



Analysis of the clinical care of patients with chronic ulcers of the lower limbs

Análise do atendimento clínico de portadores de úlceras crônicas em membros inferiores

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■ ABSTRACT

Introduction: Chronic ulcers of the lower limbs may have different etiologies, with the most frequent being venous, arterial, traumatic, infectious, and diabetic. The treatment of these wounds is dynamic and depends on the evolution of tissue repair. This treatment includes clinical and surgical methods, and dressings are the most frequently used. Dressings can range from inert covers to vehicles for actuation of active substances in the wound bed. The main indication for these substances is related to the effects of debridement and control of the bacterial population, enabling the preparation of wound beds for surgical or spontaneous resolution. **Methods:** This study is an observational, cross-sectional, retrospective study, with random sampling, aimed at assessing the care provided to patients with chronic ulcers of the lower limbs in the Outpatient Clinic for chronic wounds of the Plastic Surgery Division, HCFMUSP, between 2011 and 2013. **Results:** The clinical charts of 481 patients of both sexes, with a mean age 60 years, were analyzed; all had chronic ulcers in different stages of evolution. Comorbidities, underlying disease, size of the lesion, treatments, and evolution of wounds were evaluated. A predominance of vascular disease (69.2%) was the underlying cause. All patients were initially treated with dressings containing active agents, for preparation of the wound bed. Of these, 84% were referred for surgical management of wounds. There was no spontaneous closure in 1.5% of cases. The remaining patients (14.5%) showed worsening of lesions with topical treatment, and required other forms of preparation of the wound bed. **Conclusion:** Topical agents may be an effective outpatient/home method to prepare the wound bed of chronic ulcers for surgical management.

Keywords: Leg ulcer; Venous ulcers; Diabetic foot; Diabetic ulcers of the foot; Healing; Papain

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■ RESUMO

Introdução: Úlceras crônicas em membros inferiores podem apresentar diferentes etiologias, sendo as mais frequentes: venosa, arterial, traumática, infecciosa e diabética. O tratamento dessas feridas é dinâmico e depende da evolução da reparação tecidual. Esse tratamento inclui métodos clínicos e cirúrgicos, sendo o curativo o método não cirúrgico mais frequentemente utilizado. Curativos podem ser desde de coberturas inertes até veículos para atuação de princípios ativos no leito da ferida. A principal indicação de ativos está relacionada a efeitos de desbridamento e controle da população bacteriana, possibilitando o preparo desses leitos para resolução cirúrgica ou espontânea. **Método:** Esse estudo é observacional, longitudinal, retrospectivo, de amostra randomizada no qual pretendemos analisar o atendimento prestado aos portadores de úlceras crônicas em membros inferiores no Ambulatório de Feridas Crônicas da Divisão de Cirurgia Plástica do HCFMUSP entre 2011 e 2013. **Resultados:** Foram analisados prontuários de indivíduos de ambos os gêneros, idade média 60 anos, portadores de úlceras crônicas em diferentes estágios evolutivos. Foram pesquisadas comorbidades, doença de base, tamanho da lesão, tratamentos utilizados e evolução das feridas. Notou-se predomínio das causas vasculares (69,2%) como doenças de base. Todos os pacientes foram primeiramente tratados com curativos contendo princípios ativos, para preparo do leito das feridas. Desses, 84% foram encaminhados para resolução cirúrgica das feridas. Houve fechamento espontâneo em 1,5% dos casos. Os demais pacientes (14,5%) apresentaram piora das lesões com tratamento tópico, necessitando outras formas de preparo desse leito. **Conclusão:** Agentes tópicos podem ser uma forma ambulatorial/domiciliar efetiva de preparo do leito de úlceras crônicas para resolução cirúrgica.

Descritores: Úlcera de perna; Úlcera venosa; Pé diabético; Úlcera diabética do pé; Cicatrização; Papaína.

