TOPICAL THERAPY OF WOUNDS: AVAILABILITY AND USE IN PRIMARY HEALTH CARE CENTERS

ABSTRACT
Objective: to describe the topical therapies available and their respective wound type in primary health care centers. Method: a cross-sectional quantitative study conducted in October 2013 in 12 health care centers in a municipality in the state of Mato Grosso do Sul. Data were collected using a form with information about the topical therapy available and respective wound type, provided by nurses or the nursing team. Results: silver sulfadiazine cream and neomycin sulfate cream combined with bacitracin were the most frequently available products, followed by collagenase combined with chloramphenicol (91.6%), povidone-iodine aqueous solution 10% (33.3%), and others. Conclusion: the results show that proper material resources and specific training are required for effective therapeutic practices. Descriptors: Wounds and Injuries; Bandages; Wound Healing; Evidence-Based Practice; Nursing Care; Public Health.

RESUMO
Objetivo: descrever as terapias tópicas disponíveis e em que tipo de feridas são empregadas em uma rede de atenção primária à saúde. M étodo: estudo transversal, de abordagem quantitativa, realizado em outubro de 2013, em 12 unidades de saúde de um município do interior do estado de Mato Grosso do Sul/MS. A coleta de dados se deu pelo preenchimento de um formulário que continha informações da terapia tópica disponível e do tipo de ferida em que era empregada. As informações foram coletadas de enfermeiros e/ou equipe técnica de enfermagem. Resultados: o creme de sulfadiazina de prata e o sulfato de neomicina com bacitracina foram os produtos predominantemente disponíveis, seguidos de colagenase com cloranfenicol (91,6%), solução aquosa de iodopovidona 10% (33,3%), dentre outros. Conclusão: os resultados evocam a necessidade de aquisição de recursos materiais adequados e de treinamentos específicos para o estabelecimento de condutas terapêuticas eficazes. Descritores: Ferimentos e Lesões; Curativos; Cicatrização de Feridas; Prática Clínica Baseada em Evidências; Cuidados de Enfermagem; Saúde Pública.
**INTRODUCTION**

The term wound comes from the Latin word *vulneris*, which can be defined as any lesion disrupting the normal continuity of a body structure, that is, any soft tissue, produced by direct traumatism, with or without loss of substance. Wounds can be classified using many criteria, such as: etiology diagnosis, cause, morphology, level of contamination, healing evolution stage, characteristic of wound bed, exudate characteristic, secretion culture, presence of fistulas, progression and type of healing.1

In Brazil, wounds affect the general population, regardless of gender, age or ethnicity, with a high rate of people with skin integrity alteration, representing a serious problem of public health. In addition, wounds increase public health expenses and impact the quality of life of population.2 However, statistical data are scarce and punctual to prove this fact, due to poor records from these services.

Evolution in knowledge about the healing process physiology and the development of new materials and products for wound treatment, along with the clinical and psychosocial repercussion to patients with acute and chronic wounds, point to the selection of proper topical therapy to the needs and problems resulting from the healing process of every individual, requiring treatment and, therefore, should occur in conditions to help optimize such process.3

The products used in wound treatment include topical agents, such as ointments and solutions applied to the lesion, and coverage, whose function is to promote healing and protect the wound area from additional lesions.4

Regarding wound coverage, it can be classified as primary, when they cover the lesion and help or act with products to absorb exudate and/or secretions; or coverage with the ability to act passively, that is, without providing substances to the wound, but optimizing or improving local conditions, creating a wet environment, absorbing exudate, insulating it thermally and protecting it from trauma. Lastly, there is the bioactive coverage which, besides the functions described above, can provide substances to the wound and, therefore, actively impact the healing process.3

When choosing the most adequate topical therapy or coverage, health professionals should know the main categories of wound treatment products available in their reality, such as composition, mechanism of action, indication, contraindication, how to use it, change interval, advantages and disadvantages.5

The market of wound treatment products is in constant evolution in terms of types of coverage and topical therapies. As a result, over 2,000 products are today commercially available to prevent and treat wounds, making the selection of proper treatment a hard and challenging task for health professionals, especially nurses.4,5

This study relevance and justification are explained by the importance of knowing the topical therapies for wounds available in the public health care center investigated and in what conditions they are used. A critical analysis of the situational diagnosis by this center may help develop effective health care proposals to wounded individuals (goals, trainings, standardization of products and development of protocols) and targeted and more assertive public policies to these patients, as required. Thus, the objective of this study was:

- To describe available topical therapies and in what types of wounds they are used, in primary health care centers.

