Wound cleansing, topical antiseptics and wound healing

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ABSTRACT

Quality of care is a critical requirement for wound healing and 'good' care of wounds has been synonymous with topical prevention and management of microbial contamination. Topical antiseptics are antimicrobial agents that kill, inhibit or reduce the number of microorganisms and are thought to be essential for wounds infection control. However, they have long and commonly been used on wounds to prevent or treat infection, the merits of antiseptic fluid irrigation have received little scientific study. Unlike antibiotics that act selectively on a specific target, antiseptics have multiple targets and a broader spectrum of activity, which include bacteria, fungi, viruses, protozoa and even prions. Although certain skin and wound cleansers are designed as topical solutions with varying degrees of antimicrobial activity, concerns have been raised. Wound cleansers may affect normal human cells and may be antimitotic adversely affecting normal tissue repair. Repeated and excessive treatment of wounds with antiseptics without proper indications may have negative outcomes or promote a microenvironment similar to those found in chronic wounds. However, when applied at the proper times and concentrations, some classes of antiseptics may provide a tool for the clinician to drive the wound bed in desired directions. The present review summarises the various antiseptics in use and their negative impact on the wound healing mechanisms. It is clear that the role of antiseptics on wounds and their role in wound care management need to be reconsidered.

Key words: Wounds • Wound healing • Wound cleansing • Antiseptics • Topical wound management

Key Points

- there are no diagnostic tests to allow health care practitioners to identify whether the bacterial load in a wound is capable of causing infection
- it is believed that all wounds should undergo some form of cleansing to decrease the bacterial inoculum to levels that can be managed by host defenses
- the ideal topical therapy would include periodic reduction of bacterial contamination and removal of soluble debris without adversely impacting cellular activities vital to the wound healing process

INTRODUCTION

The practice of wound cleansing or antiseptic management has a dichotomous history anchored in tradition and science (1). It is an integral part of the management of acute traumatic wounds (2) as well a chronic wounds. Although there is a consensus that wound cleansing reduces infection rates (2) there is, however, evidence to suggest that it is not always necessary (3). There are no diagnostic tests to allow health care practitioners to identify whether the bacterial load in a wound is capable of causing infection. For this reason, it is believed that all wounds should undergo some form of cleansing to decrease the bacterial inoculum to levels that can be managed by host defenses (3). The choice of a cleansing agent, however, remains controversial. The use of antiseptics has been especially questioned (2).

'Good' care of wounds has been synonymous with topical prevention and management of microbial contamination (4,5). In fact, successful management of the contaminated wound must remove contaminants while inflicting minimal injury to tissues (3). On the premise that bacterial reduction translates to a reduced potential for infection (6) and without overlooking the deleterious effects of infection on wound repair (5), the ideal topical therapy would include periodic reduction of bacterial contamination and removal of soluble debris without adversely impacting cellular activities vital to the wound healing process (5,7,8).

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With advances in understanding of the wound healing process strategies that optimise the tissue repair process beyond the mere fact of just controlling surface bacterial contamination, it is now obvious that quality of care is a critical requirement for wound healing and for promotion of healing (5) and that the ultimate goal of wound management is to minimise the risk of opportunistic infection while promoting the development of healthy granulation tissue (9) and initiate and aid the healing process (10,11).

Topical antiseptics are antimicrobial agents that kill, inhibit or reduce the number of microorganisms and are thought to be essential for wounds infection control (6,12). However, they have long and commonly been used on wounds to prevent or treat infection (13), the merits of antiseptic fluid irrigation have received little scientific study (1). Antiseptics are considered drugs by the Food and Drug Administration (FDA) and are regulated as such (12). Topical antiseptics are active against both resident and transient flora on the skin and are able to reduce microbial numbers by mechanical removal, chemical action or both (14). Antiseptic formulations use a variety of mechanisms, act at various rates and persistence intervals, show various levels of toxicity and are more or less likely to trigger resistance (12). Unlike antibiotics that act selectively on a specific target, antiseptics have multiple targets and a broader spectrum of activity, which include bacteria, fungi, viruses, protozoa and even prions (9,13). Both the lower resistance rates and allergic risks associated with antiseptic compounds lend to their present popularity (9,13).

