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Healing Diabetic Foot Ulcers: A Comparative Review of Debridement Approaches

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ABSTRACT

Introduction and objective: More than 400 million people worldwide suffer from diabetes today. As a result of complications of this disease, diabetic foot ulcers (DFU) develop. Wound treatment consists mainly in cleansing and stimulating tissue healing processes. Depending on the method used, this process may be shorter or longer.

Review methods: In March 2023, articles found in the Medline (Pubmed) and Google Scholar databases were selected by using the following keywords: diabetic foot treatment, diabetic foot ulcers (DFU), autolytic debridement, healing DFU.

Brief description of the state of knowledge: Each of the methods described in this article has its advantages and disadvantages. Surgical debridement is used in wounds with a large amount of necrotic tissue, but it can be associated with great discomfort for the patient. Clostridial collagenase ointment has been found to be effective in reducing wound area and promoting wound closure but is more expensive. The use of autolytic debridement and larval therapy is associated with a reduction in pro-inflammatory markers, while the use of moist dressings provides a suitable environment for tissue regeneration.

Summary: The choice of the appropriate method depends on many factors such as: the patient's condition, the availability of materials and financial resources. This review paper provides a comprehensive overview of the benefits and drawbacks of different debridement methods for diabetic foot ulcers.

Key words: diabetic foot treatment, diabetic foot ulcers (DFU), autolytic debridement, healing DFU.

INTRODUCTNION

Diabetes mellitus (DM) is currently one of the main diseases of civilization. It is estimated that by 2045 there will be 700 million people affected by DM [1]. Chronic hyperglycemia and related metabolic dysfunction can lead to micro- and macroangiopathy as well as neuropathy. Diabetic microangiopathy causes impaired tissue perfusion and makes the foot more susceptible to infection and delayed healing and leads to tissue deformation and edema [2]. In patients with diabetes, the wound healing process is impaired due to such changes as: reduced production of growth factors, dysfunctions in the angiogenesis process, abnormal macrophage function, collagen accumulation, reduced amount of granulation tissue, abnormal migration and proliferation of keratinocytes and fibroblasts, peripheral nerve atrophy and imbalance between the accumulation of extracellular matrix components and their remodeling by matrix metalloproteinases [3]. As a result of these changes, diabetic foot ulcers (DFU) develop, which affect up to 34% of diabetic patients. Due to extensive infections and tissue degradation, DFU patients undergo a lower limb amputation every 20 seconds worldwide [4], [5]. To reduce inflammation, the wound must be properly debrided to remove dead tissue (this includes surgical, biological, enzymatic and autolytic debridement). It has been proven that proper wound cleansing, such as removal of contaminated or dead tissue until healthy tissue is exposed, significantly improves the healing of the remaining

healthy tissue [6]. The aim of this article is to describe the currently used methods in the treatment of diabetic foot ulcers as well as the effectiveness of the applied dressings.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Mechanical methods

Mechanical treatments for diabetic foot ulcers focus on repeated wound debridement and removal of necrotic material, wound unloading, and the use of moist dressings to help achieve a moist wound environment, essential for the healing process [7]. The choice of appropriate dressing depends on many factors such as: location, type of wound, amount of wound formation exudate and history of allergic reaction. Ensuring a moist wound environment supports granulation, autolytic processes, angiogenesis, and more rapid migration of epidermal cells across the wound base, which is why moist dressings are most often used [8]. The use of traditional dressings has many advantages, but compared to other methods, it is most often associated with a longer wound closure time. A large systematic review and meta-analysis by Elraiyah et al. compared the effectiveness of various DFU treatments. Based on three randomized controlled trials it was shown that autolytic debridement was associated with statistically significant increases in healing rates compared to standard gauze debridement. Two studies reported a reduction in amputation rates with larval therapy compared to traditional dressings. Comparing studies that used surgical methods of wound treatment and conventional dressings, it was shown that the DFU healing rate was 95% in the group using surgical treatment compared to 79.2% in the group treated with traditional dressings. In addition, surgical treatment showed significant benefits also in terms of shorter wound healing (average 46.73 vs. 128.9 days) and lower incidence of side effects (1 out of 22 [4,5%] vs 3 out of 24 [12,5%]) [9]. Another study compared 2 groups of patients who underwent partial foot amputation and had ulceration outside the amputation area, has shown that the use of moist dressings was associated with a longer granulation tissue formation. The first group was treated with Vacuum Assisted Closure (Group A) and the second was treated with conventional moist dressings (Group B). The average time to reach 90% wound granulation was longer in group B patients by approximately 3.3 ± 1.2 weeks. However, there was no significant difference in the occurrence of complications leading to re-amputation. In the VAC group, 12 patients (38.7%) required reamputation, and in the group treated with moist dressings it was 14 patients (41.2%) [10]. The multicenter study in Germany showed that the use of both negative pressure wound therapy (NPWT) and standard moist wound therapy (SMWC) was associated with a similar risk of remaining open wounds. However among patients with a large wound area, the wound closure rate over 16 weeks was significantly higher in the NPWT group (13 out of 88 (14.8%)) than in the SMWC group (5 out of 84 (6%)), but after 6 months, the percentage of patients with a closed wound was higher in the group treated with SMWC (20.7%) than in the group treated with NPWT (14%) [11].