**METHOD**

A cross-sectional quantitative census-type study was conducted in primary health care centers in a municipality in the state of Mato Grosso do Sul, in September 2013. For data collection, a script was developed including the investigated health care center identification, the topical therapy available and the types of wounds treated with every therapy.

The nurse in charge of each health care center was personally visited by one of the authors, who provided a letter with information about the study, highlighting the study approval and authorization from the Municipal Division of Health. According to the availability of the health professionals, information was then collected on the operations of the wound treatment room, from nurses and the nursing team that performed wound dressings. The products used and available in every treatment room were investigated, reporting in the script the product presentation and asking health professionals about the type of wound to be treated with every product. Descriptive statistics was used in data analysis to present quantifiable data.

As this study did not collect data from human beings - only information of products
Results

All 12 (100%) health care centers in the municipality were visited and included in this study, seven of them were Family Health Strategies, three were from Health Community Agent Programs and two were Community Agent Programs and two were indirectly and using their data, information or biological materials.

Table 1. Topical therapies available and type of wounds treated with every therapy from primary health care centers. Três Lagoas, Mato Grosso do Sul, Brazil, 2013

This study also observed the use of products not reported in the literature, for instance: vaseline and sunflower oil (kitchen use). Regarding antiseptic products, they were surprisingly available in only four centers (33.3%); they seem to be indicated for routine practice for superficial skin lesion, but without prudent evaluation; and chlorhexidine was used in practically only one center (8.3%). Industrialized products, such as hydrogel, calcium alginate, activated charcoal and hydrocolloids, were not found in any wound treatment room.
DISCUSSION

In light of the healing process evolution and understanding, the final purpose of wound treatment is to minimize the risk of opportunistic infections, promoting the development of a healthy granulation tissue to promote healing.7

This study found antimicrobial products for wound treatment in almost all centers, suggesting health professionals indiscriminately and inadequately use antibiotics in wound treatment - due to high wound vulnerability to infection, negative consequences to patients and the health system, among others.

Although systemic antibiotics are considered essential for the treatment of clinically infected wounds, topical antibiotics are not justified in the treatment of colonized or infected wounds. Topical antibiotics may cause delayed hypersensitivity reactions and superinfections and select microorganisms with multiple drug resistance (MDR). A recent review showed that the frequent use of topical antibiotics in the treatment of clinically infected leg ulcers has not produced any benefit, and there is evidence that antibiotics may be harmful, as they promote colonization of MDR strains. Another disadvantage of topical antibiotics is the frequent occurrence of contact allergy, of which neomycin is a classic example.8

Silver sulfadiazine, used by all health care units, is a topical antibiotic of broad spectrum, including MDR microorganisms and Pseudomonas spp. It was initially designed for the treatment of burns, but its current indication includes chronic wounds, with no clear effectiveness though.9 A recent systematic review10 points out the lack of evidence that attests the effectiveness of coverage and topical therapies with silver in the prevention of infections and promotion of burn healing.

Inconveniences of silver sulfadiazine include cases of resistance and problems like erythema multiforme and sensitivity to the sulfonamide fraction of sulfadiazine, as well as non-serious temporary leukopenia.3 In addition, silver sulfadiazine, alone, has been suggested to delay the healing process and present a cytotoxic effect on skin cells.10 Other authors11 have categorically stated that the use of silver sulfadiazine should be discouraged for burns, as several studies have presented its tendency to delayed healing and increased infection rates.