Antiseptic uses and indications vary; however, their use as prophylactic anti-infective agents for open wounds, such as lacerations, abrasions, burns and chronic ulcers, has been an area of intense controversy for several years (13). Currently available antiseptic products are diverse, targeted for different populations, use settings and specific indications (6). There are many types of topical antiseptics designed for various purposes; each may be used for health care, veterinary workers, food handlers or public consumers (14). Several antiseptic agents intended for health care personnel mainly focus on cleansing intact skin and are used for prepping patients preoperatively and prior to intramuscular injections or venous punctures, pre- and postoperative scrubbing in the operating room and hand washing by medical personnel. In clinical practice, antiseptics are broadly used for both intact skin and wounds (13). The usefulness of antiseptics on intact skin is well established and broadly accepted. However, the use of antiseptics as prophylactic anti-infective agents for open wounds, such as lacerations, abrasions, burns and chronic ulcers, has been an area of intense controversy for several years. Citing cytotoxicity data, many authors have advised against their use on open wounds (13). Some may even contain detergents, which render them too harsh for use on non intact skin (13).

Although certain skin and wound cleansers are designed as topical solutions with varying degrees of antimicrobial activity, concerns have been raised. Wound cleansers may affect normal human cells and may be antimitotic, adversely affecting normal tissue repair (4,5,13). Some authors strongly disapprove the use of antiseptics in open wounds. On the other hand, others believe antiseptics have a role in wound care, and their use may favour wound healing clinically (13). Two official guidelines have been released recently concerning antiseptic use on wounds. Povidone-iodine has been FDA approved for short-term treatment of superficial and acute wounds. The statement includes that povidone-iodine has not been found to either promote or inhibit wound healing. On the other hand, guidelines for the treatment of pressure ulcers by the US Department of Health and Human Services strongly discourage the use of antiseptics and promote the use of normal saline only for cleansing pressure ulcers (13). There is still much to learn about the effectiveness of different methods currently used for the irrigation of open wounds (15) be it acute or chronic.

Several antiseptic categories exist, including alcohols (ethanol), anilides (triclocarban), biguanides (chlorhexidine), bisphenols (triclosan), chlorine compounds, iodine compounds, silver compounds, peroxygens and quaternary ammonium compounds. The most commonly used products in clinical practice today include povidone-iodine, chlorhexidine, alcohol, acetate, hydrogen peroxide (H_2O_2), boric acid, silver nitrate, silver sulfadiazine and sodium hypochlorite (13). Although acetate (a radical) and silver sulphadiazine (an antibiotic) as well as other products are not really antiseptics, they are however listed

Key Points

- the ultimate goal of wound management is to minimise the risk of opportunistic infection while promoting the development of healthy granulation tissue and initiate and aid the healing process
- unlike antibiotics that act selectively on a specific target, antiseptics have multiple targets and a broader spectrum of activity, which include bacteria, fungi, viruses, protozoa and even prions
- both the lower resistance rates and allergic risks associated with antiseptic compounds lend to their present popularity
- the use of antiseptics as prophylactic anti-infective agents for open wounds, such as lacerations, abrasions, burns and chronic ulcers, has been an area of intense controversy for several years
- there is still much to learn about the effectiveness of different methods currently used for the irrigation of open wounds be it acute or chronic

Key Points

- the purpose of this review is to critically examine value as well as potential harm to patient outcome by the use of topical antiseptic preparations on open wounds

by several reports discussing topical preparations for wound care as such creating some confusion in the classification of topical disinfectants, antiseptics and antibiotics. Disinfectants have a broad spectrum effect on all vegetative forms of microorganisms, including spores, but usually have a toxic effect on tissues and probably are not suitable for use in open wounds. Antiseptics have as well a broad spectrum antimicrobial effect. They are toxic to multiple components of bacterial cell metabolism rather than to the more specific sites of antibiotic action such as enzyme inhibition and are believed to be relatively non toxic to tissues. They may even have the effect of promoting healing (16). The purpose of this review is to critically examine value as well as potential harm to patient outcome by the use of topical antiseptic preparations on open wounds.

COMMONLY USED ANTISEPTIC COMPOUNDS

Alcohol

Although several alcohols have been shown to be effective antimicrobials, ethyl alcohol (ethanol, alcohol), isopropyl alcohol (isopropanol, propan-2-ol) (used in the United States) and *n*-propanol (in particular in Europe) are the most widely used for both hard-surface disinfection and skin antisepsis (12,17). Classified as Category I, they are safe and effective for health care personnel handwash, surgical hand scrub and patient preoperative skin preparation (12). These alcohols have excellent in vitro bactericidal activity against most gram-positive and gram-negative bacteria. They also kill *Mycobacterium tuberculosis*, various fungi and certain enveloped viruses; however, they are not sporicidal and have poor activity against certain non enveloped viruses (12,17). Generally, the antimicrobial activity of alcohols is significantly lower at concentrations below 50% and is optimal in the 60–90% range (17). The alcohol killing mechanism appears to stem from membrane damage and rapid denaturation of proteins, with subsequent interference with metabolism and cell lysis protein coagulation and denaturation (12,17).

