Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i3.5097

HYPERBARIC OXYGEN THERAPY IN CHRONIC ULCER MANAGEMENT

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Abstract:
Objective: This review explores the evolving landscape of therapeutic interventions for chronic ulcers, emphasizing the importance of understanding etiology and optimizing patient outcomes in dermatological therapy.
Background: Chronic ulcers present a significant challenge in dermatological therapy, necessitating a comprehensive understanding of their etiology for effective treatment. While addressing underlying pathology is crucial, local therapy, exceptionally moist wound healing, plays a pivotal role in managing these wounds.
Scope: Current treatment strategies prioritize moist wound healing and encompass various modalities to promote tissue repair and mitigate complications. This review explores established practices such as cleaning, debridement, infection control, and emerging techniques, including biological skin substitutes, growth factors, laser therapy, hyperbaric oxygenation, electrical stimulation, and negative pressure dressings.
Critical Interventions: The review highlights traditional and novel approaches to managing chronic ulcers, providing insights into optimizing patient outcomes and advancing dermatological condition management.
Significance: Understanding the evolving landscape of therapeutic interventions for chronic ulcers is essential for dermatologists, healthcare professionals, and researchers. This review aims to provide valuable insights for optimizing patient care and improving treatment outcomes by examining established and emerging techniques.

Keywords: Chronic ulcers, Dressings, Compression treatments, Biological skin substitutes.

Introduction

As we have already mentioned, an ulcer is a loss of substance that affects the entire skin structure, with erosion and ex-ulceration corresponding to more superficial attacks. Classically, the term "wound" is used to denote ulcers of exogenous cause, generally traumatic, and "ulcer" for those of endogenous cause, but the truth is that they are used interchangeably. Therefore, the term ulcer is purely descriptive and must always be accompanied by its etiological cause: vascular, post-phlebitis, diabetic, pressure, etc. In this work, we will not go into the diagnosis of ulcers, but we will directly address their treatment. Still, there is no doubt that establishing the etiology and the correct diagnosis is an absolute priority. Years ago, we discussed the diagnosis of "leg ulcers" in a monograph that may still be useful for the uninitiated. Skin ulcers can be acute or chronic. The former are generally traumatic and are usually repaired by surgical techniques or granulation by secondary intention. However, chronic ones suffer from a phenomenon of stagnation in their healing mechanisms that makes them incapable of completing it. In them, external manipulation using various techniques is essential to bring the repair to a successful conclusion. We will mention these types of techniques (Carter, DaVanzo, et al., 2023).

Transcendence of The Problem

There is no doubt that chronic ulcers represent a significant problem if one considers their incidence, the deterioration they produce in patients' quality of life, and their economic impact. The prevalence of ulcers of vascular origin in the United States is between 600,000 and 1,500,000.[2]. Every year, 3% of people with diabetes develop foot ulcers, and between 15 and 20% do so throughout their lives; of them, 90% end up requiring limb amputation[3,4]. Different studies carried out on the quality of life in patients with chronic ulcers have shown a significant deterioration based fundamentally on the pain of the injuries, loss of time necessary for their care, and impact on their physical, work, and social activity. [5] The economic impact of chronic ulcers is significant, not only due to healthcare costs but also due to the loss of working hours. Recently, Eisenbud et al. [6] estimated that in the United States, it represents a cost of 5 billion dollars per year (Carter, Frykberg et al. 2023).

REPAIR MECHANISM OF THE WOUNDS

As soon as the loss of substance occurs, a series of complex mechanisms are set in motion, only partially known and which can be synthesized in three phases.[7,8]: inflammatory, proliferative, and longer lasting. The first phase, which lasts approximately 72 hours, aims to plug the wound (clot formation) and clean it; platelets and different inflammatory cells, mainly granulocytes and macrophages, participate in it. Also, during this stage, a series of soluble mediators are released that initiate the healing process. The proliferative stage has the increase in collagen and angiogenesis to constitute granulation tissue as its fundamental mission. At this stage, the participation of endothelial cells is of great importance. The maturation stage can last years and is fundamentally based on collagen production and subsequent destruction. In all these stages, there is a participation of keratinocytes that tend to migrate both from the edges and the epithelial remains of the wound through multiplication and maturation systems (Chen, Yu et al., 2023).

In chronic ulcers, there are alterations in healing mechanisms. Thus, in studies using exudate from these lesions, the levels of metalloproteinases, which determine an increase in proteolytic activity and inactivation of the growth factors necessary for healing, have been shown. Collagen is the main component of the dermis and some extracutaneous structures such as tendons, bones, or ligaments. The production of collage is optional in creating the new scar. Unfortunately, the skin does not recover elasticity in this process, usually reaching 70 or 80% of its original situation. The balance between the synthesis and degradation of this dermal protein is essential in the scar's characteristics. In diabetic patients, collagen synthesis is altered, which has an impact on healing mechanisms. In the inflammatory phase, there is a tremendous cellular activity of resident cells (epithelial cells, fibroblasts, dendritic cells), as well as the production of different mediators that attract platelets,

neutrophils, lymphocytes and macrophages to the wound area, and They favor the phenomena of angiogenesis and the production, ultimately, of granulation tissue.

