WOUND CLEANING AND WOUND HEALING – A CONCISE REVIEW

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Background

- Three procedures; debridement, irrigation, and cleaning form the basis of standard wound care and are widely held to improve the healing of chronic wounds.
  - Debridement describes the mechanical removal of dead tissue;
  - Irrigation the application of fluid streams under pressure to the wound; and
  - Cleaning (also termed "cleansing") the more gentle application of any fluid to the wound.
- Published literature shows that cleaning improves the wound environment and accelerates healing. Although the cleaning of wounds with antiseptic solutions prevents infection[1] it is not well established that irrigating wounds with antiseptic solutions enhances wound healing.

Objective

- The objective of this review is to evaluate the safety and efficacy of currently available wound cleaning agents and their ability to enhance wound healing.

Methods

- This review is based on a literature search for studies addressing cleaning of chronic wounds. The search was performed in February 2012 at PubMed using the following terms: Chronic[All Fields] AND ("wounds and injuries"[MeSH Terms] OR ("wounds"[All Fields] AND "injuries"[All Fields]) OR "wounds and injuries"[All Fields] OR "wound"[All Fields]) AND (cleaning[All Fields] OR cleansing[All Fields] OR washing[All Fields]) AND "humans"[MeSH Terms].

  One hundred and sixteen papers were found and 31 were analyzed in detail following a preliminary review. Further relevant papers were cited in these 31 publications, and have been included. Classification of the evidence of the effect of the cleaning agents was that proposed by the American Association of Chest Physicians Task Force (AACP).

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Results & Summary

Options for Wound Cleaning

- Efficacy in enhancing wound healing is reported in a number of ways: time to complete healing or percent reduction in wound area at a given time point; by the use of surrogate markers such as infection or colonization rates; or by the use of subjective markers such as wound appearance or degree of encrustation. Many studies are small, uncontrolled or anecdotal, and are often old: of the 116 studies initially identified only 36 (31%) had been published in the last five years.
- There is a wide range of solutions available to clean a wound. Water and saline have been widely used, but are ineffective in reducing the bio-burden associated with wounds, and their use is not associated with improved wound healing. Tap (potable) water is as (in)effective as sterile saline. Disinfectants such as povidone iodine, ionized silver (alone or in an activated charcoal dressing), chlorhexidine, alcohol, acetic acid, hydrogen peroxide, and chlorine-based agents such as sodium hypochlorite and N-chlorotaurine, have also been used in spite of their *in vitro* toxicity to human fibroblasts. Chlorhexidine, povidone iodine and hydrogen peroxide have been shown to delay wound healing. There are no adequate studies documenting the efficacy of alcohol, acetic acid or hydrogen peroxide in enhancing wound healing.
- Alternative agents such as tea tree oil have been evaluated in pilot studies, with no success in eliminating methicillin resistant Staphylococcus aureus (MRSA). As well as liquid cleansing agents, solids applied to the wound may be effective. In a pilot study application of sugar to the wound subjectively improved wound healing, *in vitro* evaluation showed reduced bacterial growth[2]. Honey is similarly effective.

Silver, chlorhexidine and alcohols

- Silver, when ionized, is an effective antimicrobial. However, its duration of action may be shortened by binding to proteins or chloride ions, and there is no evidence that it accelerates healing[3]. Chlorhexidine is available both as a dilute (0.05%) solution for wound irrigation, and as a 2 or 4% skin scrub. The latter is sometimes inappropriately used for wound care. There is some evidence of toxicity and little evidence of efficacy at either concentration[4]. Ethanol, isopropanol and n-propanol are widely used for surface disinfection and skin antisepsis; antimicrobial activity requires a concentration of > 50% and ideally in the range 60-90%[5].