Iodine

For more than a century, iodine has been regarded as one of the most efficacious antiseptic to reduce infectious complications and topical iodine forms have been used for wound treatment. The simplest form of iodine is Lugol's solution, which has irritating and caustic properties (18). Tincture of iodine, containing approximately 2% iodine, has been long used as a preoperative skin preparation (12). Iodophors are the most common form of topical iodine and depend on the release of free iodine as the active agent. The complexing molecule acts only as a carrier. Iodophors increase the solubility of iodine and allow for sustained-release (12). The iodophor, povidone-iodine, a complex using 1-vinyl-2-pyrrolidinone polymer and a halogen-releasing agent is a time-release formulation of iodine that attacks key proteins, nucleotides, and fatty acids in the bacterium eventually causing cell death (9,12,17). The iodine released when the complex is in contact with the skin is not only available to kill microorganisms, but is also adsorbed by dead skin cells or other organic material. The killing spectrum of iodines and iodophors is broad and includes gram-positive and gram-negative bacteria, fungi, viruses and protozoa (12). Povidone-iodine absorption has been a concern in the treatment of pregnant and lactating mothers because of the possibility of induced transient hypothyroidism (12).

Cadexomer-iodine is a hydrophilic modified-starch polymer bead where molecules of iodine are immobilised. Upon application the polymer beads are swollen by wound exudates and gradually release incorporated iodine (18). Its most general indication is for the treatment of sloughy, exudating or infected ulcers (19). Preparations that could prolong the topical antibacterial effect would offer an obvious advantage (16), however, the iodine contained in these products has different chemical structures, their effects are assumed to be equivalent (18). Through bactericidal and bacteriostatic mechanisms, iodine products effectively reduce bacterial load and are active against most species, certainly those encountered in chronic wound care (16). Despite the antimicrobial advantages obtained through the use of iodine products, several potential disadvantages were observed in their clinical application for wound treatment with different and controversial results (18).

Biguanides: chlorhexidine gluconate and polyhexanide/polyhexamethylene biguanide

Chlorhexidine, a biguanide antiseptic, is probably the most widely used biocide in antiseptic products, in particular, in hand washing and oral products but also as a disinfectant and preservative (9,17). It is produced in two forms: a 0.05% dilution for wound cleansing and a 4% solution for use as a surgical skin preparation and hand scrub. Recently 2% solutions have been made available for surgical skin preparation (10,12). Chlorhexidine gluconate (CHG) has been used for more than 30 years in the clinical setting. It has a high level of antimicrobial activity, low toxicity and strong affinity for binding to the skin and mucous membranes (12). It seems to impart its antimicrobial activity at the membrane level, damaging both outer and inner bacterial membranes, causing leakage and possibly disrupting membrane potentials critical for ATP generation (9,17). It disrupts the microbial cell membrane and precipitates the cell contents. CHG (0.5–4%) is more effective against gram-positive than gram-negative bacteria and has less activity against fungi and tubercle bacilli. It is inactive against bacteria spores, except at elevated temperatures. Numerous studies indicate that CHG is not absorbed through the skin and has a low skin-irritancy potential. However, CHG should not come into contact with eyes, the middle ear or meninges. The immediate bactericidal action of CHG surpasses antiseptic preparations containing povidone-iodine, triclosan, hexachlorophene or chloroxylenol (12).

Polyhexanide/polyhexamethylene biguanide (PHMB) is considered to be highly histocompatible non cytotoxic and is one of the most frequently used wound antiseptics nowadays (20). Polyhexanide in a hydrogel preparation has gained much attention after it was shown that methicillin-resistant *Staphylococcus aureus* detected on skin or wounds just as a contamination or as colonisation without clinical and/or serological signs of infection could be successfully eradicated (21). Polihexanide proved also clinically and histologically superior to povidone-iodine and silver nitrate for the treatment of second-degree burns. Its antiseptic efficacy does not inhibit the re-epithelialisation process (22). However, it was also shown that the exposure of human osteoblasts and endothelial cells to polyhexanide at concentrations with questionable antibacterial activity resulted in severe cell damage raising some questions about the feasibility of using antiseptics in bone cement for the treatment of total arthroplasty infections (23) and probably about the effect of PHMB on wound healing (23).