Many factors are released within the ulcer, but we will only comment on those that may be of interest from the point of view of their therapeutic application:

Growth factors such as platelet-derived growth factor (PDGF-B), essential fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), and nitric oxide (NO) are found in the exudate from ulcers and are responsible for promoting chemotaxis, migration, stimulation, and cell proliferation.

Recombinant growth factor-BB derived from human platelets (PDGF-B) or becaplermin (PDGF) is the only growth factor accepted by the Food and Drug Administration (FDA) for the treatment of diabetic ulcers of the feet. It has been established that PDGF is in low concentration in the exudate of chronic ulcers, and it has been shown that its topical application provides a favorable effect on their healing. PDGF is a potent mitogen and chemotactic agent that increases vascularisation and endothelial proliferation.[9].

bFGF is one of the most essential factors in the inflammatory phase of healing since it is a potent mitogen that acts on many cells and, therefore, has a proven role in migration, cell proliferation, and glial endothelium[10]. The topical application of bFGF has demonstrated a favorable action on forming granulation tissue and epithelial regeneration in burns. Still, its efficacy on diabetic ulcers is not superior to placebo. [11]. Possibly, the failure of this monotherapy lies in the need to use more than one growth factor.

VEGF determines endothelial cell proliferation and migration in the wound repair process. It is secreted in different cells: keratinous cells, macrophages, fibroblasts, and endothelial cells, a secretion that usually takes place in a hypoxic environment. This secretion reaches its highest concentrations on day seven and is the fundamental stimulus for angiogenesis.

NO is an essential factor in fibroblast proliferation and collagen production. It is secreted by the fibroblasts themselves and fibroblasts and macrophages.

Vascular ulcers, especially venous ulcers, are due to the appearance of venous hypertension that leads to valvular insufficiency and, therefore, to passive vasodilation of the veins with slowing of circulation. This explains why compression cures are the most appropriate treatment for this process. The demonstration of fibrin cuffs around the vessels results in a decrease in transcutaneous oxygen. Be that as it may, the resulting tissue ischemia favors the trapping of leukocytes and the release of proteolytic substances that induce skin changes (ulceration and the well-known changes of stasis dermatitis).1.

TYPES OF HEALING

Classically, two types of healing are established that correlate with the size of the defect and are reciprocal with the healing time and the quality of the resulting repair. The healing by *first intention* is performed in wounds with an approximation of the edges, either because they are small or because this proximity is achieved surgically. Healing is obtained quickly, and the aesthetic and functional results are promising. This type of healing usually occurs in minor wounds with clean edges and without necrotic remains. On the contrary, the second healing intention is performed on large wounds with rough edges that are generally contaminated. Healing is a slow, long, and complex process. The aesthetic and functional result could be better since the epithelial coating is usually fragile and very different from its original appearance. Pressure ulcers and vascular ulcers are the ones that typically carry out this type of healing. Healing by first intention requires little medical intervention. However, sluggish or chronic ulcers are favored by correct manipulation, which will be discussed in the present work (Cui, Zhang, et al., 2023).

RELATED FACTORS WITH THE HEALING PROCESS FROM A WOUND

Wound healing is a long, complex, and dynamic process that many factors can influence, some known and others not. Even those labeled as known are not completely consensual or supported by scientific

evidence studies. It is essential to know them since it is in our hands, in most cases, to correct them. We will review the most notable ones[12]. (Li, Xing et al. 2023)

General situation of the patient

Usually, a well-nourished, healthy, young patient is more likely to achieve adequate healing.

nutritional status

All nutritional deficiencies delay the healing of ulcers. Still, states of hypoproteinemia and hypovitaminosis are incredibly influential, especially A, C, and K. Alcoholism is also a risk factor for suffering from chronic ulcers.

Age

Older people have a lower capacity for cell proliferation, neovascularisation, and collagen genesis, so their capacity for tissue repair is diminished.

Coagulopathy

Protein C and S deficiencies and coagulation disorders, in general, are obstacles to healing.

endocrine processes

Of all these signs, the increase in pain and re

Obesity, diabetes, pituitary and adrenal disorders alter the intimate mechanisms of wound healing.

Neuropathies

The presence of ulcers in neurological patients, both central and peripheral, is well known.

