Assessment of a Wound Cleansing Solution in the Treatment of Problem Wounds

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Abstract: Chronic wounds will heal in most cases if provided an optimal local wound environment and therapy that addresses underlying disease. The quality of topical wound management will influence the speed of the wound healing process. The value of cleansing chronic wounds is considered a basic principle in modern wound management. Several methods are available for wound cleansing and debridement. Currently, there has been focus on measures of wound cleansing whereby debris and exudate are gently and continuously removed to prepare the wound bed for wound closure. For this purpose, physiological solutions or specific disinfectants may be used. This retrospective analysis of existing data was performed looking at the clinical efficacy and cost-effectiveness of using a wound antiseptic to treat problem wounds. Wound cleansing upon dressing changes using a polyhexanide containing solution (Prontosan®, B Braun, Melsungen AG, Germany) in venous leg ulcers was compared to cleansing with either Ringer's solution or saline. The wounds of the patients treated with polyhexanide solution healed faster and in more cases (97% versus 89%). The Kaplan-Meier mean estimate (and associated standard error [SE]) demonstrated a statistically significant difference between treatment groups ($P < 0.0001$) in time to healing. The Kaplan-Meier mean time to healing for the study group (SG) was 3.31 months (SE = 0.17) compared to 4.42 months (SE = 0.19) for the control group ([CG], saline/Ringer's solution).

Problem wounds are rarely affected by a single factor.[1] Delay in closure of a wound can result from problems such as poor perfusion, infection, pressure, and chronic venous hypertension.

To support wound healing, systemic factors and local factors should be addressed.[1-4] Local barriers to healing must be removed before attempting wound closure.

Sometimes a wound may present as healthy and granulating and yet does not heal. This could be due to the wound bed containing nonviable (senescent) cells or cells of the wrong phenotype. In either case, they are not responding to biochemical signals in a manner conducive to the wound healing process, leading to so called weak or problem wounds.[1-6]

The importance of individual matrix metalloproteinases (MMP) in the epithelialization process is not fully understood. Commonly, many MMP-9 positive neutrophils are observed in close proximity to the negative MMP-9 epithelium. Excess MMP-9 in a wound may deprive the keratinocytes of signals by extracellular matrix molecules. Additionally, MMP-9 can degrade a1-proteinase inhibitor, which can result in elevated neutrophil elastase activity. Thus, MMP-9 can contribute to unfavorable conditions in several ways and lead to delayed epithelialization.

IL-8 is a member of the α-chemokine family and is a potent neutrophil chemoattractant. Neutrophils, as "early responders" to wounds and infections, release enzymes to remodel the extracellular matrix of the tissues through which they migrate to reach the site of the wound. It is proposed that the host's cellular response to IL-8 enhances angiogenesis, but if these cells are of the wrong phenotype, wound healing could be delayed.[3,6]

There have been several studies investigating the contents of both problem and acute wound fluid in order to distinguish their differences.[5-7] Protease activity appears to be the major area of disparity between fluid types.

Chronic or problem wounds may develop due to an underlying disease that is complicated by relevant cofactors.[5-9] Wound healing may also be delayed due to the underlying disease, eg, chronic venous stasis, chronic lymphatic congestion, or arterial circulation disorders on a macro or micro level.

Chronic wounds that are not (clinically) infected are assumed to be colonized.[9] In the process of becoming chronic, the pathogens present in wounds are of different etiology, independent of the actual cause of the wound condition and may present with similar issues.[9-11]

More attention must be paid to the complex synergistic biotope in a problem wound.[11] Local reduction and/or elimination of isolated species is not useful and is frequently counter productive.[10]

An optimal wound healing environment is free of debris and nonviable tissue. The presence of necrotic tissue influences the wound environment and increases the risk for infection, even when aseptic wound management is carried out.[1,12]

Materials and Methods

A retrospective review was conducted on 59 patient records on the effect on venous leg ulcer healing using polyhexanide solution (study group). The retrospective analysis reviewed the clinical efficacy of wound cleansers in problem wounds. Wound cleansing upon dressing changes using polyhexanide solution in venous leg ulcers was compared to cleansing with either Ringer's solution or saline (control).

The results of the study group (SG) were compared with 53 control group (CG) patients, who were selected in adherence to the same inclusion/exclusion criteria. In the CG, wounds were cleansed using either Ringer's solution or saline, initiating the wet-to-dry phase. The healing pattern of the ulcers was evaluated for time to healing, wound bed condition, pain, and patient comfort during dressing changes and wound cleansing. A comparison of the SG and CG was made by assessing the percentage of healed wounds in relation to the time to ulcer closure.

