Addressing the challenge of wound cleansing in the modern era

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Abstract
Over the past two decades a body of evidence has been generated to support the traditional use of water in cleansing wounds, with studies showing that the use of clean water does not increase the risk of infection or delay healing. However, recent advances in the understanding of wound management have encouraged reforms and led to the development of wound cleansing agents that have the potential to improve clinical outcomes. This article draws on in vitro and in vivo evidence including comparative studies of patients with acute and chronic wounds to consider the evidence supporting alternatives to water in wound cleansing.

Key words: Antimicrobial • PHMB • Biofilm • Wound cleansing

Over the last 20 years, a body of evidence has been produced that supports the use of water as the wound cleanser of choice in the management of acute and chronic wounds. This research has generally focused on relative wound healing rates, and the comparative incidence of infection following wound cleansing with water or alternative cleansers. The comparative data produced in respect of post cleansing infection rates was produced following the diagnosis of infection using accepted Celsian clinical signs of infection, and/or in light of supportive laboratory culture of wound sampling. This work has been welcomed, and has broadly indicated that provided the water used in the cleansing process is at least of potable quality, wound healing will not be delayed. However, increasing insight over recent years as to how bacteria 'behave' when residing in and on soft tissue has indicated that although cleansing a wound with water may not be harmful, it may not play an active role in the promotion of healing, especially when managing chronic wounds where infection may be present without an associated host response. Is it now time to reconsider our approach to wound cleansing, and to contemplate an alternative to water as the cleansing agent of choice?

Why and when wounds require cleansing
It has been suggested that a wound may require cleansing when there is problematic excess exudate, the exudate is obviously infected, foreign body contamination, gross contamination by dirt or bacteria, and when slough or necrotic tissue is present (Cutting, 1990). The value of water as a wound cleansing agent during the late 1980s and early 1990s should be viewed against the backdrop, at that time, of increasing in vitro evidence that the use of topical antiseptics was harmful to healing tissue (Brennan, Foster et al, 1986; Brennan and Leaper, 1985; Deas, Billings et al, 1986), and therefore caution in use was advised. Less clear, however, was the answer to the question of when in the history of a wound cleansing should take place, and the relevance of variations in practice in cleansing acute and chronic wounds. The advances made in our knowledge and understanding of wound care management in the last 20 years have encouraged reforms, and led to the introduction of wound cleansing agents that have the potential to improve clinical outcomes.

Background to wound infection
The human body contains an estimated $10^{14}$ cells, of which only 10% are mammalian (Teitelbaum and Walker 2002). The remainder are resident microbial flora, engendering an associated potential for disease that is always present despite the fact these microbiota have a role to play in maintaining individual health.

The potential for a wound to become infected is high as a wound surface is always heavily contaminated with a variety of bacterial species which may be aerobic and anaerobic (Bowler, Duerden et al, 2001). This, together with availability of fluid and nutrients found in wound exudate and the moist environment, contribute to an ideal setting for bacterial proliferation. Maintaining the wound bioburden at a level where the host remains in control is therefore an important aspect of management if avoiding the onset of wound infection with associated increase in patient morbidity is to be achieved.