Drugs

Some drugs such as steroids, cyclosporin, colchicine, and some antiseptics, paradoxically widely used in the treatment of wounds, can be toxic to macrophages and inhibit neovascularisation and collagen synthesis, thereby delaying healing...

Local factors

Humidity

The humid environment is the most suitable, as we will later comment, for the healing of wounds [13] since it favors cell conservation and migration, which is not achieved in a dry environment.

oxygen tension

Hypoxia promotes wound healing[14,15], which determines that a closed cure is more valuable than an open one. This aspect is controversial since some authors use hyperbaric chambers to treat wounds, especially arterial ones.

pH titular

The acidity benefits healing[15] since it represents an excellent barrier against bacterial invasion. Consequently, one of the most common maneuvers on wounds, washing with homemade and, therefore, alkaline soap, is detrimental to the healing process.

Infections

The presence of germs in wounds is a controversial topic. There is no doubt that wounds, especially chronic ones, are colonized by germs, and it is not always easy to decide whether this presence results from colonization or infection. Many authors consider as a sign of infection the presence of classic clinical signs such as erythema, edema, heat, purulent exudate, and pain, to which have been added delayed healing, discoloration or friability of the granulation tissue, formation of pockets in the basis of the ulcer and unpleasant odor[16].delay in healing are the most reliable[17]. To be evaluable, the culture should not be taken, as usual, by brushing, but rather through needle aspiration or biopsy, considering

the presence of infection when more than 10^5 bacteria/g[18,19]. Another critical problem is using antibiotics to treat chronic ulcers, which usually leads to bacterial resistance (Saboia-Dantas, Dechichi, et al., 2023).

On the other hand, using local antiseptics is not only not helpful but counterproductive. As can easily be deduced, using topical antibiotics prophylactically is useless and is a risk factor for developing resistance. Therefore, when suspecting a bacterial infection, we should act according to what is listed in Table 1 (Wang, Zhang et al., 2023).

Others

The complexity of the wound itself, inadequate cures, etc.

GENERAL CONCEPTS ABOUT THE TREATMENT OF CHRONIC ULCERS

Classically, two healing systems have been established for chronic ulcers: traditional healing or dry healing, based on the use of antiseptics and "leaving the wound in the open air," and healing in a humid environment or moist healing, which proposes the use of products that generate a humid environment in the wound bed, control exudate and stimulate more physiological healing. Most experts believe this last method is the most appropriate and should replace the first (Carter, DaVanzo, et al., 2023)

The treatment of chronic ulcers has a double aspect: that of the underlying disease and local treatment. Etiological treatment is necessary, but it will not always solve the presence of chronic ulcers since these frequently appear as a consequence of an irreversible vascular injury, such as diabetic ulcers. Cleaning wounds is an essential step in wound care. It is not a purely mechanical act, but its success or failure will depend on its correct execution. The American Agency for Health Care Policy and Research (AHCPR) dictates standards for cleaning pressure ulcers that can be extended to the rest of chronic ulcers (Table 2). The use of antiseptics is a controversial issue since, as mentioned previously, their use can be harmful. However, some molecules such as iodine ca dexomer have proven useful and even toxic, so their use in chronic ulcers is not contraindicated[22]. We consider the use of antiseptics inappropriate given their known toxicity and aggressiveness on monocytes, fibroblasts, granulocytes, and granulation tissue, and instead, the use of physiological saline that must be applied with a certain pressure is recommended. In this sense, the GNEAUPP (www.gneaupp.org) suggests that the most appropriate vacuum pressure is that of gravity itself or using a 35 ml syringe with a 0.9 mm needle with a pressure achieved. 2 kg/cm^2. The safety pressure for washing ulcers ranges between 1 and 4 kg/cm^2.

Debridement is necessary if debris, slough, or necrotic remains are a breeding ground for the development of bacteria and trigger a phagocytic response detrimental to wound healing. It can be done using larvae by mechanical, enzymatic, chemical, surgical, or surgical methods. Although this step is widely accepted and practiced, studies have yet to demonstrate its effectiveness23 (Chen, Yu et al., 2023).

Exudate control is essential since, although a humid environment in the wound is advisable, it should not be excessive, as it could cause maceration of the edges and even the granulation tissue. This excessive exudate can also be a sign of infection. Today, different types of dressings on the market help control ulcer exudation. Infection control has already been discussed. Maintaining a moist and aseptic environment is advisable during the healing and re-epithelialization phases, favoring faster repair. It is also advisable to use dressings that allow the treatments to be spaced out since, in this way, damage to the newly formed tissues will be avoided.

WET CURE

As mentioned, maintaining a humid environment inside the ulcer favors angiogenesis, cell migration, granulation, and epithelialization (Table 3). Therefore, it seems reasonable to replace the classic dry cure of leaving the lesions in the air and covering them with absorbent dressings, of which many are on the market without significant differences being established between them.[12].