The polyhexanide wound rinsing solution (Prontosan®, B Braun, Melsungen AG, Germany) contains a preservative that prevents bacterial growth and ensures sterility for up to 8 weeks. The product contains undecyleneamidopropyl betaine, as a surface-active substance that penetrates difficult coatings and removes debris and bacteria. The proposed mechanism of action for this wound cleansing solution is based on its low surface tension, supporting physical removal of debris and bacteria.[13,14]

Polyhexanide, a polymerized form of chlorhexidine, has been shown to have microbicidal activity and good tissue compatibility for its activity against acid lipids of bacterial cell membranes and its minor effect on the neutral lipids of human cell membranes.[15]

Polyhexanide solution is reported to support wound healing[16] and has demonstrated efficacy in the management of nonhealing chronic and/or refractory wounds (eg, second degree burns), as well as for lavages.[15-19]

The product may be combined with various dressings such as alginates and hydrofiber. Due to tissue compatibility and the absence of irritation, application under semiocclusive and occlusive dressings is possible.[20] Polyhexanide solution is available as a raw material to manufacturer pharmacy-prepared solutions and as a ready-to-use solution for wound antisepsis (Prontosan W® MIC). The product is classified as a class II medical device. Polyhexanide solution may not be used in combination with other wound cleansing soaps, ointments, oils, enzymes, etc.

The wounds included in the study were cleansed utilizing a "wet" phase and a short resting phase or "dry" phase, in order to restore periwound skin integrity.[14] During the short cleansing phase (15 minutes) the need to warm the cleansing fluid to room temperature is not

mandatory. The aim is not necessarily to create an optimal physiological wound environment or temperature. The wet to dry phase is a wound cleansing measure that also aims at reducing itching and inflammation.[14]

In case of extensive inflammation, patients have reported this cooling phase, which begins after the wet phase, to be soothing. The wet phase may be a topical measure as part of the wound treatment regimen. The rinsing fluid used should be clinically effective, nontoxic, nonirritant, and hypoallergenic. Ringer's solution is another rinsing option apart from the use of saline.

Two or 3 layers of gauze or nonwoven material may be used as a fluid carrier medium. As an alternative, a moist wound healing dressing, such as a hydrofiber, may be used. Depending on the wound bed condition the fluid is selected with which the gauze or carrier is moistened.

Phase 1: fluid is donated from the moist wrap to the wound bed and the periwound skin for about 10 to 15 minutes.

Phase 2: the remainder of the fluid is released from the wrap, leading to wound cleansing and cooling, as well as reduction of inflammation.

Phase 3: in the following minutes (up to a maximum of 6 hours), evaporation continues and the dressing is saturated with debris, exudate, and pathogens and will require changing.

Dry phase: the wound is covered with a dry dressing (sterile gauze); this phase takes about 15 minutes, after which the wound is covered with a moist dressing.

The patients included in the evaluation had venous leg ulcers. They were recruited from a community wound healing clinic (Gesundheitsmanager, Schwaig/Nuremberg, Germany) and were selected from outpatients of the authors' practice. Patients were recruited to the study using inclusion and exclusion criteria. The ulcer had to be present for at least 3 months. Each patient's clinical history was evaluated. A physical examination was performed on all patients. A duplex scan was used to confirm presence of chronic venous hypertension. Patients with persistent, severe, arterial circulatory disorders (Stage II and higher according to Fontaine) were excluded.

All patients received standardized compression therapy using under-padding and 2 layers of short stretch bandages.[21] Bandages were changed every 5 days on average. Depending on the ulcer stage and exudate production, an absorbent moist wound healing dressing such as an alginate and/or foam dressing, was used to cover the wound. The evaluation focused on clinical efficacy, time to ulcer closure, and wound evolution. The patients were followed until ulcer closure. The maximum observation period was 6 months. All cases that were analyzed had complete follow-up documentation. Cases for which there was no follow-up documentation were not included.

Results

Patient population. The CG included 14 men and 39 women (n = 53) with an age range of 47 to 89 years (mean = 75). The SG included 17 men and 42 women (n = 59) with an age range of 55 to 93 years (mean = 77).

In the CG (saline/Ringer's solution), 47 of 53 wounds (89%) healed completely during the 6-month observational period (Table 1 and Figure 1).

In the SG (polyhexanide solution), 57 of 59 wounds (97%) healed completely during the 6-month observational period (Table 2 and Figure 1). A direct comparison of healing performance is shown in Figure 1.

Wound infection was defined as the presence of typical clinical signs of infection (eg, redness, swelling). With regard to the frequency of infections during the course of treatment, regardless of the condition at the beginning

Table 1. Evolution of ulcer closure for the control group (n = 53).

Months of treatment	Evolution of ulcer healing (control group)		
	Patients/month	%/months	Cumulated %
1	1	2	2
2	4	7	9
3	10	19	28
4	12	23	51
5	9	17	68
6	11	21	89
	Total		%
Ulcer not closed after 6 months	6		11

Table 2. Evolution of ulcer closure for the study group (n = 59).