Halophenols (chloroxylenol)

Chloroxylenol (4-chloro-3,5-dimethylphenol; p-chloro-m-xylenol) is the key halophenol used in antiseptic or disinfectant formulations (17). Chloroxylenol is bactericidal (17). Surprisingly, its mechanism of action has been little studied despite its widespread use over many years. Because of its phenolic nature, it would be expected to have an effect on microbial membranes (17). At concentrations of 0.5–4.0% it acts by microbial cell wall disruption and enzyme inactivation. It has good activity against gram-positive bacteria, but it is less active against gram-negative bacteria, *Mycobacterium tuberculosis*, fungi and viruses (12).

Bisphenols (triclosan)

Triclosan and hexachlorophane are the most widely used biocides in this group, especially in antiseptic soaps and hand rinses. Both compounds have been shown to have cumulative and persistent effects on the skin (17).

Hexachlorophene is primarily effective against gram-positive bacteria. It is a chlorinated bisphenol that interrupts bacterial electron transport, inhibits membrane bound enzymes at low concentrations and ruptures bacterial membranes at high concentrations. (17,24) Three percent hexachlorophene kills gram-positive bacteria within 15–30 seconds, but a longer time is needed for gram-negative bacteria (12). Hexachlorophene has been associated with severe toxic effects, including deaths. It can be absorbed through damaged skin of adults and the skin of premature infants (23). Baby powder accidentally contaminated with 6% hexachlorophene has caused infant deaths (12).

Triclosan is a diphenyl ether (12). It exhibits particular activity against gram-positive bacteria. Its efficacy against gram-negative bacteria and yeasts can be significantly enhanced by formulation effects. The specific mode of action of triclosan is unknown, but it has been suggested

Key Points

- in any wounding process, the divided edges of the wound are more susceptible to infection than the unwounded tissue
- soft-tissue injuries because of shear forces of cuts by either a piece of glass or the metal edge of a knife resulting in a linear laceration that require very little energy to produce tissue failure exhibit considerable resistance to the development of infection
- wounds in which the mechanism of injury is compression or tension rather than shear forces requiring considerably greater energy and with characteristic stellate laceration with abrasions of adjacent skin to the wound and reduction in blood flow have an increased susceptibility to infection
- the environs in which the injury occurred are also predictive of the number of pathogens in the wound and the likelihood of developing wound infection same as the presence of foreign bodies
- it is argued that all wounds are contaminated with bacteria and that this alone will not disrupt the wound healing process
- it is when this contamination changes to a state of critical colonisation or infection that the bioburden in the wound is the most important contributing factor that impedes healing

that the primary effects are on the cytoplasmic membrane (12,17).

Silver compounds

In one form or another, silver and its compounds have long been used as antimicrobial agents (17). Currently, the antibiotic silver sulfadiazine is the most clinically relevant silver compound. It is thought to mainly act at the DNA level as silver ions bind to the helix thereby blocking transcription (9,17). Irrespective of the source of silver, whether released from solutions, creams and ointments or nanocrystalline silver, silver is highly toxic to both keratinocytes and fibroblasts (24).

Hydrogen peroxide

H_2O_2 is a widely used biocide for disinfection, sterilisation and antisepsis. It is a clear, colourless liquid that is commercially available in a variety of concentrations ranging from 3% to 90% (17). This readily available oxidant is rapidly converted to the highly reactive hydroxyl radical that damages an array of cellular components. Although widely considered innocuous and environment friendly, relatively high concentrations need to be applied because of the significant catalase activity of several key pathogenic bacteria (9,17).

WOUND CONTAMINATION AND WOUND INFECTION

In any wounding process, the divided edges of the wound are more susceptible to infection than the unwounded tissue. The magnitude of this enfeebled resistance, however, varies with the mechanism of injury (14). Soft-tissue injuries because of shear forces of cuts by either a piece of glass or the metal edge of a knife resulting in a linear laceration that require very little energy to produce tissue failure exhibit considerable resistance to the development of infection, with the infective dose being 10^6 bacteria per gram of tissue or greater. Wounds in which the mechanism of injury is compression or tension rather than shear forces requiring considerably greater energy and with characteristic stellate laceration with abrasions of adjacent skin to the wound and reduction in blood flow have an increased susceptibility to infection (10^4 bacteria per gram of tissue) (14). The environs in which the injury occurred are also predictive of the number of pathogens in the wound and the likelihood of developing wound infection same as the presence of foreign bodies (14).