INTRODUCTION

Several diseases can cause the formation of chronic ulcers in the lower limbs, and include venous, arterial, traumatic, infectious, and diabetic etiologies¹. Despite the wide variety of etiological factors, the main causes of chronic ulcers of the lower limbs are venous and arterial diseases. Ulcers of venous origin affect 1% of the world's population and correspond to 75% of all chronic ulcers².

Various studies have reported a prevalence of active, unhealed venous ulcers of approximately 0.3%, i.e., around one case per 350 adults, while the incidence of healed ulcers, regardless of their etiology, is approximately 1% in the adult population. This prevalence increases with age, and is more than 4% in people older than 65 years. When not properly managed, approximately 30% of the healed venous ulcers recur in the first year, with the rate rising to 78% after two years³.

These ulcers have significant socioeconomic impact owing to their recurrent nature and long healing time. The patient needs care from health professionals, is frequently absent from work, and often takes early retirement. All these factors are a significant burden on health and welfare systems, in addition to interfering with the patient's quality of life; the high cost of treatment or absenteeism and loss of employment do not take into account the decrease in enjoyment of daily activities³.

Venous insufficiency is the result of long-term venous hypertension caused by valve insufficiency and/or obstruction³. Ulcers due to venous insufficiency involve the skin and subcutaneous tissue, and they are predominantly found in the gaiter area, which is the region between the ankle and the lower half of the calf, and the medial leg above the medial malleolus.

Their clinical characteristics include edema that worsens at the end of the day and improves with limb elevation, hyperpigmentation or dermatitis, lipodermatosclerosis, acute and progressive pain, eczema, and single or multiple ulcerations. In general, these wounds have an irregular surface shape, initially with well-defined borders and yellowish exudate. After six weeks without healing, the wound is considered chronic⁴.

Wound treatment depends on the evolution of the healing process, and includes clinical and surgical methods; dressings are the most common clinical treatment⁵.

Dressings are used to improve the condition of the wound bed, and can sometimes be definitive treatment. However, in many situations, this is only an intermediate step before surgical treatment.

Papain has been used in Brazil as a dressing for wound treatment since 1983⁶. This extract has topical activity, primarily providing enzymatic and autolytic debridement, and acting to control the bacterial population during the preparation of the wound bed. Papain is extracted from the leaf and fruit latex of green papayas, *Carica papaya*, and the fruit extract is more effective than the leaf extract. Papain is a complex mixture of proteolytic enzymes and peroxidases. This active agent causes proteolysis or degradation of proteins to amino acids in devitalized and necrotic tissue, without affecting healthy tissue. Other properties of this extract are its anti-inflammatory, bacteriostatic, and bactericidal activities. The antibacterial action is only demonstrated at a concentration of 10%, by inhibiting the growth of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. There are also reports of antibacterial action against *Escherichia coli*⁷.

Hydrogel is composed of water, carboxymethylcellulose (CMC), and propylene glycol (PPG); its main function is to soften and remove devitalized tissues (autolytic debridement). The water keeps the environment moist, CMC facilitates cellular rehydration and debridement, and PPG stimulates the release of exudate. Its best indication is for the treatment of superficial wounds with moderate or low exudate. Hydrogel can be combined with calcium alginate. In this situation, sodium in the exudate and blood interacts with calcium in the dressing. This ionic exchange assists in autolytic debridement, and has great capacity for absorption, thus resulting in the formation of a gel that keeps the environment moist for healing and induces hemostasis⁸.

The closure of the wound should be performed as soon as possible in those who present with clinical conditions and locations requiring surgical procedures. The main surgical options for resolution of these ulcers are skin grafts and local and/or free flaps⁹.

OBJECTIVE

The objective of this study was to retrospectively analyze the care provided to patients with chronic ulcers in the Outpatient Clinic for chronic wounds of the Division of Plastic Surgery at HCFMUSP.

METHODS

This was an observational, longitudinal, retrospective study with a randomized sample. The study was approved by the Ethics Committee for Research of the Hospital das Clínicas, Faculty of Medicine, Universidade de São Paulo (HCFMUSP), CAAE: 35417614.1.1001.0068.