Months of treatment	Evolution of ulcer healing (study group)		
	Patients/month	%/months	Cumulated %
1	4	7	7
2	13	22	29
3	18	31	60
4	13	22	82
5	7	12	94
6	2	3	97
	Total		%
Ulcer not closed after 6 months	2		3

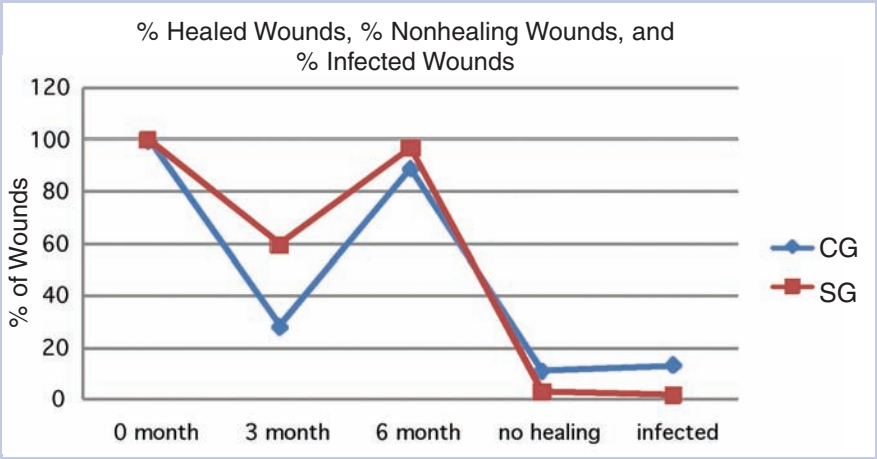

Figure 1. Results after 6 months of treatment for the patients with wounds in the control group ([CG], n = 53) and the study group ([SG], n = 57).

of therapy, the following was observed:

- CG (saline/Ringer's solution, n = 53), infection during the course of treatment occurred in 7 cases (13%). No signs of infection were noted during the course of treatment in 46 cases (87%).
- SG (polyhexanide, n = 59), infection during the course of treatment was noted in 2 cases (3%). There were no signs of infection noted during the course of treatment in 57 cases (97%).

The wounds of the patients treated with polyhexanide solution healed in more cases during the 6-month period (97% versus 89%) and healed in a shorter time (60% versus 28% for CG) within the first 3 months of treatment. Additionally, the healing time was compared between the 2 treatment groups using a log-rank test. Patients not reporting a healing time had their data censored at 6 months. The Kaplan-Meier mean estimate (and associated standard error [SE]) were calculated for both treatment groups. There was a statistically significant difference between treatment groups ($P < 0.0001$) in time to healing. The Kaplan-Meier mean time to healing in the SG group was 3.31 months (SE = 0.17) compared to 4.42 months (SE = 0.19) for the CG (saline/Ringer's solution).

Discussion

Wound treatment, especially in an outpatient setting, may present organizational and hygienic problems. Infections in the course of treatment of secondary healing wounds occur frequently. Infection rates of secondary healing wounds in relation to place, type, and duration of treatment, as well as wound etiology, are reported to be almost 10% of wounds treated.[10] Precaution must be taken to exclude patients from treatment that are known with hypersensitivity to polyhexanide.

Currently, a focus has been placed on measures of wound cleansing as part of wound bed preparation that gently and continuously removes debris and exudate to prepare the wound bed for closure.

One measure to prevent secondary wound infection is cleansing during dressing changes;[1,2] physiological solutions or specific cleansing fluids and disinfectants may be used.

More attention must be paid to the complex, synergistic biotope in a problem wound.[4] The application of a wound antiseptic or a wound cleansing fluid may be useful to support prevention of infection for these so called weak wounds. Therefore, the use of anti-infectious measures (local and/or systemic) may be needed less frequently.[1,14]

According to current research, local reduction and/or elimination of isolated species may not be useful and even counterproductive, as an existing balance may be disturbed.[16]

The use of a wound cleansing solution such as polyhexanide, which has low surface tension, may support physical removal of debris and bacteria.[16] This mechanism may help to explain why wound infection was less frequent in the SG (n = 2/59, 3%) when compared to the control group (n = 7/53, 13%). Furthermore, the percentage of healed wounds after 6 months (97%) was significantly higher ($P < 0.0001$) in the study group when compared to the control group (89%).

Overall, healing rates reported for both groups were in line with healing rates reported in the literature,[20] as the selected population for the present study had venous leg ulcers and received adequate compression therapy with short stretch bandages.

When comparing the performance of polyhexanide solution to conventional saline/Ringer's wound cleansing, it should be noted that wound healing is a highly complicated multifactorial process and is not exclusively defined by the wound dressing materials and the creation of optimal local wound bed conditions. However, it is recognized that local wound management measures play an important role.[1,10,12]

Moist wound treatment is considered the standard in topical wound therapy.[1] Typically, neutral physiological solutions are used for wound cleansing. A new approach to wound cleansing must be at least comparable to this standard. The patient population treated with polyhexanide solution in the present study had more ulcers closed and their time to healing was significantly less in comparison to the control group.

Conclusion

Wound cleansing with polyhexanide solution contributed significantly to optimization of the local wound environment. Wound cleansing was effective and helped prevent secondary infection, especially in "weak" wounds. This may help to prevent complications and thus shorten total treatment duration.

Polyhexanide solution in a modern wound treatment regimen seems to be useful and safe for wound cleansing in between dressing changes and may be combined with wound dressings, especially in the management of "weak" wounds.

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