The role of antimicrobial wound dressings

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Since George Winter described the value of the prevention of scab formation to promote the epithelialisation of experimental superficial wounds by using a moist wound environment (Winter, 1962), there has been a progressive exponential increase in the numbers and types of dressings available in clinical practice.

A major factor, common to all wound care, is the prevention of infection, or the creation of a wound environment that does not promote infection. However, infection control is a contentious issue, particularly against a background of the continuous and expanding number of resistant organisms. Systemically administered antibiotics should be reserved for treating invasive infection, and, wherever possible, topical antibacterials used for superficial, local management of an open-wound surface (European Wound Management Association, 2006). Topical antibacterials have been used for centuries and are still in widespread practice within both human healthcare, as well as veterinary practice.

WHAT IS INFECTION?

Infection is the main cause of delayed healing in primarily closed (surgical), traumatic and burn wounds. The recognition of a surgical site infection (SSI) is relatively easy when an incised wound presents with an extended, raised inflammatory margin (cellulitis) around the wound, sometimes associated with lymphangitis, raised local or systemic temperature and local pain. It is not so easy to define an open wounds healing by secondary intention (Gardner et al, 2001; Cutting and Harding, 1994). This over-expressed, inappropriate and uncoordinated inflammatory response relates to invasion of microorganisms through the normally intact resistant skin barrier. The bacteria release toxins and proteases, depending on their pathogenicity, which facilitates their spread. The host response, locally and systemically, may be overwhelmed, particularly in immunosuppressed patients, leading to bacteraemia, systemic inflammatory response syndrome, sepsis, organ failure or death.

SILVER DRESSINGS

Although silver has been used for centuries in water recycling and sanitisation, in complementary healthcare and to inhibit bacteria in food. However, the introduction of silver into wound care as an antibacterial, particularly in burns, is relatively recent. There are growing numbers of silver dressings (see Figure 1), which are already available and are presented as creams, foams, hydrogels, hydrocolloids and polymeric films and meshes(eg. Silvercel Ag (Systagenix), Acticoat (Smith and Nephew).

Figure 1: Silver dressing in situ – this dressing needs to be covered with a secondary layer (eg. foam dresing).

Each preparation claims different advantages, with the common effect to all, perhaps, being the antibacterial action of silver. This latter characteristic is also being exploited in other medical devices (Furno, 2004), eg. central (jugular) catheters. Elemental silver (Ago) appears to have no antibacterial action or ionic charge, whereas its cation ($Ag+$)is highly reactive (Wright et al, 1998a). Unlike antibiotics, silver is toxic to multiple components of bacterial cell metabolism. Including causing damage to the bacterial cell wall. Altering membrane permeability leads to gross cellular structural changes, causing blockage of transport and enzyme systems, such as the respiratory cytochromes, alteration of proteins and binding of microbial deoxyribonucleic acid and ribonucleic acid to prevent transcription and division. Like other antiseptics, silver is soon inactivated by protein binding, but this inactivation can also be caused by tissues and anions, such as chloride, phosphate and sulphide. It is probable that the presentation of an immediate, large bolus of silver with sustained release promotes the speed of bacterial kill (Ovington,1999) and that rapid or sustained release of silver ions gives a wide spectrum of activity (Wright et al,1998b). Dressings that can sustain release of silver do not need to be changed so often therefore their use is beneficial to both patient and owner. Organisms do vary in their susceptibility to silver, but there is good evidence that silver has activity against the common pathogens, Staphylococcus aureus and Pseudomonas spp, which are commonly encountered in chronic wound care. The newer dressings present silver ions differently from silver nitrate and silver sulphadiazine (SSD; [Lansdown and Williams, 2004]).These include forming unique Ag+/Ago complexes by the use of nanocrystalline technology, or a high-silver availability (Ag+) through other means, to give a large and effective sustained bolus delivery (Wright et al, 1998). The development of resistance is unlikely, as it is with other antibacterials such as povidone-iodine, as the antiseptic actions affect at least three bacterial cell systems (Ovington,1999). Systemic toxicity, argyria (skin condition caused by improper exposure to chemical forms of silver), is unlikely as absorption from dressings is so small and probably depends on wound size (Lansdown et al, 2005).