From 2011 to 2013, 467 patients with chronic lower limb ulcers were treated in the Outpatient Clinic.

Using software specific for this purpose (Microsoft Excel random function RANDBETWEEN [1]), a sample of 68 patients was selected randomly. The patient sample had wounds in the lower limbs, included both sexes, were 42 to 86 years old (mean 60 years), and had an average presentation of approximately 7 months. The patients' medical records were evaluated for the following data: etiology, comorbidity, size of ulcers, treatment used, clinical outcome, and complications.

The treatment specified the use of different active principles and concentrations of papain formulated gel for topical use. We also evaluated the variation in treatment time with these topical agents, in addition to their use alone, or in association with other agents, and the effect on the progress of the lesion.

RESULTS

The etiological factors of chronic ulcers included vascular insufficiency, *diabetes mellitus*, and immunological diseases (lupus, scleroderma, psoriatic arthritis, and cutaneous tuberculosis). There was a predominance of vascular causes (69.2%). Among these, there was a higher incidence of venous ulcers (67.7%) compared to ulcers resulting from arterial occlusion (1.5%), as shown in Figure 1.

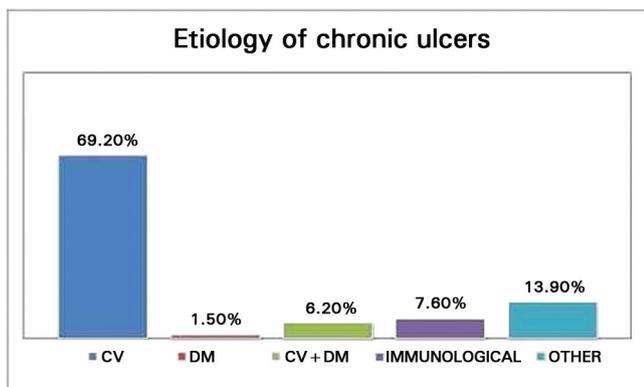


Figure 1. Etiology and incidence of diseases leading to formation of chronic ulcers of the lower limbs. Note the predominance of vascular causes in association with *diabetes mellitus* (CV + DM) and immunological disorders (IMMUNE). Other etiologies include traumatic ulcers and burns.

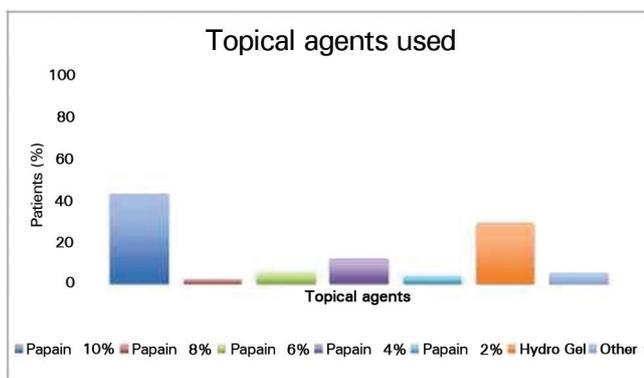


Figure 2. Description of the various topical agents used as first choice in the treatment of chronic ulcers.

The topical agents used in the initial treatment of these wounds, as well as the variation in their concentrations, are specified in Figure 2, and were always used in daily dressing changes.

The most common active agent used was 10% papain (in 19.1% of patients), followed by hydrogel (in 13.3%). In 41.2% of cases, the initial agent required replacement with a second agent to complete the treatment. Nevertheless, in 3 patients (4.5% of the cases treated with a second agent), the response was inadequate, requiring treatment other than topical management.

The initial size of the wounds evaluated was $38.75 \pm 5.69 \text{ cm}^2$. An average reduction of 6.68 cm^2 was observed with topical treatment, with adequate preparation of the bed for surgical treatment after the use of dressings for a mean of 7 months. A total 4.5% of the patients had worsening of the lesions despite topical treatment, with the presence of necrotic tissue in 1.5%, and/or clinical signs of infection in 3%, leading to a

mean increase of 3.53 cm^2 in the original wound size. This phenomenon showed no apparent relationship with the mean age of the individuals or etiology of the lesions. Other forms of wound bed preparation were used in these patients (such as subatmospheric pressure therapy) before surgical coverage.