Dressings are essential in carrying out a wet cure. There are many of them on the market, and their main drawback lies in their high price. However, they have another series of virtues that make their use advisable and do not necessarily make the treatment of chronic ulcers more expensive. Does not exist

MANAGEMENT OF A CHRONIC ULCER WITH SUSPECTED INFECTION

1. If there is clinical suspicion of infection (foul dour, abundant or purulent exudation, abnormal granulation tissue, pain, arrest of the healing phenomenon, etc.), proceed to culture/antibiogram by taking it with aspiration or biopsy.
2. The isolation of various germs does not necessarily indicate infection, nor does it interfere with wound healing, only isolating more than 10^5 colonies/g is the index of infection and indication for treatment with systemic antibiotics
3. Topically, we must consider the use of antibiotic therapy for ulcers that do not evolve adequately with the correct topical treatment: – Choose an effective antibiotic against gram-negative, gram-positive, and anaerobic (e.g., argent sulfadiazine)

– Do not use dressings that do not allow gas exchange. Today, there are dressings available that They generally contain silver or activated carbon, with bactericidal capacity.

– No study has demonstrated the usefulness of local antiseptics in local infections; on the contrary, the use of them (povidone-iodine, sodium hypochlorite, hydrogen peroxide, acetic acid) is toxic for many of the cellular elements involved in the mechanisms.

Healing

TABLE a.AHCPR RECOMMENDATIONS FOR CLEANING ULCERS
Cleaning should be the first act in wound treatment and done constantly at each dressing change. It should be done gently, exerting the most minor mechanical force possible to allow the automatic removal of necrotic remains without causing trauma to the wound bed.
Do not use antiseptics such as iodinated derivatives, sodium hypochlorite, hydrogen peroxide, and acetic acid.
Use an isotonic saline solution.

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TABLE 3. ADVANTAGES OF WET CURE
Increased supply of oxygen and nutrients endogenously through angiogenesis
Medium acidification
Ease of cell migration
Exudate control
Maintain the appropriate temperature, stimulating fibrinolysis.
Pain reduction
Protection of wounds against infections Reduction of healing time
Decrease in local cures

An ideal dressing (Table 4), but the different types available will be discussed. Dressings can be classified into passive, active, and interactive. The lethargic dressing only has a protective function, while the others create an adequate environment, a microclimate that favors wound healing by favoring debridement, avoiding infections, and facilitating healing. We will try to synthesize the different types of dressings, paying particular attention to their indication (table 3).

Conventional (passive)

Gauze

They are the most used dressings. They are composed of cotton fibers, considered dry dressings with great absorbent capacity. They are inexpensive, and their main drawback is that they damage the granulation tissue during changes. This defect can be avoided by soaking the gauze in saline or paraffin solution.

Viscose

They are not very adherent; some are infused with silicone to reduce it further.

Specials (active and interactive)

Hydrocolloids

It is the first type of interactive dressing introduced on the market. Its elemental composition is carbohydrate.

TABLE 4. PROPERTIES OF THE IDEAL DRESSING
Create a humid environment.
Promote wound healing
Do not adhere to the wound.
Being able to renew itself without causing trauma or pain Ability to absorb excessive exudate Maintain gas exchange
Impermeability to microorganisms
Patient acceptability
Easy to use
Acceptable cost

Methylcellulose, to which other variable substances are added to increase its absorption and adhesion capacity. The polyurethane cover may be permeable to oxygen (semi-occlusive and occlusive, respectively). In contact with the exudate from the wound, they form a gel, which causes them to gradually lose permeability and effectiveness and even cause the wound's edges to deteriorate. They exist on the market in different presentations: plates of various sizes and thicknesses, paste to fill cavities, absorbent granules, and even in the form of ribbons known as "hydrofibers." They are indicated in pressure ulcers in the initial stages and not infected. They also act as autolytic dependants and promote granulation and healing of wounds since different studies have shown the presence of growth factors in the exudate that remains in contact with the ulcer.

Alginates

They are derived from natural algae *(Phaeophyceae)* and comprise polysaccharides that associate mannuronic and glucuronic acids with a base of calcium alginate. They are dressings with a high absorbent capacity, around 10 to 20 times their weight, and have a particular antibacterial action. Upon contact with an exudate containing sodium salts, calcium alginate, which is insoluble, is transformed into sodium alginate, which constitutes a hydrophilic gel that creates a humid and hot environment in the wound bed, providing optimal conditions for ideal for the healing process. They are sold as dressings of different sizes, tapes for cavities, and are associated with hydrocolloids in plate and liquid form. Its indications are exudative, bad-smelling, and even infected wounds, as well as if debridement is required.

