate wearing shoes made of pleasant fabrics and of larger size.

The calluses are removed by removing this "natural" pressure point from both the centre and the periphery of the ulcer, which is already open, as the initial step in treating the NU. Debridement products (collagenases and fibrinases) are utilised if there is still devitalized tissue following this process. Although NU are usually painless, there may be neuropathic pain in patients with chronic decompensated diabetes mellitus and leprosy with recurrent reactionary neuritis, especially following treatment. Amitriptyline at 25 to 75 mg/day or nortriptyline at 25 to 150 mg/day are utilised as first-line therapeutic alternatives for these patients. **Figure 4** depicts the approach to leg ulcers.<sup>17</sup>

### 3. Conclusion

This article discusses about various types of chronic leg ulcers. Emphasis is laid on aetiology, clinical features and diagnostic techniques in various types of ulcers. Skin grafting, PRP and PRF dressings are effortless and cost effective yet very useful procedures in the management of chronic ulcers. Managing ulcers by these simple methods brings a vast improvement in improving the quality of life of the affected individuals. Finally, it highlights the diverse options in the management of chronic leg ulcers on the outpatient basis.

### 4. Conflicts of Interest

None.

### 5. Source of Funding

None.

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