Polyhexanide/Betaine

- Solutions or gels containing 0.1% of the antimicrobial agent polyhexanide and 0.1% of the surfactant betaine, are used for wound cleaning and have been recently shown to enhance wound healing. Polyhexanide causes expansion and fluidization of negatively charged phospho-lipid bi-layers, making the bacterial cell membrane leak and ultimately causing cell death[6]. Polyhexanide / betaine in concentrations of up to 2µg/mL does not inhibit human keratinocytes[7], and, thus, the healthy skin. Polyhexanide has a biocompatibility index >1 indicating that tissue toxicity is low. Polyhexanide / betaine remove coagulated plasma protein deposits more effectively than Ringer's solution and saline. In a randomized controlled porcine study, cleaning with polyhexanide was associated with the most rapid closure of superficial wounds, significantly ($p<0.05$) reducing the time to closure to 22.9 days to 24.1 days compared to placebo (Ringer's solution)[8].
- Polyhexanide is well tolerated with sensitization rates of about 0.5%. In an open study of ten patients with chronic wounds who had previously been treated with saline cleansing, polyhexanide / betaine cleansing produced improvement in patient quality of life, reduction in wound odor, exudate, pain and wound size[9]. In a retrospective case-controlled study of 112 patients with chronic leg ulcers, polyhexanide / betaine was compared with cleansing with saline or Ringer's solution[10]. In a single blind, randomized, controlled study of 40 patients with chronic leg ulcers polyhexanide / betaine was compared with saline cleaning. Follow-up was restricted to four weeks, after which time no difference in wound size was observed; however polyhexanide / betaine patients reported significantly less wound pain, and had significantly lower wound pH values, a factor associated with improved wound healing. Laboratory data showed anti-bacterial effects[6,11].

Povidone Iodine

- Povidone iodine preparations are effective antimicrobial agents, but positive effects on wound healing are not well defined, and systemic iodine absorption may produce clinically significant side-effects. Comprehensive reviews describe the conflicting results of multiple animal and human studies assessing the potential toxicity and the effect on healing rates associated with povidone iodine preparations[12,13]. One explanation may be that povidone iodine solutions do not inhibit wound healing *in vivo*, but many commercially available preparations also include detergents, which do delay wound healing, and the wound must be irrigated with water or saline after use if povidone iodine cleansers with detergent are to be used[14]. No studies have shown a statistically significant benefit from the use of povidone iodine in wounds other than burns although pooled data from two studies in the healing of lacerations suggest that povidone iodine might be superior to saline.

Implications for Clinical Practice

- The efficacy of the various agents for wound cleansing is summarized in Table 1 together with the strength of evidence classification. While all active agents are effective antimicrobially effective *in vitro*, efficacy in enhancing wound healing is uncertain. The one exception seems to be polyhexanide / betaine, with several studies indicating efficacy in enhancing wound healing. Water and electrolyte solutions are ineffective.
- To summarize, some level of effectiveness regarding wound healing in vivo has only been documented for polyhexanide / betaine (1B) and to a lesser degree (2C) for povidone iodine and silver, which is in line with their anti-microbial activity *in vitro*, while for the remaining compounds no positive clinical effects on wound healing have been demonstrated.

Table 1: Summary of Cleaning Agents

Cleansing Product	Improves Wound Healing	Effective Anti-microbial Against Common Wound Contaminants *in vitro*	Toxicity *in vitro*
Acetic Acid	Ineffective: 2C[1]	Effective: 1B[1]	Toxic: 1B[1,15]
Alcohol	Ineffective: 2C[1]	Effective: 1B[5]	Toxic: 1B[15]
Chlorhexidine	Ineffective: 2C[1,4,16]	Effective: 1B[5]	Toxic: 1B[1,4,15]
Hydrogen peroxide	Ineffective: 2C[1,16]	Effective: 1B[1]	Toxic: 1B[1,15,17]
Polyhexanide / betaine	Effective: 1B[1,8,10,18]	Effective: 1B[5,6,11]	Low Toxicity: 1B[5,6,19]
Povidone Iodine	Effective: 2C[1,5,12,13,16,20]	Effective: 1B[5]	Toxic: 2C[15]
Saline	Ineffective: 1A[21,22]		
Silver (ionized)	Effective: 2C[3,23,24]	Effective: 1B[1,24]	Toxic: 2C[5,15]
Sodium hypochlorite	Ineffective: 2C[1,21,26]	Effective: 1B[1,21]	Toxic: 1B[1,15,17]
Water	Ineffective: 1A[22]		

Conclusions

- There are very few adequate studies on the wound cleaning properties of most of the agents discussed in this review, and thus insufficient evidence of their clinical effects on wound healing.
- With more credible evidence of local toxicity, consensus opinion rejects the routine use of antiseptics in chronic wound care.
- Recent data suggests that polyhexanide / betaine may be both effective and non-toxic.
- Data from *in vitro* studies may be indicative but are no proof of clinical efficacy.

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- **Additional references are available upon request.**