Surgical debridement

Surgical debridement is the preferred method for wounds that contain a significant amount of necrotic tissue, particularly those that are associated with infected tissue or exhibit visible tendons or bone. This technique involves the removal of dead, non-responsive tissue to transform the chronic healing environment into an acute one, thereby improving the wound's response to topical treatment and accelerating the healing process. In a randomized trial that enrolled 122 patients, the effectiveness of weekly sharp debridement versus debridement every two weeks was investigated to determine the required healing time for DFUs. The study results indicated that, following a 3-month period, 10% fewer patients experienced complete healing with debridement every two weeks compared to weekly debridement. The benefits of surgical debridement include the improvement of granulation tissue healing as well as more accurate wound examination, which in turn reduces pressure on the wound [12]. Debridement may be performed in the operating room when it's supposed to be more advanced and requires deep sedation or as an ambulatory surgical procedure when it's supposed to be more superficial. In this method sharp tools are used, such as scalpels or special scissors, for mechanical removal of abnormal tissue. Speed and specificness are the advantages of this method. Indications include removal of the source of infection and sepsis, the need for collection of deep cultures taken post debridement to choose specific antibiotic treatment, stimulation of the wound to accelerating the healing process, preparation for grafts [13]. In patients who have an intact scar with no evidence of an underlying infection, the surgical debridement method is contraindicated. Major bleeding from the wound, complications of deep sedation, pain during and after the procedure are disadvantages of this debridement. One of the studies has shown that due to anesthesia used during the debridement, operative mortality was 2% and long-term mortality was as high as 68% [14] . In a randomized controlled trial involving 14 patients, it was demonstrated that non-surgical sharp debridement resulted in faster wound healing compared to low-frequency ultrasonic debridement by almost 2 months, along with a notable improvement in patients' quality of life as ulcers healed [15] . Two independent clinical cases of patients with infected diabetic foot with multiple lesions and irreparable damage showed that surgical debridement alongside other treatment methods such as maggot therapy, the Negative Pressure Wound Therapy (NPWT), and silver foam dressing, allow for satisfactory treatment results. A monotherapy strategy could lead to a very low level of recovery and the use of surgical debridement definitely increases positive results and the patient's quality of life [16], [17].

Enzyme debridement

Enzyme debridement, a method involving the topical application of enzymes that digest fibrin, elastin, and collagen, has shown promising results in the treatment of diabetic foot ulcers (DFU). Clostridium Collagenase Ointment (CCO) is currently the only FDA-approved product for this type of wound debridement in DFU. CCO, a type of clostridial collagenase, hydrolyzes collagen molecules to remove detritus without damaging healthy tissue, promotes the formation of granulation tissue and epithelialization, and reduces the level of pro-inflammatory cytokines. With its potential to accelerate wound healing and improve patient outcomes, CCO is an important agent to consider in the treatment of DFU [18]. Several studies have investigated the effectiveness of CCO in the treatment of DFU. Montley et al. conducted a randomized, prospective study that showed patients

who received CCO in combination with sharp debridement had a significantly faster reduction of wound area compared to patients who received only sharp debridement. The mean wound area reduction of patients treated with CCO monotherapy was 50% from baseline, while patients treated with a combination therapy of selective sharp debridement with saline dressings did not show such a reduction [19]. [20]In addition to promoting faster wound healing, CCO has also been found to have a significant benefit in terms of wound closure. Waycaster et al. reported a higher percentage of wound closure in patients treated with CCO than in patients treated with hydrogel dressings [20]. Furthermore, CCO has shown promising results in treating non-healing chronic wounds. A randomized controlled trial was conducted to compare the efficacy of collagenase and hydrogel for debridement of nonviable tissue in institutionalized adults with pressure ulcers. The study enrolled 27 nursing home residents over a period of one year. Subjects were randomized to receive either daily dressing changes with hydrogel or collagenase for up to 42 days. The results showed statistical significance in favor of collagenase for achieving full debridement by Day 42, despite not cross-hatching eschar. This study suggests clinical utility of collagenase in settings without clinician availability for the cross-hatching procedure [21]. CCO has also been found to have an anti-inflammatory effect. In a study by Galperin et al., patients treated with CCO had lower levels of pro-inflammatory factors (TNF-α and IL-6) and higher levels of anti-inflammatory factors than patients treated with hydrogel dressings [22]. One major concern in the treatment of DFU is the incidence of wound infection. Patients treated with CCO had more than twice the rate of wound infection compared to patients treated with silver dressings [19].