Although it has been widely recognised for centuries that severe bacterial infection often develops in wounds containing dirt and soil, there has been little knowledge until recently of the role of components of soil in this infection process (14). Specific infection-potentiating factors have been identified in the soil, which include its organic components as well as its inorganic clay fractions. For wounds contaminated by these fractions, only 100 bacteria are necessary to elicit infection (14). Their ability to enhance the incidence of infection seems to be related to their damage to host defenses. In the presence of these fractions, leukocytes are not able to ingest and kill bacteria. This deleterious effect on white blood cell function is a result of a direct interaction between the highly charged soil particles and white blood cells. Soil infection-potentiating fractions also have considerable influence on non specific humoral factors. Exposure of fresh serum to these fractions eliminates its bactericidal activity. As expected, these particles, which are highly charged species, react chemically with amphoteric and basic antibiotics, limiting their activity in contaminated wounds (14,25).

The major inorganic infection-potentiating particles are the clay fractions, which reside in heaviest concentration in the subsoil rather than in topsoil (14). Consequently, traumatic soft-tissue injuries occurring in swamps or excavations run a high risk of being contaminated by these fractions, which predispose the wound to serious infection (14). A corollary to these observations is that some soil contaminants, such as sand grains, are relatively innocuous. This fraction, which has a large particle size and a low level of chemical reactivity, exerts considerably less damage on tissue defenses than do the other infection-potentiating fractions. Surprisingly, the black dirt on the surface of highways also seems to have minimal chemical reactivity (14).

CHRONIC WOUNDS

It is argued that all wounds are contaminated with bacteria and that this alone will not disrupt the wound healing process (9,26,27).

Interestingly, studies have suggested that colonisation of the wound with microflora of the skin can actually enhance healing (9,13). It is when this contamination changes to a state of critical colonisation or infection that the bioburden in the wound is the most important contributing factor that impedes healing (26). Unfortunately the progression of colonisation into infection is a multifactorial process involving many host and microbial components (9), nevertheless, prevention of wound infection is considered the most important contributing factor if an acute wound is to be prevented from becoming chronic (26).

Many chronic wounds seem to be confined to the inflammatory phase of the healing process (9) and present a challenge that is costly in terms of quality of life to the patient and in financial terms for the National Health Service (26). Three factors contribute to the development of a chronic wound. These are firstly, cellular and systemic factors that occur because of ageing; secondly, repeated ischaemia and reperfusion injury often with underlying ischaemia; and thirdly, bacterial colonisation, also known as bioburden (26,28). It is also claimed that in addition to the wound's bioburden other factors, such as foreign matter or necrotic tissue, if present in a wound, can delay or prevent normal healing by production of metalloproteases (26). It is known that various types of bacteria are sustained in chronic wounds (26,27). Recent developments in wound care have identified that many of these bacteria live in communities known as biofilms. Biofilms are highly resistant to cleansing by irrigation and by treatment with antibiotics (26,29).

EVIDENCE-BASED BEST PRACTICE OF WOUND CLEANSING

Mechanical forces are usually used to rid the wound of bacteria and other particulate matter retained on the wound surface by adhesive forces (14). Under most circumstances, debridement alone will reduce bacterial loads with the added benefit of removing necrotic tissue that may otherwise increase inflammation and delay healing (9,30). If cleansing is required, an appropriate solution should be selected to optimise the healing process and minimise the risk of damage to viable tissue (10).

Even though there is no strong evidence that cleansing wounds per se increases healing or reduces infection (31) it is almost universally recommended and applied. The two cleansing techniques generally used are irrigation and scrubbing. Although irrigation with a large amount of saline and brushing are recommended, excessive brushing to remove sand, debris or fragments will damage soft tissues and impairs the wound's ability to resist infection and allows residual bacteria to elicit an inflammatory response (14,32).

Irrigation has long been considered one of the most appropriate methods of cleansing a wound. Substantial evidence exists that this should involve irrigation with a fluid that has a similar osmotic pressure to that found in living cells (26). Wound cleansing solutions must be non toxic to human tissues, remain effective in the presence of organic material, reduce the number of microorganisms, not cause sensitivity reactions and be widely available and cost effective (10). Suggested cleansing agents are normal saline, sterile water and even simple tap water (10). In austere environments such as mobile military hospitals, supply lines may not be able to meet these requirements, especially in a mass casualty situation. Alternative irrigation solutions may be necessary in the absence of saline, or in a situation where a limited saline supply is reserved for casualty intravenous resuscitation (33). The use of potable water as an irrigant has been studied in contaminated skin lacerations using an animal model and showed no difference in bacterial reduction between potable water and sterile saline (33–35). It has been even recommended for the irrigation of complex musculoskeletal wounds and open fractures (33). An experimental study established indeed that potable water is as effective as normal saline in removing bacteria from a contaminated musculoskeletal wound (33). In the absence of potable tap water, boiled and cooled water as well as distilled water can be used instead as wound cleansing agents (31).