Hydrogels

Water is its main component, up to 80%, to which starch-type polysaccharides, polyethylene oxide, or carboxymethylcellulose are added. They can also contain alginates. They fundamentally have absorption functions in the case of very exudative wounds or rehydration in the case of dry lesions. They are also effective in debriding wounds, so they are indicated for substance losses of these characteristics. They come in liquids, plates, granules, or an amorphous structure (water plus polysaccharides or carboxymethylcellulose plus alginates). They generally require a secondary dressing for fixation.

Polyurethanes
They are thin sheets of adhesive polyurethane, generally transparent and semi-occlusive, since they are permeable to gases but not to liquids and do not absorb exudate. They are flexible, so they adapt well to the wound and are washable, allowing them to be reused. They are indicated for superficial substance losses in the epithelialization phase, not exudative, and as prophylaxis in risk areas.

Polymeric foams
They are semipermeable dressings, impervious to liquids, and permeable to water vapor. Its main properties are the absorption of exudate, the maintenance of a humid environment, and the prevention of maceration. They do not break down with exudate and are flexible and, therefore, adaptable to different types of wounds. Depending on its composition, there are different types available:
1. Dressings with non-adherent acrylic internal layer, highly absorbent hydrophilic middle layer, and externally gas-permeable polyurethane.
2. Dressing with an internal layer of polyurethane foam or gel and externally with semipermeable gas polyurethane.
3. Dressings have a trilaminar structure, a micro-perforated polyurethane sheet internally, a hydro-cellular absorbent layer, and external polyurethane in the middle zone.
These dressings should not be used with oxidizing agents containing hypochlorite, ether, or hydrogen peroxide.

Silicones
They consist of a polyamide network covered in silicone. It comes in sheets of various sizes. The hydrophobic properties of silicone mean that it does not adhere in wet areas, that is, the wound, and it does in dry areas, that is, at the edges of the wound. This property is known as micro adhesion. They reduce the sensation of pain; they do not dissolve on contact with the exudate; as they do not adhere, they do not cause detachment of the epidermal cells with the
change of dressings. The sheet can remain in the wound for about five days. They are indicated in any wound in the granulation phase, painful lesions, and even in the fixation of grafts or repair of graft donor areas.

Charcoal dressings
Its base is activated carbon but can also contain silver, alginate, and hydrocolloids. They have excellent absorption capacity, especially for odors and microorganisms. They need better adherence. They are applied directly to the wound but require an additional fixation dressing. Logically, its indication is very exudative, smelly, and super-infected wounds.

silver dressings
They come with silver on carbon mesh, Hydro fiber, and silver polyethylene meshes covered with nanocrystalline silver or silver on a hydrocolloid base. Depending on their composition, they have different properties, and common characteristics are the antimicrobial or bactericidal effect and the control of exudate and foul odor. They are, therefore, indicated in wounds with slow evolution, whether or not there is suspicion of infection and the production of an unpleasant odor.

Collagen
They are dressings that produce an adequate environment and gradually dissolve in the ulcer. You only have to change them once they have entirely loosened.

Dextranomer
It is a three-dimensional network of dextran polymers in porous microspheres with excellent absorption capacity when coming into contact with exudate. They also absorb cellular and bacterial

debris present in the wound by capillarity. They also have a debriding capacity, eliminating necrotic tissue without damaging the living tissue.

The large number of products present on the market is evident. Each has its advantages and disadvantages that we have tried to comment on. Still, it seems appropriate to conclude this section by summarising some of the conclusions obtained in a study by Carlos III University, which aims to evaluate the effectiveness and the cost-effective relationship. The use of special dressings in the treatment of pressure ulcers and vascular ulcers, both venous and arterial[12]:

- Similar efficacy on the variables of healing or wound size reduction between specific dressings, social and conventional, except in the case of hydrocolloids in pressure ulcers.
- Absence of significant differences between the different types of special dressings.
- Although the cost of the material per treatment unit is higher in the case of special dressings, in general, there seems to be a decrease in indirect expenses reflected in less use of nursing time, which favors a better cost ratio -effectiveness.
- Need for further studies to validate or not these results.

COMPRESSION THERAPY

Compression therapy in venous ulcers, although old, is the most effective, cheap, and used treatment in the control of hypertension and venous insufficiency.[26,27]. The use of compressive therapy is not incompatible with the use of different types of dressings[28,] not even with surgical therapy[29]. In the opinion of most experts, compression therapy is the only effective treatment for chronic ulcers.

Bandage, in the case of venous ulcers, aims to reduce edema and improve venous return. To achieve this, it is advisable to combine exercise and leg elevation while resting. Compression therapy is comfortable for the patient since he can continue with his work, allowing for spaced cures and, therefore, reducing the treatment cost. It is also practical since it provides rapid granulation of the ulcer. Before applying it, arterial compromise must always be ruled out (Carter, DaVanzo et al., 2023).