In an immune-competent individual who is wounded, a cascade of cellular and biochemical activity is activated with the initial objective of cleansing the wound. This process includes the removal of micro-organisms and tissue debris from the wound bed and is associated with the generation of the Celsian signs of inflammation; redness, swelling, heat and pain. Temporal extension of the acute inflammatory response will be observed if infection intervenes. A range of factors increase the risk of supervening infection, including age, systemic disease, poor nutrition, down-regulation of the immune response and poor tissue perfusion of oxygen. In addition to the signs identified by Celsus, subtle indicators of infection have been categorized (Cutting and Harding, 1994; Cutting, White et al, 2005). The related accuracy of these subtle signs of infection has been tested (Cutting, 1998; Gardner, Frantz et al, 2001).
Sub clinical infection (biofilms)
Accurate clinical assessment of a wound is a necessary and regularly repeated responsibility. Although acute wounds are easy to identify by virtue of their aetiology; chronic wounds may only be verified retrospectively. A corollary of this is the difficulty in determining the specific cause of the delay in healing. This has contributed to the generation of a classification system whereby wound features or characteristics are appraised. Such characteristics may include (among others) type and level of exudate, condition of the wound edge, wound bed tissue type, and ‘infection’. Although the features of wound infection have been characterized (Cutting and Harding, 1994; Cutting, White et al, 2005), recent publications investigating wound biochemistry and cellularity (Armstrong and Jude 2002; Diegelmann 2003; Schultz, Mozingo et al, 2005; Smith, 2006; Yager, Kulina et al, 2007) indicate that chronic wounds are ‘fixed’ in a state of chronic inflammation, suggesting that a link exists between chronic wounds of different aetiologies. How can this chronic inflammatory state (which delays healing) exist without eliciting an obvious response from the host? A number of mechanisms have been proposed and three are referred to here. Allen et al (2005), have construed that pyocyanin (a virulence factor) expressed by P. aeruginosa is capable of suppressing the acute inflammatory response and is therefore able to immuno-evoke. Stephens et al (2003) have identified the importance of anaerobic organisms in chronic wounds and the related suppression of cellular wound healing responses. Wound biofilm provides a robust explanation for delayed healing. It has been reported that biofilms prevail in chronic wounds but are rare in acute wounds (James, Swogger et al, 2008). The view that biofilm is a significant barrier to healing (Bjarsholt, Kirketerp-Moller et al, 2008) would be supported by replication studies, particularly in vivo, exploring the differences in healing between acute and chronic wounds.

Biofilms’ role in delayed healing
Biofilms are complex microbial communities that are embedded in an extracellular matrix of proteins, nucleic acids and polysaccharides (slime) and are attached to a surface (Cooper and Okhiriia 2006). Within the extracellular polymeric substance (EPS) a biological diversity may be found. The rison d’etre of the biofilm is survival, and the EPS provides protection to the community from chemical and neutrophil attack. In addition to the maintenance of a chronic inflammatory state the sessile (attached) bacteria release proteases. The potential exists for these bacterial (exogenous) proteases to work in tandem with human (endogenous) proteases and degrade growth factors and tissue proteins that are integral to the healing process. It has also been proposed that effete neutrophils release proteases which inhibit the ‘search and destroy’ function of macrophages. The resulting tissue destruction and additional production of pro-inflammatory cytokines sustains the chronic inflammatory state (Wolcott, Rhoads et al, 2008).

Biofilm management
The concept of Biofilm Based Wound Care (BBWC) has been suggested as an effective method of managing biofilm infections (Wolcott, Rhoads et al, 2008). Integral to this concept is the utility of debridement (Eldor, Raz et al, 2004; Williams, Enoch et al, 2005; Wolcott and Rhoads, 2008) in order to realise physical removal and suppression of biofilm. As a diagnostic tool for biofilm is currently not available, much debate exists around ‘when to treat’. The significance of delayed healing as a result of biofilm presence is becoming recognised (Percival and Dowd, 2010; Schierle, De la Garza et al, 2009), and as such the relationship of delayed healing and the need for debridement is being acknowledged (Wolcott and Rhoads, 2008). Discussion continues over whether it is possible to ‘see’ a wound biofilm. As biofilm communities are microscopic it needs to be emphasised that it is not possible to visualise wound biofilm with the naked eye. However, it has been proposed that visual cues may be present that suggest biofilm presence. Cutting et al (2010) propose that the presence of slough in a chronic wound provides a visual indication of biofilm existence in a wound and that slough itself is a living bioburden conglomeration that necessitates debridement of the wound.

An additional component of BBWC is concurrent use of antimicrobials (Wolcott and Rhoads, 2008). Concern has been raised about a possible association between bacterial resistance and the widespread and sometimes indiscriminate use of antimicrobials (Russell, Tattawasart et al, 1998), (Tambe, Sampath et al, 2001). It has also been stated that through the implementation of appropriate policies, inappropriate antimicrobial use can be reduced (Jarvis, 1996). The focus of this paper was on improving clinician use of antimicrobials through the development and implementation of antimicrobial use committees. Extensive and acceptable use, in microbiological and clinical terms, of antimicrobials is vital. Antiseptics have been reported as having a positive contribution to make in the control of wound bioburden in wounds that are clearly infected or those that are at risk of infection (White, Cutting et al, 2006).

When deciding whether or not to use an antiseptic, it is important that wound chronicity as a result of biofilm presence is considered (Nelson, 2003).