Even though various solutions have been recommended for cleansing wounds, normal saline is favoured as it is an isotonic solution and does not interfere with the normal healing process. Tap water is commonly used in the community for cleansing wounds because it is easily accessible, efficient and cost effective, however, there is an unresolved debate

Key Points

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- recent developments in wound care have identified that many of these bacteria live in communities known as biofilms. Biofilms are highly resistant to cleansing by irrigation and by treatment with antibiotics
- irrigation has long been considered one of the most appropriate methods of cleansing a wound
- substantial evidence exists that this should involve irrigation with a fluid that has a similar osmotic pressure to that found in living cells
- suggested cleansing agents are normal saline, sterile water and even simple tap water

Key Points

- the benefits of pressurised irrigation are well recognised
- the bacterial removal efficiency of the irrigating stream is proportional to the pressure experienced by the wound surface
- the benefits of high-pressure irrigation must be weighed against potential side effects such as the dissemination of bacteria into soft-tissue wounds
- routine unnecessary cleansing can traumatize fragile new tissue in and around the wound bed

about its use (31). To date, there is no evidence that using tap water to cleanse acute wounds in adults increases infection on the contrary, some evidence suggests that it reduces it (31). Invariably, if cleansing is required, an appropriate solution should be selected to optimise the healing process and minimise the risk of damage to viable tissue (10). Antiseptic solutions may be used exceptionally and caution is advised as their toxicity might outweigh any benefits (10,36). In fact, it has been suggested that, rather than the product used itself, it is the physical action of cleansing that removes debris, contaminants or unwanted exudate from a wound bed (10,37).

Although there is no clear consensus of opinion as to which is best, cleansing of chronic wounds to remove foreign matter, necrotic tissue or bacteria is usually either with normal saline or tap water (26). For chronic wounds, the relative risk of developing an infection when cleansed with tap water compared with normal saline is 0.16 (31). It is claimed, however, that because of the complexity of factors influencing a chronic wound, no single therapeutic intervention will have any significant impact on improving the wound (26,28). Recently a consensus paper became available that advocated the use of an active substance, polyhexanide, as a first choice treatment for chronic, hard-to-heal wounds suitable for wound bed preparation to remove biofilm prior to further treatment and appears to offer, in the majority of patients, a safe and cost effective method of cleansing wounds which is more efficient than normal saline (26).

Although most surgeons prefer to treat contaminated wounds as soon as possible, the effect of timing on the ability of irrigation to reduce the amount of bacteria in an acute wound is not fully known (38), although recently superior bacterial removal with earlier irrigation was shown in an experimental contaminated wound model (38).

The benefits of pressurised irrigation are well recognised (14,39). It takes significantly smaller hydraulic pressures to rid the wound of large foreign bodies than it does to remove small particles and bacteria (14) and the bacterial removal efficiency of the irrigating stream is proportional to the pressure experienced by the wound surface (14). Low-pressure irrigation (0.5 pounds per square inch – psi) is best for clean wounds, and high-pressure irrigation (7 psi) can be used instead for dirty or heavily contaminated wounds (14). The cleansing effect of the bulb syringe irrigation is negligible because the wound bacterial concentration is not significantly affected by this low-pressure irrigation system. High-pressure syringe irrigation effectively decreases the level of bacterial contamination and markedly reduces the incidence of wound infection in contaminated wounds (14). High-pressure irrigation removes 80% of the soil infection-potentiating factors from the wound (14). Changing the composition of the wound irrigation solution by adding chelating agents, flocculants and dispersants or a non ionic surfactant does not significantly enhance the efficiency of removal of soil infection-potentiating factors from wounds (14).

In the clinical setting, high-pressure irrigation is accomplished with an inexpensive disposable irrigation assembly consisting of a 19-gauge plastic needle or catheter attached to a 35-mL syringe. This would exert a pressure equivalent to 7 psi on the wound surface. In contrast, the pressure encountered by a surface irrigated by a bulb syringe is only 0.5 psi (14). To minimise exposure to biologically hazardous material during wound irrigation, an overturned plastic gallipot from a sterile wound dressing pack may be used as a splashguard during the irrigation process (14,40–42).