The fundamental basis of compression therapy is the bandage. Before starting it, it is essential to check the existence of distal pulses. The bandage should be performed when the venous pressure on the walls of the blood vessels is as low as possible, which occurs when the patient is in the Trendelenburg position, which is undoubtedly the best position to perform it. It should not be used in patients sitting or with the leg in a decline. In the presence of edema, it is advisable to keep the patient in Trendelenburg until it decreases.[30]. All bandages must follow an ascending direction, starting at the base of the fingers and ending after exceeding the cleft space or reaching the groin.[31]. The turns of the bandage can be made in a circular way, the most advisable since they always maintain the same pressure, or in a herringbone, which creates an ascending turn and a descending one, so it does not meet the criterion of keeping the pressure following the same sense. The optimal pressure, which is also usually well tolerated by the patient, is 35-40 mmHg, equivalent to 5 layers of a standard 10 cm wide bandage. The pressure should progressively decrease as you ascend distally to maintain the leg's physiological pump (Wang, Zhang et al., 2023).

In compression therapy, the first thing is the treatment of the ulcer itself, using the cleaning and dressing methods already mentioned. Immediately, we proceed to the bandage, which can be done with different types of material:

Elastic stockings

It is a valuable and comfortable material, although the patient has to get used to it in many cases. Four types on the market are classified according to their compression capacity as light, moderate, firm, and extra vigorous, and their properties are summarised in Table 6. Generally, the more force, the more effective, but worse tolerance. For this reason, starting with light or moderate compression stockings and gradually increasing them is advisable. Likewise, full panty-type stockings provide more excellent protection than "tights" or socks. Like bandages, they provide more excellent compression at the ankle, 100%, which progressively decreases to the thigh, 50%, acting like the natural impulse exerted by the leg muscles. The stocking should be placed, like the bandage, after prolonged rest and when there is no edema; the best time is as soon as you get up, and it is advisable

to shower at night. In summer, they are uncomfortable, but this is also true when vascular insufficiency worsens, so it is advisable to continue using them, at least for a few hours. The useful life is about six months (Saboia-Dantas, Dechichi et al. 2023).

Sales

The therapeutic pressure achieved with the use of bandages depends on the characteristics of each one and, above all, on its composition and elastic capacity. Rubber or polyurethane bandages retain their elasticity for longer than those made of stretchy fabric, which are generally made of crepe that are difficult to adjust and progressively decrease their tension, making it necessary to change them frequently. The bandaging technique is critical, which we will not comment on and refer readers to various texts.[31]. However, we will consider some particular types, such as the Lin ton, Unna's boot, and Duke's boot (Li, Xing, et al. 2023).

Linton type bandage

It is a classic form of bandage that exerts pressure when standing and, to a lesser extent, when the patient is lying down. Before performing the bandage, Protecting the skin with an insulating cream such as water-based paste or Vaseline is advisable. The ulcerated area can be treated in the way that is considered most appropriate since this type of bandage is compatible with any local cure. The first layer of bandage should be made with cotton, and then an adhesive elastic bandage is applied in a circular shape. Once the bandage is finished, it is advisable to check the color of the fingers, both when the patient walks and when he is at rest, and to ask him if he feels too much pressure or tingling in the fingers. If so, it should be loosened until a good tolerance is found. The dressing change is weekly, although it can be carried out more frequently if the ulcer exudate requires it (Cui, Zhang et al., 2023).

Bota de Unna

It is also a classic system for treating skin ulcers but is no less valid. It positively affects venous hypertension during orthostatism but not during rest. The Unna boot results from the combination of a wet paste in contact with the wound and the external compression of the bandage itself. The paste used, although variable, can ideally be a water-based paste with which the entire bandage is impregnated, which must be adjusted perfectly but without excessively compressing. Once the first layer is placed, a bandage is made with zinc glue, resulting in moist internal and complex external parts. It is advisable to check the bandage after 24 hours to ensure no signs of ischemia. The patient should be informed to attend the consultation if they notice pain, tingling, or other striking subjective signs. The care of the bandage is like any canola; depending on the wound's exudation, it should be removed between 3 and 15 days (Chiu, Zimmer, and Chiu, 2023).