Neomycin is an aminoglycoside with bactericidal activity in Gram-negative bacteria. It inhibits protein synthesis and is presented in tablets, suspension, and topical ointment. It is indicated for the prevention of gastrointestinal tract and skin tissue infections. It has also been used in the treatment of a wide variety of localized infections, including infected dermatoses, infected burns, skin ulcers, impetigo, furuncles and external otitis. The indiscriminate use of neomycin should be avoided, as it may promote sensitization (rash, erythema, pruritus) and resistance to various microorganisms.12

A study1 whose purpose was to describe the resources used by nurses from the public health system in the treatment of venous ulcers in two distinct socioeconomic realities - Brazil and Portugal - showed that neomycin sulfate/bacitracin was used by 83.3% of the health care centers in Brazil and not used in Portugal. According to the authors, the study found a higher availability and variety of industrialized therapeutic resources in Portugal, such as hydrocortisone, hydrogel, hydropolymer (polyurethane), hydrofiber with silver (Ag), gauze impregnated with povidone-iodine, oxygenated gauze, iodophor dressing, idoform, zinc oxide ligature and activated charcoal with Ag. The results of this study (Chart 1) do not differ from the results found in another Brazilian reality.1

Another therapy available in most health care centers was collagenase ointment. Collagenase ointment, a metalloproteinase produced from bacterium Clostridium histolyticum, has been extensively studied, given its ability to degrade devitalized tissues in the clinical context, high availability, and low cost. It is a water-soluble protease, indicated for enzymatic debridement of devitalized tissues and with low effectiveness in large areas of necrosis. Collagenase is comprised of three polypeptide chains that create a triple helix. It specifically hydrolyzes peptide bonds and degrades the triple helix of collagen, not degrading any other protein without a triple helix. This is an exclusive characteristic of collagenase, as no other currently available protease can digest collagen.13

In vitro and in vivo studies have shown that the enzyme can liquefy the necrotic tissue, without damaging the granulation tissue. Collagenases digest the lower portion of the devitalized tissue, following a bottom-up pattern. Thus, it shows a slower action than other debriding agents. In both in-vitro and in vivo investigations, collagenase has shown a
minimally aggressive effect on viable cells, and it may promote angiogenesis and epithelialization. Enzymatic agents like collagenase are believed to remove substrates required for bacterial proliferation or to encourage migration of antibodies, leukocytes and a better access of antimicrobial agents to the infected area.\textsuperscript{13}

Studies\textsuperscript{14-15} have shown the ability of \textit{in vitro} collagenase to promote fibroblast proliferation, keratinocyte migration, and preservation of growth factor and non-denatured collagen. An article\textsuperscript{16} published by Wounds, one of the most important journals on wounds worldwide, reported that several investigations, when analyzing collagenase selectivity, indicate this enzyme has great affinity for cleaving peptide bonds associated with collagen type I. This characteristic is considered favorable, just as its selectivity that can prevent degradation of other proteins present in the wound bed, for instance, growth factors. Therefore, intact collagen, surrounded by mucopolysaccharides, is minimally affected.

The enzymatic activity of collagenase is negatively impacted by detergents, ions of heavy metals (mercury, zinc or silver) and antiseptic solutions like povidone-iodine. However, hydrogen peroxide, Dakin’s solution, sodium chloride solution at 0.9%, polymyxin B, and bacitracin do not affect its activity. It should be noted that these studies providing such relevant information investigated ointments containing collagenase only, therefore, information not applicable to products with collagenase associated with chloramphenicol.\textsuperscript{13}

Topical antiseptics are essential antimicrobial agents in wound treatment rooms. They eliminate or inhibit microbial growth and they are developed to primarily control infections. In this sense, they have been used on wounds to prevent or treat infections for a long time.\textsuperscript{7,17} On intact skin, their use is consolidated and largely accepted. However, their prophylactic use as anti-infectious agents on open wounds, such as lacerations, excoriations, burns and chronic ulcers, has caused controversy for decades.\textsuperscript{17}

Unlike antibiotics that act selectively on a specific target, antiseptics have several targets and a broad spectrum of action, including bacteria, fungi, viruses, protozoans and even prions. Lower rates of resistance and risk of allergy associated with antiseptic agents favor their current popularity.\textsuperscript{17,18}

As reported by health professionals, antiseptics seem to be improperly used as a prophylactic measure to infection on superficial wounds, that is, without a systematic evaluation of patient and lesion. It can be a problem due to increased costs and the possible presence of MDR strains. Also, clinical observations and a growing number of authors suggest antiseptics may delay the healing process, with well documented cytotoxic effects of antiseptics on fibroblasts and keratinocytes, important cells for the healing process.\textsuperscript{7}