There was no spontaneous closure in 1.5% of clinically managed patients. However, 84% of the patients (n = 57) were referred for surgical management, with the need for hospitalization on our service, which advocates surgical treatment as early as possible, when indicated.

All patients in the study remained in follow-up in other medical specialty clinics for their underlying pathologies; however, patients with ulcers of vascular origin did not receive adjuvant treatment by the referring surgical clinic.

DISCUSSION

Chronic lower limb ulcers of venous origin affect 1% of the world's population, and correspond to approximately 75% of all chronic ulcers¹⁰. This distribution in the population was reflected in our sample, with a predominance of venous ulcers (67.7%).

These ulcers may take months or years to resolve, despite being treated appropriately. Once healed, there is the possibility of recurrence in 18% to 28% of cases if there is no follow-up and treatment of the cause. It is also well known that the size and duration affect the prognosis of these lesions¹¹.

There are several products on the market to treat wounds, which makes the choice of a correct dressing a difficult and challenging task. In this regard, some factors should be considered¹². Factors related to the wound and the adjacent skin include etiology, size, depth, anatomical location, volume of exudate, risk or presence of infection, and condition of the adjacent skin. Factors related to the patient include nutritional status, underlying diseases, need for pain control, and patient preferences. Factors related to the dressing include indications, contraindications, advantages and disadvantages, availability, durability, adaptability, and ease of use.

From the data analyzed, it is notable that topical treatments significantly improved the healing process. The literature reports that papain has been used as a topical agent in various types of

wounds, in patients of different age groups, with positive effects in the stimulation of the healing process, and with a low incidence of side effects¹³.

Nonetheless, we should stress that the use of papain in different concentrations during different treatment phases allows better management of the progress of the ulcer, resulting in a decreased healing time and a more aesthetic appearance.

Patients who have allergic reactions to the latex of *Carica papaya* may present a similar reaction to papain. However, individuals who do not have this reaction can definitely apply papain to the skin^{14,15}.

The healing time of the wound is another important factor discussed in the literature. Several studies¹⁶ have shown that treatment of chronic wounds with papain shortens the healing time. Salomé¹⁷ associated the use of EFA with papain, noting that these products are valuable resources in the treatment of wounds. In agreement with that data, our study observed an 85.5% reduction of lesions among the patients analyzed.

Papain is used in various pharmaceutical formulations in the treatment of wounds, such as powder, gel, cream, and solutions at a concentration of 2% to 10%¹⁶. Currently, a concentration of 2% is recommended for stimulation of the formation of granulation tissue, 4% to 6% to remove liquefactive necrosis, and 8% to 10% for coagulation¹⁸. In our hospital, we use papain as a gel, because this formulation maintains a moist wound environment, which is a precondition for the healing process; in addition, this avoids the inconvenience of preparation at the time of application, and it may be stored for long periods. Furthermore, it can be easily applied within the limits of the wound, and is easily removed from the lesion by washing with saline¹⁹.

This results in a net cost that is 10% of that of hydrogel, making the use of papain more in accord with the reality of the Brazilian health services.

A second agent was used to treat the injuries when there was no further need for proteolytic action or stimulation of granulation tissue or when there was an adverse response after the use of the first agent.

With regard to unsuccessful results, it is important to note that some patients interrupted treatment or were noncompliant owing to complaints of hyperalgesia or bleeding. In these cases, early surgical debridement was proposed for wound bed preparation²⁰.

CONCLUSION

Topical agents may be an effective outpatient or home-based means of preparing the wound bed of chronic ulcers for surgical management. This treatment could reduce the need for hospitalization and reduce the socioeconomic impact of these lesions. The possibility of a shorter hospital stay has a positive effect on the quality of life of these patients, and can increase personal satisfaction in daily activities.

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