TREATMENT THROUGH THE USE OF SKIN GRAFTS

The surgical repair of vascular ulcers is undoubtedly a provocative idea, but it initially clashes with an obvious fact: the poor vascularisation of the area. The use of thin autologous grafts is, without a doubt, a valid option. Still, it provides delicate skin that can easily ulcerate again.[32]. Recently, there is an evident development of so-called biological skin substitutes (SBC)[33] which provide a wide therapeutic possibility to which dermatologists must, of course, adapt since it will be an undoubted help in the treatment of substance losses in which classic skin grafts cannot be used. SBCs, known as live skin equivalents, are commercially offered as autologous and allogeneic substitutes. The latter is obtained from genetic engineering and can be epidermal, dermal, or mixed (epidermal my and dermis). SBCs offer a series of advantages over traditional grafts: it is a non-invasive technique, it does not require anesthesia nor the patient's admission, and, of course, a donor area, thus avoiding the production of a new wound. It is, without a doubt, an expensive product, but the savings in indirect costs (with consultations and hospital expenses) can compensate for this (Chen, Yu et al., 2023).

Epidermal SBC

They are available as autografts and obtained from the patient's keratinocyte cultures. It has been available in the United States since 1988 as Epicel and can provide large amounts of tissue. It is used in the treatment of burns and leg ulcers. Its drawbacks lie in the delay in performing the treatment, the need for a prior biopsy and culture, and the quality of the skin obtained since it is thin and fragile. To avoid delay in treatment, cultures of allogeneic keratinocytes from neonatal foreskin skin have been made, which are cryopreserved until implantation (Carter, Frykberg, et al., 2023).

Dermal SBCs

They are allogeneic grafts and, therefore, immediately available. They positively affect epithelial migration, differentiation, and adequate granulation tissue production that allows grafts' subsequent use. Classically, cadaver skin has been used as a donor, which can be chemically treated to eradicate its antigenic components (Alloderma). Based on genetic engineering, a current alternative is dermal grafts made of bovine collagen and chondroitin-6-sulfate polymer with a coating of human keratinocytes or fibroblasts (In tegra). The FDA recently authorized a Derma graft for the treatment of diabetic ulcers. This product comprises cultured neonatal dermal fibroblasts *in vitro and* a bioabsorbable polyglactin mesh[34]. The exact operation mechanism of these substrates is not well known. Still, the studies carried out, especially on Derma graft, suggest that, although they do not survive inside the ulcer, they promote the release of a series of cytokines that stimulate healing (Carter, DaVanzo, et al. 2023)

Composite grafts

They consist of bilayers made up of epidermal and dermal components. The best-known group is Apligraft , which contains an external layer of allogeneic epidermal keratinocytes and an internal layer of human fibroblasts dispersed in a protein matrix; it does not have skin attachments. App graft It acts by producing cytokines and growth factors that accelerate the healing process. Cel It is another allogeneic SBC with a similar structure to Apligraft, made on a porous matrix of bovine collagen I, which is also indicated in vascular, diabetic ulcers, and epidermolysis bullosa[32]. Various studies have shown that using SBC on venous ulcers is well tolerated and produces excellent results. [35,36,] so it is a future technique that must be considered. Table 7 shows the products that currently exist in the American market (Wang, Zhang et al., 2023).

OTHER THERAPIES

Other therapeutic measures have been used in the treatment of chronic ulcers. They include the laser, electrical stimulation, negative pressure, and the hyperbaric chamber. There are also some more curious ones, among which honey or insect larvae can be considered, as well as the use of new medications.

The laser in chronic ulcers has been used as an adjuvant to other measures with mixed results. Attempts have been made to use helium-neon, diode, carbon dioxide, and KTP lasers. The wavelengths used have ranged between 590 and 950 nm. In the literature, there are references to complete closure of diabetic neuropathic ulcers in 4 weeks using a 670 nm diode laser.[37], along with others that do not find significant differences concerning other treatments. In a Cochrane Foundation publication from 2000[38,] No benefit is demonstrated in treatment with low laser intensities compared to other therapies or non-coherent light. Only one study, with a few cases, suggests that combining laser and infrared light can promote healing ulcers in the lower extremities. It helps reduce pain. Thus, the 904 nm diode laser has been used with good results since it produces an increase in the prostate gland in 12 or epoprostenol.[39]. In conclusion, it can be stated that, although the laser is indeed not effective as monotherapy, it is useful when used in a complementary manner with other treatment measures (Saboia-Dantas, Dechichi, et al. 2023).

Hyperbaric oxygen therapy (HBO) is "physical therapy based on obtaining high partial pressures of oxygen, inside a hyperbaric chamber, in which a pressure higher than atmospheric is reached." [40]. Numerous experimental and clinical studies demonstrate that hyperbaric oxygen therapy increases the

partial pressure of oxygen (PO).2) in hypoxic and infected tissue, reaching levels greater than 30-40 mmHg (Li, Xing, et al. 2023).