Polyhexamethylene biguanide (PHMB)
Polyhexamethylene biguanide (PHMB) is also known as polyhexanide and polyaminopropyl biguanide. It is a commonly used antiseptic that is now incorporated into a number of dressings. PHMB compounds (polymeric biguanides) have a broad spectrum of biocidal activity and have a wide range of uses. They have been used as contact lens cleansers, in mouthwashes and as an antiseptic including use in wounds (Fabry, Trampenua et al, 2007; Motta, Milne et al, 2004; Nascimento, Tanomaru et al, 2005; Salas Campos, Gómez Ferrero et al, 2006; Santodomingo-Rubido, 2007). PHMB is regarded as being safe to use following exposure committees. Extensive and acceptable use, in microbiological and clinical terms, of antimicrobials is vital. Antiseptics have been reported as having a positive contribution to make in the control of wound bioburden in wounds that are clearly infected or those that are at risk of infection (White, Cutting et al, 2006).

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Evidence of Prontosan efficacy
In an in vitro study comparing efficacy of four sterile wound
cleansing solutions (saline, Ringer’s solution, Prontosan and
Octenisept) on a wound coating model, Prontosan was the only
solution that fragmented the test coatings and solubilised the
denatured proteins (Kaehn 2009). The author concluded that this
is an indispensable asset in order to achieve thorough yet gentle
wound cleansing.
In an in vivo animal study Prontosan’s activity on biofilms of
metillin resistant Staphylococcus aureus using a porcine partial
thickness wound model was evaluated (Davis, Rivas et al, 2007).
Mean counts of wound MRSA were recorded at 48 and 72
hours in four treatment groups; untreated control, sterile saline,
Ringer’s solution and Prontosan. A comparative reduction in
MRSA at 48 and 72 hours was found in the Prontosan treated
group. The reduction in the Prontosan group at 48 and 72
hours was found to be statistically significant compared to the
other groups (p<0.05). The study report records that the largest
reduction of MRSA, following cleansing with Prontosan, was
found from 48 to 72 hours signifying that extended irrigation
may provide additional reduction in wound bioburden.
In a retrospective review of venous leg ulcer healing in 112
patients the clinical efficacy of wound cleansers was examined
(Andriessen and Eberlein, 2008). At dressing change the study
group received the wound rinsing solution Prontosan (n=59)
and these were compared with the control group who received
either Ringer’s solution or saline (n=53). Inclusion/exclusion
criteria were applied to both study and control groups and the
healing pattern of the ulcers was evaluated. The results show that
more patients in the study group healed in the 6 month period
when compared with the controls – 97% v. 89%. A shorter time
to healing was also recorded in the study group when compared
with the control group – 60% v. 28% within the first 3 months
of treatment. Mean time to healing was 3.31 months (study
group) compared to 4.42 months (control group) p<0.0001.
These findings sustain the results found in the Kaehn (2009) in
vitro study.
Out-patients (571 women, 382 men) were recruited to a
retrospective study examining efficacy of PHMB rinsing solution
and PHMB-containing wound gel (Moller, Nolte et al, 2008).
Wound types included diabetic foot – 62%, venous leg ulcers
– 10%, pressure ulcers – 8%, post operative wound dehiscence –
16%, and radiotherapy wounds – 4%. At every dressing change
the wound was cleansed with the PHMB irrigation solution and,
depending on clinician decision, the PHMB gel or solution was
used. The wounds were dressed with a foam dressing if lightly
discharging or a fibrous dressing if more heavily exuding. On
entry into the study 41% of patients (391) had a wound infection
as determined by classical signs of inflammation (local infection)
or systemic signs – raised CRP, ESR, leucocytosis, or fever.
One hundred and five patients (11%) had heavily contaminated
wounds. These patients received systemic antibiotics in addition
to PHMB solution/gel. Following treatment the wound infection
rate fell from 41% to 3% and antibiotic therapy was not required.
Wound closure was achieved in 80% of wounds and 3% showed
no improvement. Patient evaluation shows that PHMB solution/
gel was painless in 99% of cases, and almost 66% reported an
improvement in wound odour. The treatment was well tolerated
with an improvement in patient quality of life.
Wound cleansing and infection with biofilm
phenotype
A recent Cochrane Collaboration Review (Fernandez, Griffiths
et al, 2010) reviewed randomised and quasi randomised controlled
trials that compared water (cooled boiled water, distilled water
and tap water) with the use of sterile saline and with another
solution used for wound cleansing (*procaine spirit) in patients
with acute and chronic wounds.
Their conclusions are not surprising, stating that there is no
evidence that tap water increases infection when used to cleanse
acute adult wounds and some evidence that it reduces it. The
authors also added that there is not strong evidence that cleansing
wounds per se increases healing or reduces infection. However,
as with all systematic reviews the report needs to be read bearing
in mind the associated confines that are imposed on this type of
work. Cleansing was defined as ‘the use of fluids to remove loosely
adherent debris and necrotic tissue from the wound surface’. Yet,
Rodeheaver and Ratliff (2007) offer a more detailed definition
of wound cleansing as ‘remove surface contaminants, bacteria and
other materials surrounding skin’. As the Cochrane review included studies
that compared wound healing outcomes/infection rates in wounds
cleansed with the aforementioned agents it would seem that the
latter definition would have been more appropriate.