The benefits of high-pressure irrigation must be weighed against potential side effects such as the dissemination of bacteria into soft-tissue wounds. In fact, the irrigation fluid disseminates into the interstices of the wound, predominantly in a lateral direction. This lateral spread occurs within the loose areolar tissue, contributing to the development of postoperative oedema. Paradoxically, high-pressure irrigation may make the wound more susceptible to infection, so this technique should be reserved for heavily contaminated wounds only (14). However, in a recently published experimental study about the effectiveness of different methods currently used for the irrigation of open wounds comparing normal saline solution, bacitracin solution, castile soap and benzalkonium chloride with use of a pulsatile lavage device (19 psi) then using the same animal model to compare bulb syringe and pulsatile lavage irrigation with saline solution it was concluded that approaches used to remove bacteria from wounds, such as irrigants other than saline solution or high-pressure devices, may not have the best clinical outcome (15).

Routine unnecessary cleansing can traumatise fragile new tissue in and around the wound bed (10). Moreover, it is well established now that wound exudate may contain bactericidal properties and growth factors that will help promote wound healing and should only be removed if copious amounts are present or there are clinical signs of infection (10).

Disinfection of the skin around the wound by antiseptic agents should be initiated without contacting the wound itself (14). Two widely used groups of antiseptic agents, containing either an iodophore or chlorhexidine, exhibit activity against a broad spectrum of organisms and suppress bacterial proliferation. The superiority of one antiseptic agent over another has not been shown. Although these agents can reduce the bacterial concentration on intact skin, they seem to damage the wound defenses and invite the development of infection within the wound itself. Consequently, inadvertent spillage of these agents into the wound should be avoided (14).

ANTISEPTIC CYTOTOXICITY AND THE EFFECT ON WOUND HEALING

Anecdotal clinical observations and an increasing body of literature suggest that application of antiseptics is not as benign as originally accepted. The cytotoxic effects of antiseptics on many of the key cellular participants in the wound healing process, such as keratinocytes and fibroblasts, have been well documented (5,8,9,43,44). Moreover, exposure of the wound to either Hibiclens™ (Mölnlycke Health Care US, LLC, Norcross, GA) or Betadine® (Purdue Products L.P., Stamford, CT) surgical scrub solution has been shown to damage tissue defenses, and cause pain or irritation to tissues (14).

In a recently published important experimental study, reductions in proliferation of normal human dermal fibroblasts (NHDF), pivotal to the wound healing process, were observed when the cells were cultured in the presence of various antiseptic compounds for 96 hours with a few notable exceptions (9). Both H_2O_2 and povidone-iodine treatment led to dose-dependent reductions in proliferation with complete attenuation achieved at 500 μmol/L and 0.2% final concentrations, respectively. Silver-containing compounds and chlorhexidine solutions exhibited a different trend. High doses still elicited a decrease in proliferation, but, at lower doses, an increase in proliferation was observed (9). In all instances, the highest doses tested for all the biocides approached 100% inhibition, indicating potential cytotoxicity at these concentrations (9). All of the antiseptics in a dose-dependent manner reduced also migration of the NHDF cells which under normal culture conditions would rapidly invade the vacant spaces, filling the void within 24–48 hours (9). H_2O_2 was the most effective compound tested with complete attenuation achieved at a 1000 μmol/L concentration. Chlorhexidine and povidone-iodine were also effective at reducing migration. On the other hand, silver sulfadiazine was the least effective compound at inhibiting migration, however, a reduction in migration of $36\% \pm 2\%$ was observed at a dose of 10 μmol/L (9). Cells exposed to H_2O_2 and povidone-iodine completely lacked important foot-like projections characteristic of normal polarised motility and migration of cells (9,45). Silver sulfadiazine and chlorhexidine-treated cells as well presented with fewer and less developed filopodia at the leading edge as compared to none treated normal cell (9).

The same study also showed that Chlorhexidine is a strong inhibitor of pro-MMP (matrix metalloproteinase)-9 and pro-MMP-2 release in stimulated NHDF cells with 10 ng/mL tumour necrosis factor-α and 10 ng/mL transforming growth factor-β1. Exposure of the cells to 250 and 500 μmol/L H_2O_2 reduced the pro-MMP-9 release by 70% and 99%, respectively. A 66% reduction in pro-MMP-2 release was also seen in both H_2O_2 treatment groups (9). A dynamic range of effects was exhibited with silver-containing compounds and povidone-iodine. When exposed to low levels of silver, a reduction of pro-MMP-2 and an increase in pro-MMP-9 was observed. Silver sulfadiazine had a more pronounced effect than silver nitrate in up-regulating pro-MMP-9 (18% increase versus 5%). High doses, however, attenuated the pro-MMP-9 release and greatly reduced pro-MMP-2 levels below those of resting levels. Low-dose iodine exposure of these cells resulted in almost a threefold increase in pro-MMP-9 release from stimulated cells.