A study on the effects of antiseptics on fibroblast function reported reduced proliferation of normal human dermal fibroblasts in the presence of several antiseptics for 96 hours with some notable singularities. Hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}) and polyvinylpyrrolidone-iodine (PVP-I) reduced fibroblast migration and proliferation in a dose-dependent manner, fully interrupting these actions at final concentrations of 500μmol/l and 0.2%, respectively. Compounds with silver and chlorhexidine solutions showed a different tendency, with reduced proliferation only at high concentrations and increased proliferation at lower doses. Compounds with silver and chlorhexidine also presented a small impact on migration. In general, in all cases, most doses tested for all biocides reached 100% inhibition, indicating potential cytotoxicity at these concentrations. All antiseptics, in a dose-dependent manner, also reduced cell migration.\textsuperscript{18}

Experimental data suggest the effects of antiseptics on fibroblasts are more comprehensive than their toxicity only. Therefore, repeated and excessive treatment of wounds with antiseptics without proper indication may have negative results or promote a similar microenvironment to that found in chronic wounds. However, when used in proper moments and concentrations, some classes of antiseptics may help health professionals in the healing process of wounds. While antiseptics cannot be removed from the products for wound treatment, a risk-benefit evaluation should be conducted when using these products.\textsuperscript{18}

Iodine is an antiseptic agent of broad spectrum, available in alcoholic, aqueous and degemming solutions. An aqueous solution is used in wound treatment, usually as PVP-I, which contains 10% polyvinylpyrrolidone (which limits the availability of iodine, making it less toxic) and 1% free iodine, slowly released. The spectrum of action of products with iodine is broad and includes Gram-positive and Gram-negative bacteria, fungi, viruses, and protozoans. The absorption of PVP-I has been a concern in the treatment of
pregnant and lactating women, due to a possibility of transient hypothyroidism.\textsuperscript{7,17}

Through bacteriostatic and bactericidal mechanisms, products with iodine effectively reduce the bacterial load and are active against most species, certainly those found in the treatment of chronic wounds. Despite the antimicrobial advantages from products with iodine, several potential disadvantages have been observed in their clinical application in wound treatment, with different and controversial results.\textsuperscript{7}

A classic study\textsuperscript{19} demonstrated the cytotoxicity of PVP-I for fibroblasts unless diluted at 0.001%, as well as delayed epithelialization and reduced tensile strength of the wound. In several in vivo studies on iodine compounds, the authors concluded that, in humans, PVP-I has no negative impact on wound healing and may be effective in lowering the number of bacteria, thus reducing infections. They highlight that studies with animals have more conflicting results, as they depend on several variables and, therefore, should be interpreted with precaution.\textsuperscript{17}

In addition, it should be noted that, regardless current knowledge of proper microenvironment for wound healing, antiseptics in solutions should not be used, as they may cause cell damage and have not demonstrated benefits when compared to irrigation with saline solution.\textsuperscript{20}

Alcohol 70% was mentioned as a topical therapy for wounds in two health care centers (16.7%), used in the insertion of orthopedic pins and clean and dry surgical sites. Although several alcohols have demonstrated effective antimicrobial activity, ethyl alcohol (ethanol), isopropyl alcohol (isopropanol, 2-propanol) and n-propanol are the most commonly used in surface disinfection and skin antisepsis. They are safe and effective in hand hygiene, pre-surgery hand antisepsis and pre-surgery patient skin preparation. Still, they have an excellent bactericidal activity in vitro against most Gram-positive and Gram-negative bacteria; also acting against \textit{Mycobacterium tuberculosis}, several fungi and certain enveloped viruses. However, they are not sporicides and have weak activity against certain non-enveloped viruses. In general, the antimicrobial activity of alcohols is significantly lower in concentrations below 50% and excellent in the range of 60-90%. A negative aspect is the absence of a residual effect.\textsuperscript{7}

Of particular note, cleansing the sites of orthopedic fixator insertion using a saline solution, alcohol, H$_2$O$_2$ or an antibacterial soap to prevent infections was not effective when compared to no cleansing at all.\textsuperscript{11} It should be noted that alcohol was used in clean and dry surgical sites, a practice without scientific support.