*Procaine spirit is procaine HCL 2% with alcohol 70%. Anecdotal evidence
suggests that it is commonly prescribed as a wound cleansing agent following
surgery in Australia and Singapore.
In addition, the Cochrane review was unable to provide any insight into the impact of the cleansing modalities on wound biofilm. Recent attention has focussed on biofilms, (Cooper and Okhira, 2006) – bacterial communities that reside on and possibly in the wound bed, and that exhibit resistance to traditional antimicrobial therapy (Percival, Cooper et al, 2010). Biofilms are becoming recognised as a major inhibitor to wound healing (Cutting et al, 2010), and as such their management in the wound environment needs to be addressed.

In respect of anti-biofilm efficacy of PHMB, some research is available. Clinical isolates of E. coli and S. epidermidis were exposed to five biocides at various concentrations and the biocidal activity was recorded. PHMB and peracetic acid were found to be the most active towards planktonic (free floating) cells and demonstrated a corresponding activity towards biofilm phenotype bacteria (Gilbert, Pemberton et al, 1990; Gilbert, Das et al, 2001).

In a clinical evaluation of 10 community patients with longstanding wounds (1–5 years; mean 2.6 years) Prontosan was used as the wound cleanser replacing normal saline that had been used for at least one month previously (Horrocks, 2006). Objectives of the evaluation included achieving a visible wound bed within 3 weeks of treatment, reducing wound size, ascertaining patient comfort with Prontosan, ease of application, and the recording of any adverse reactions. Achieving a visible wound bed was correlated with removal of wound biofilm in this cohort evaluation, and although this association cannot be conclusively confirmed this outcome does complement a number of the findings. These findings included an overall reduction in wound size (confirmed by photography and wound tracings); previous malodorous wounds were no longer odorous; and all patients reported considerable reduction or elimination of wound pain. Patients also reported considerable improvement in quality of life, and a reduction in community nurse visits. Horrocks (2006) concludes that Prontosan appears to offer a safe and cost-effective method of wound cleansing, being more efficient than normal saline.

Conclusions

Choice of cleansing solution should reflect the individual requirements of the wound and the patient and be underpinned by a sound knowledge/experience base. Numerous investigations have explored the merits of water or saline in wound cleansing, with the most profound conclusion being that wound cleansing with potable quality water appears to do no harm. The question that has yet to be answered is, which wound cleanser supports optimal healing so that patient morbidity is reduced, and expenditure in terms of both human and material resources is maintained at an economic level? If current thinking, that all chronic wounds are biofilm wounds (Wolcott and Rhoads, 2008), is sustained then we will need to rethink our approach to wound cleansing, as the studies examined above indicate that PHMB, in conjunction with a surfactant, is superior to isotonic solutions. In addition, there is evidence emerging that Prontosan is an effective wound cleanser in longstanding (chronic) wounds and has been found by patients to be pain-free, improve patient quality of life, effectively manage wound infection and to reduce the overall time to healing.


Pizurio-Guzmán NM (2009) Rhamnolipid biosurfactant production from glycerol: new methods of analysis and improved dentrifying fermentation. The Graduate Faculty of The University of Akron