In conclusion, CCO has been found to be an effective agent in the treatment of DFU, promoting wound healing, wound closure, and reducing the level of pro-inflammatory cytokines. Despite the higher incidence of wound infection, CCO has shown advantages over other dressings in the treatment of DFU. Further studies are required to confirm the safety and efficacy of CCO in the treatment of DFU. The limitations of existing studies, such as small sample sizes and inconsistent study designs, suggest the need for larger randomized controlled trials with standardized protocols. The promising results from existing studies suggest that CCO can be an important addition to the armamentarium of wound care professionals in the management of DFU.

Maggot debridement therapy

In recent years, larvatherapy has been gaining increasing interest as a method of treating chronic wounds. Ease of access to maggot therapy makes it more and more attractive to implement. Maggot therapy should be considered for faster wound debridement, development of granulation tissue and reduction of wound surface area, and in the presence of surgical contraindications [23], [24] . Maggot debridement therapy (MDT) is a selective technique that involves the use of Lucilia sericata larvae to digest dead tissue and pathogens through proteases present in their saliva. Larval secretions contain antibacterial and antifungal peptides, including lucifensin and lucimycin. MDT is administered by applying 50-1000 sterile larvae, aged 24-48 hours, 2-4 times a week, depending on wound size and depth, for 24-72 hours. In patients with diabetic foot ulcers (DFU), a 2-week course is typically used [25] . Wounds are treated with free larvae and in pouches. There are no obvious differences between the approaches that used loose or bagged larvae. Maggot therapy has facilitated faster and more effective clearance of non-viable tissue. This allowed for faster granulation tissue development and increased wound surface reduction compared to hydrogel dressings [24] .It is an alternative to conventional

methods of therapy due to the increasing multi-drug resistance of bacteria and the observed allergic reactions to antibiotics and disinfectants. The use of larvatherapy allows for shortening the treatment time, reducing the consumption of antibiotics and reducing the cost of treatment [26]. Malekian et al. studied the effectiveness of maggot therapy on Staphylococcus aureus and Pseudomonas aeruginosa in DFU. They concluded that the number of S.aureus-infected cases in the treatment group was significantly reduced after 48 hours compared to the control group. The number of infected cases of P. aeruginosa was significantly reduced after 96 hours [27]. The disinfection of bacterial growth is confirmed by the elimination of pathogenic microorganisms, with the exception of bacterial spores, on the wound bed [24].

Autolytic debridement

Autolytic debridement is a key component in the effective management of chronic wounds, such as pressure ulcers and diabetic foot ulcers. Autolytic debridement involves the use of occlusive or semi-occlusive dressings such as hydrocolloids, hydrogels, and transparent films. The main aim of this kind of therapy is maintenance of a moist wound environment due to their ability to hold a large amount of water and preserve viable healthy tissue simultaneously. The moist wound environment allows the host's neutrophils and macrophages to remove devitalized tissue through their own body enzymes [28]. Additionally wound debridement is pushing by liquefy hard eschar and loosen the necrotic tissue. Granulation, epithelialization, and autolytic debridement are promoted too [29] . The advantages of hydrogels include their high selective which causes little or no damage to the surrounding skin, making it a safe and pain-free option for patients. However, hydrogel dressings may not be suitable for all types of wounds, because autolytic debridement is not as fast as surgical debridement. Moreover, the wounds require close monitoring for signs of infection or anaerobic growth. In addition, use of occlusive hydrocolloids may promote a possible adverse effect - maceration of surrounding skin [28]. In some a single-blind randomized controlled trial with a 12-week follow-up period, involving 26 patients who were randomly assigned to either the control group (cleaning and a simple dressing) or the experimental group (hydrogel treatment), the results didn't show significant difference between the two groups in terms of wound area. Participants healing by hydrogel dressings had larger initial median wound area and the research come out the wounds like these have lower Chance of healing. Therefore, we cannot be sure of the quality of this evidence. On the other hand, microscopic analysis revealed a decrease in inflammatory infiltrates in the hydrogel group after 12 weeks of treatment, indicating that the hydrogel promoted wound debridement [30]. The results of other randomized studies showed autolytic debridement was associated with a statistically significant increase in healing rates compared with standard wound debridement by gauze and conventional wound care. It should be taken into account that these studies differed in follow-up time and ulcer severity. Another study compared hydrogel dressing with larval therapy. Larval therapy tended to a significantly reducing a wound size area, but the number of completely healed ulcers between larval and autolytic debridement was similar. Another study found no significant difference in healing between hydrogel and platelet-derived growth factor. Although hydrogels dressings have many advantages, they will not be affective in all cases The authors recommend that the choice of debridement method should be selected individually for each patient and be based on the available expertise, cost and patient preferences [31], [32].

SUMMARY

Effective wound management is essential for DFU treatment. Mechanical methods, such as debridement and moist dressings, create a favorable wound environment for healing. Surgical debridement is preferred for wounds with necrotic tissue or infection. Enzyme debridement using clostridial collagenase has shown promise in promoting wound healing but carries a higher risk of infection. MDT has gained interest due to its efficacy in removing dead tissue and pathogens. Autolytic debridement with occlusive or semi-occlusive dressings is a viable option but may not be as fast as surgical methods. Further research is needed to validate the safety and effectiveness of these treatments for DFU management.

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