Key Points

- it is well established now that wound exudate may contain bactericidal properties and growth factors that will help promote wound healing and should only be removed if copious amounts are present or there are clinical signs of infection

Key Points

- although the type of open-wound management must be individualized for each wound (14), cleansing bacteria, soil and other debris from traumatic wounds, as well as surgical debridement cannot be overemphasized
- although certain skin and wound cleansers are designed as topical solutions with varying degrees of antimicrobial activity, wound cleansers may also be antimitotic and adversely affect normal tissue repair
- available experimental data suggest that the effects of antiseptic treatment on fibroblasts are more encompassing than just toxicity
- wound management strategies address the delicate balance between cytotoxicity and cellular activities
- despite cytotoxicty data, most antiseptics have not been shown to clearly impede healing, especially newer formulations like cadexomer iodine (which speeds healing) and novel silver delivery systems. These compounds appear to be relatively safe and efficient in preventing infection in human wounds
- the continued unjustified use of antibiotics will have to be addressed if the rise of resistant and emergent organisms is to be controlled
- topical antimicrobials, such as the antiseptics,could be used more often to avoid the need for antibiotics particularly in wound care and management protocols
- unfortunately, given this review, it is not possible to formulate rigid guidelines or to propose an algorithm regarding the use of antiseptics for routine wound cleansing
- the role of antiseptics on wounds and their role in wound care management should be critically reconsidered

No significant change in pro-MMP-2 release was observed at this dose. High-dose exposure to iodine was strikingly different. No MMP release was detected in these cells (9). In addition, low-dose silver, H_2O_2 and iodine all increased the conversion of the pro-MMP-2 into the truncated, active form (9).

CONCLUSION

Quality of care is a critical requirement for wound healing. Strategies that optimise the tissue repair process have evolved with advances in understanding of the wound healing process (5). Although the type of open-wound management must be individualised for each wound (14), cleansing bacteria, soil and other debris from traumatic wounds, as well as surgical debridement cannot be overemphasised. Debridement removes tissue heavily contaminated by soil infection-potentiating fractions and bacteria, and excises devitalised tissues that impair the wound's ability to resist infection (14).

It is argued that wound cleansing has three elements, namely, the technique, the solution and the equipment (46,47). Techniques used include high-pressure irrigation, swabbing, low-pressure irrigation, showering, bathing and washing the affected area under a running solution or total immersion in a whirlpool bath. Different cleansing solutions are also used, for example, normal saline, water and antiseptic solutions. Furthermore, wound cleansing requires the use of equipment such as syringes, needles, catheters and pressurised canisters (46,47). Some have argued that wound cleansing can have a positive impact on wound healing outcomes, however, it is conducted mostly without a clear rationale underpinning the practice (46,48). Although certain skin and wound cleansers are designed as topical solutions with varying degrees of antimicrobial activity, wound cleansers may also be antimitotic and adversely affect normal tissue repair (5).

Skin cleansers are most toxic to fibroblasts (5). Available experimental data suggest that the effects of antiseptic treatment on fibroblasts are more encompassing than just toxicity (9). Keratinocyte monolayers, representing the in vivo basal layer of the epidermis that epithelialises the wound surface after injury, are more sensitive to wound cleansers such as H_2O_2, modified Dakin's solution (0.025%) and povidone (10%) (5). Repeated and excessive treatment of wounds with antiseptics without proper indications may have negative outcomes or promote a microenvironment similar to those found in chronic wounds (9). However, when applied at the proper times and concentrations, some classes of antiseptics may provide a tool for the clinician to drive the wound bed in desired directions (9). Wound management strategies address the delicate balance between cytotoxicity and cellular activities. Irritation of intact healthy tissue could seriously impact the rate and quality of tissue repair (5). Although the removal of antiseptics from the wound bed management arsenal cannot be advocated, care should be used when administering these products (9). Despite cytotoxicty data, most antiseptics have not been shown to clearly impede healing, especially newer formulations like cadexomer iodine (which speeds healing) and novel silver delivery systems. These compounds appear to be relatively safe and efficient in preventing infection in human wounds (13).

The continued unjustified use of antibiotics will have to be addressed if the rise of resistant and emergent organisms is to be controlled. Topical antimicrobials, such as the antiseptics, could be used more often to avoid the need for antibiotics particularly in wound care and management protocols (16). Unfortunately, given this review, it is not possible to formulate rigid guidelines or to propose an algorithm regarding the use of antiseptics for routine wound cleansing. On the contrary, the role of antiseptics on wounds and their role in wound care management should be critically reconsidered (13).

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