The solution of H$_2$O$_2$ at 10 volume (3%) is commonly used as an antiseptic for wounds. It has an oxidizing effect that destroys anaerobic bacteria but loses its effect in contact with an organic material, such as pus or cotton gauze.\textsuperscript{4} Its use to remove blood from skin - mentioned by studied health professionals - is not supported by the literature, being probably an empirical practice. This solution at 3% shows the effectiveness of broad spectrum among \textit{in vitro} studies. Its strongest activity is for Gram-positive bacteria, but the presence of catalase in these bacteria make concentrations below 3% less effective. Likewise, catalases present in tissues may further reduce the bactericidal activity of H$_2$O$_2$ \textit{in vivo}. Although H$_2$O$_2$ is commonly used, few studies have analyzed its effect on the healing process of wounds and its effectiveness as an antiseptic agent.\textsuperscript{17,8}

In conclusion, H$_2$O$_2$ does not seem to have a negative impact on wound healing, but it is not effective in reducing bacterial density. It may be useful as a chemical debriding agent,\textsuperscript{17} however, it is not adequate for wound cleansing. Thus, this antiseptic has not been largely used, as there is no clear evidence that demonstrates its efficiency, and there are other deeply studied and widely accepted options in the market.\textsuperscript{4}

Two health care centers (16.7%) used antiseptic chlorhexidine, in degerming form, for cleansing of surgical incisions with secretion. It is a synthetic compound derived from a biguanide that has been indicated as a first-choice antiseptic for skin preparation for invasive interventions, partially due to its residual effect of six to eight hours and its high antimicrobial activity, low toxicity, and strong affinity for bonding to skin and mucous membranes. It is an effective solution against Gram-positive and Gram-negative bacteria, particularly for the first microorganisms. It presents weaker activity against fungi and tubercle bacilli and it is inactive against bacterial spores, except at high temperatures. Several studies indicate that chlorhexidine is not absorbed through the skin and has low skin irritation potential. However, it should not be in contact with eyes, middle ear or meningis. Its immediate bactericidal action is superior in relation to antiseptic solutions with PVP-I.\textsuperscript{7,21} It presents 0.05% dilution for wound cleansing and solution at 4% when used in surgical site preparation and hand hygiene.
Solutions at 2% have been recently made available for surgical site preparation. However, low concentrations (0.02%) are recommended for wound irrigation. For open wounds, an aqueous non-detergent formulation is recommended, as reported in this study.

Chlorhexidine seems to be relatively safe, with minor side effects for the healing process, and it may favor healing of open wounds with risk of infection. However, the results of studies conducted so far are not sufficient to draw conclusions about the use of chlorhexidine in open wounds. Clinical controlled studies must be conducted to evaluate its efficiency and safety.

Another product used in wound treatment reported by health professionals was essential fatty acids (EFAs). This fatty substance is comprised of linoleic acids (Omega 6) and linolenic acids (Omega 3), and it can be associated with vitamins A, E, and soy lecithin. EFAs are precursors of pharmacologically active substances, involved in the process of cell division and epidermal differentiation. They have the ability to change inflammatory and immunological reactions, altering leukocyte functions and speeding up the tissue granulation process, and they favor growth factors, promote mitosis and cell proliferation, help autolytic debridement and are bactericidal for *Staphylococcus aureus*. Linoleic acid is important for the transport of fats and maintenance of the function and integrity of cell membranes. They can be used directly on the wound bed or impregnated in gauzes, which should be changed every 24 hours at the latest.

With scarce clinical randomized controlled studies with human beings, it is not possible to generalize in clinical practice that EFAs positively affect the healing process or have an antimicrobial action. Thus, robust studies have to be conducted, with stronger methodological rigor, comparing the different formulations available containing fatty acids and their influence on the healing process.

It should be noted that the EFAs present in the wound treatment rooms were of kitchen use (sunflower oil). This fact is a point of concern, as this presentation is not authorized by the Brazilian Health Surveillance Agency (ANVISA, as per its acronym in Portuguese) for wound treatment.