Tissues improve healing, angiogenesis, fibroblast activity, and collagen synthesis**.** It also enhances the antimicrobial defense of the host, with the more excellent phagocytic activity of leukocytes, inhibition of the growth of anaerobic bacteria, and the effect of some antibiotics. It is, therefore, a valid therapeutic option. The administration of high-pressure oxygen can be done locally using small pressurized chambers specifically designed to insert an extremity. Although they have the advantage of low cost and excellent manageability, they should be considered something other than HBO since their supposed benefits are not based on the physiological effects of breathing oxygen at high pressures. The usefulness of this system is controversial since while some authors have reported good results in diabetic foot, its use in combination with other therapies makes it challenging to know your real benefit[41]. On the contrary, randomized studies show that not only are they not beneficial, but they can reduce the release of oxygen in the affected limb (Cui, Zhang, et al., 2023).

Electrical stimulation has been recommended for the treatment of chronic pressure ulcers. However, its real value in other types of ulcers has yet to be definitively established. Gardner et al.[43], through a meta-analysis, verified that said stimulation produces a substantial improvement in ulcers, especially in pressure ulcers, without significant differences between the different machinery used. Recently, in 2003, Houghton et al. [44] Showed that applying this therapy three times a week reduces the size and healing time of chronic leg ulcers. Therefore, this therapeutic modality should be considered another weapon in our treatment arsenal for this disease. Topical treatment of chronic negative pressure ulcers has been available since the late 1990s. This technique can accelerate granulation tissue formation, decrease edema size, increase blood flow, and accelerate healing. It is instrumental in reducing the length and depth of ulcers.[45,46]. Harmful pressure devices (suction cups) consist of glass, metal, or rubber applicators or suction cups in the form of caps of different diameters depending on the treatment area, in the upper part of which the aspiration-compression tube is connected. It joins the vacuum-producing mechanism. Due to the risk of dissemination, its use is contraindicated in recent thrombophlebitis and phlebothrombosis, circulatory disorders of cancerous origin, and acute infections (Chiu, Zimmer, and Chiu, 2023).

Honey has been used to treat ulcers for over 2,000 years based on its antibacterial capacity. Recently, with the resurgence of natural medicine, the trend is awakening again to revive the use of medicinal honey (honey on sterile dressings) in treating chronic ulcers. Various studies demonstrate its acceptability by the patient[47,48] and shortening epithelialization time[48], as well as antibacterial capacity even against methicillin-resistant germs (MARSA) (Chen, Yu et al. 2023)

Insect larvae (biosurgery) are another alternative, despite the undoubted social rejection it can entail. It is a unique debridement technique that must be taken into account. Different types of larvae are applied to the wounds, but the Lucilita laughs. It is the most used to debride the wound. Its effects are quick and effective, and it has no side effects, except possibly the psychological ones of knowing that one finds maggots in one's wounds. Its contraindication is the presence of gangrene areas.[51]. The mechanism of action is not well established; Prete demonstrates that the digestive juices secreted by these larvae have a favorable effect on fibroblasts and stimulate the production of EGF and interleukin-.[5 (Carter, Frykberg et al. 2023)2].

Some antiepileptics, such as phenytoin[53] and the pirate uncle[54,] have demonstrated effectiveness in the speed of healing and its quality. The usefulness of becaplermin and the various growth factors in neuropathic and diabetic ulcers has already been discussed, and its usefulness may be extended to other chronic ulcers.[9]. Therefore, the treatment of chronic ulcers is an area of great interest in whose knowledge and therapeutic possibilities is advancing rapidly. We do not doubt that it is a multidisciplinary disease in which the dermatologist must participate. Possibly, this aspect depends, to a large extent, on ourselves (Carter, DaVanzo, et al., 2023).

Conclusion

Ulcers, characterized by loss of skin substance, present a significant clinical challenge due to their diverse etiologies and complex healing mechanisms. Despite the interchangeability of the terms

"wound" and "ulcer," understanding their underlying causes remains crucial. Chronic ulcers, in particular, pose substantial burdens on patients' quality of life and healthcare systems due to their high prevalence and associated complications.

The repair mechanisms of wounds involve intricate processes encompassing inflammatory, proliferative, and maturation phases. In chronic ulcers, aberrations in these mechanisms impede healing, necessitating targeted interventions. Growth factors such as PDGF-B, bFGF, VEGF, and NO play pivotal roles in promoting cellular proliferation and tissue regeneration, offering therapeutic potential for ulcer management.

Vascular ulcers, including venous ulcers, constitute a significant portion of chronic ulcers and require comprehensive management strategies, notably compression therapy. Understanding the factors influencing wound healing, such as nutritional status, age, coagulopathy, and local factors like humidity and infection, is crucial for optimizing treatment outcomes.

Moist wound healing, as opposed to traditional dry healing methods, is increasingly favored for its physiological benefits and efficacy in promoting tissue repair. Evidenced-based approaches, including proper wound cleansing, debridement, exudate control, and infection management, are essential components of ulcer care.

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