Another therapy observed by this study was dexamethasone, a corticosteroid indicated for the treatment of inflammatory skin lesions: it acts on inflammation and pruritus. It is important to point out the use of this substance on wounds of non-inflammatory etiology may be harmful or useless, as it affects inflammatory reactions - characteristics of the first stage of the healing process, reduces or inhibits the immunological activity, nefibroplasia and neoangiogenesis, affects protein synthesis and reduces epithelialization.

Vaseline is a compound of saturated hydrocarbons of semisolid consistency derived from petroleum. It can retain water in the epidermis and prevent transcutaneous water loss, favoring moisturizing and growth of keratinocytes, as it penetrates the interstice of stratum corneum and allows it to grow after damages. However, using this substance in wound treatment has no support in the revised literature regarding its therapeutic action.

Despite the reality presented by this study, another study conducted in seven out of the eight health care centers located in one municipality in the state of Rio de Janeiro, Brazil, found only EFA, collagenase and/or iruxol<sup>6</sup>, sterile Vaseline and silver sulfadiazine for the treatment of chronic ulcers.

Due to the cost of modern topical therapies, it is not difficult to find in health care institutions a limited variety of products for wound treatment. However, when considering a cost-benefit evaluation, savings will probably be obtained from products and fewer nursing professionals to conduct the same activity, optimizing them to provide comprehensive health care and promoting a better quality of life for these patients.

Several products have been launched in the market in the last years for wound treatment. According to their context, the health care team should define the products that will provide better well-being to people with these lesions. Also, considering there is not a single topical therapy for all wounds, due to the specificities of every type of healing stage, nurses should learn about and test new technologies and resources available in the market and analyze their practices to enhance their power of argumentation with administrators and other health professionals to ensure proper conditions for effective therapeutic interventions for patients with wounds.

Of particular note, a study conducted in the city of Recife, Pernambuco Brazil, had the aim of evaluating the aspects related to the Basic Health Care structure for the treatment of patients with wounds. Specifically regarding the material resources for wound treatment, the centers were equipped with basic items, many times of controversial use.
This study\(^1\) found products like (topical and degerming) PVPI, silver sulfadiazine, neomycin sulfate, EFA, and collagenase, which, in some aspects, agree with the findings of our investigation.

We hope these results will help wound professionals analyze their therapies to increment with more adequate topical options to this population, discouraging empirical and inefficient treatments.

The limitations of this study are: being developed in a single city, which does not allow general conclusions; on the other hand, this study allowed to know the topical therapies currently used in wound treatment in the reality studied. Another limitation was collecting data from only one nursing professional from each health care center, although he was the one to provide wound care on the visit day to the centers, but the possibility of other professionals informing different therapies should not be discarded. Also, no information was obtained about what professional provided wound care, in terms of therapy selection or care provision and result evaluation.

**CONCLUSION**

This study observed that many topical therapies for wounds are used with no scientific support but standardized for wounds by the professionals providing wound care. This situation indicates training is needed for health professionals that treat patients with wounds to enhance safety and knowledge of patient care and the main characteristics and performance of available products for proper use, according to the epidemiological profile of patients treated in the health care centers, and consequently, prevent inadequate use or unnecessary expenses with products not indicated for wound healing.

In addition, this study observed that a stronger involvement of administrators is required aiming for investments in innovative topical therapies that favor healing and quality of life of this population, as the acquisition of proper products to fulfill such demand - like hydrogel, calcium alginate, activated charcoal, hydrocolloids, among others - is mandatory, considering the significant increase in the number of chronic wounds reported by the primary health care centers in Brazil, for instance, venous, neuropathic and pressure ulcers.

In the treatment of people with wounds, primary health care nurses should closely follow the patient through systematic evaluations, indications of proper therapies/coverage to the clinical conditions of the wound and patient, analysis of comorbidities and socioeconomic conditions of patients, prevention of complications, prescription of self-care actions, healthcare education, among others. However, it is not a definitive remedy; it should be recognized that healing some chronic wounds is beyond nursing actions. In these cases, nurses should request multiprofessional support to provide better, complete and decisive health care.

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