HONEY

The use of honey to treat wounds dates back to 2000BC (Forrest, 1982). Numerous reports document the efficacy of honey in wound healing, and several studies even indicate that honey appears to be superior to many modern methods of treatment (White et al,1963; White,1966; Molan,1999; Cooper and Molan,1999). Honey is currently used worldwide to treat human patients with contaminated wounds or infected body cavities. Mechanisms associated with wound cleansing and healing properties of honey include decreased inflammatory oedema, attraction of macrophages to further cleanse the wound, accelerated sloughing of devitalised tissue, provision of a local cellular energy source, and formation of a protective layer of protein over the wound and a healthy granulation bed (Kamat,1993). Honey also has antibacterial properties that have been attributed to its high osmolarity, acidity, and hydrogen peroxide (H_2O_2) content (White,1966).The effect of osmolarity in contaminated wounds is based on the low-water content(or high osmolality) created in the wound (Chirife et al,1982). As the high osmolarity of honey draws lymph from a wound, dissolved nutrients within the lymph provide nutrition for regenerating tissue (Molan, 1999). The antibacterial factor inhibine has been isolated from honey produced from several different plant sources (White et al,1963). Inhibine, which was determined to be H_2O_2, is produced by the natural glucose oxidase in honey. Glucose oxidase produces gluconic acid(which is the principal acid in honey)and H_2O_2 from glucose. Although H_2O_2 is primarily responsible for the antibacterial properties of honey, it is present at harmlessly low levels. H_2O_2 is continuously produced by the activity of the glucose oxidase enzyme, which is only activated when diluted (White et al, 1963). The concentration of H_2O_2 that accumulates in one hour is approximately 1,000 times less than that found in the H_2O_2 solution (3%) that is commonly used as an antiseptic (Cooper and Molan,1999), which means it does not damage tissues. The generation of low levels of H_2O_2stimulates angiogenesis and the growth of fibroblasts. This increased angiogenesis increases oxygen delivery to tissues, which is a limiting factor for tissue generation (Molan,1999).Topical acidification of wounds has been shown to promote healing (Kaufman,1985); honey's low pH (3.6 to 3.7) will accelerate healing as well as increase antibacterial effects. Most honey used in wound management is manuka honey (see Figure 2) and there are a number of dressings containing manuka honey(see Figure 3), eg. Activon (Dechra), Manuka ND and Manuka AD (Kruuse UK). The unique antimicrobial properties of manuka honey have been attributed in large part to the presence of methylglyoxal (MGO), which has been shown to originate from the high levels of dihydroxyacetone present in the nectar of manuka flowers (Adams et al, 2009; Mavric et al, 2008).

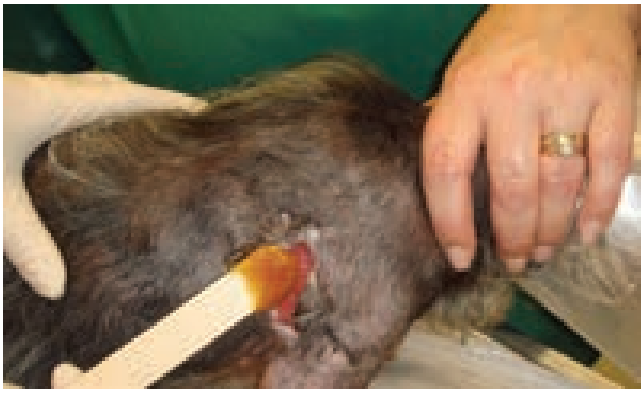

Figure 2: Use of manuka honey – applied using a sterile spatula.

Figure 3: Removal of the honey dressing, the wound should then be lavaged to remove exudate and remnants of dressing.

POLYHEXAMETHYLENE BIGUANIDE (PHMB) DRESSINGS

ANTIMICROBIAL PEPTIDES

Naturally occurring antimicrobial peptides (AMPs) were discovered about 25 years ago and are produced by the majority of living organisms. These AMPs have a broad spectrum of activity against bacteria, viruses and fungi and have been suggested as therapeutic alternatives to antibiotics (Hancock and Sahl, 2006). AMPs are positively charged molecules that bind to bacterial cell membranes and induce cell lysis by destroying membrane integrity; in effect, rupturing the bacterial cell membrane meaning the bacteria can no longer survive. This mechanism of cell killing is similar to that found with antibiotics such as the penicillins and cephalosporins, which act by interfering with cell wall synthesis to cause cell fragility and lysis. A number of synthetic compounds with the antimicrobial activity of AMPs have been produced as alternatives to conventional antibiotics. One of these — PHMB — has a chemical structure similar to AMPs. This allows it to insert into bacterial cell membranes and kill bacteria in the same way as AMPs.

PHMB IN WOUND MANAGEMENT

PHMB has been incorporated into a range of wound management products from several companies (see Figure 4). The AMD range of infection control dressings (Tyco Healthcare, Basingstoke)is impregnated with 0.2% PHMB. The product range includes Telfa AMD non-adherent wound dressings, Kerlix AMD gauze dressings and AMD Foam dressings, another range of PHMB dressings is Suprasorb X + PHMB (Activa Healthcare), which contains 0.3% PHMB.

Figure 4: PHMB foam dressing in use.

CONCLUSION

Resistant bacteria pose a continual problem in veterinary medicine, as much as human medicine. Healthcare professionals need to seek alternatives to the administration of antibiotics to patients, for their own health, as well as their patient's. The availability of antimicrobial dressings means there is now a first line alternative to antibiotics in the treatment of wounds, and the variety available means there are options for every stage of wound healing in veterinary patients. Topical antimicrobials should be used as first line in wound management in veterinary patients.

REFERENCES

Adams CJ, Manley-Harris M, Molan PC. The origin of methylglyoxal in New Zealand manuka (Leptospermum scoparium) honey. Carbohydrate Research 2009; 344(8): 1050–1053

Chirife J, Scarmato GA, Herszage L (1982) Scientific basis for use of granulated sugar in treatment of infected wounds. The Lancet 1: 560-561

Cooper RA, Molan PC. Honey in wound care. J Wound Care 1999; 8(7): 340

Cutting KF, Harding KG. Criteria for identifying wound infection. J Wound Care 1994; 3: 198–201

Forrest RD. Development of wound therapy from Dark Ages to the present. J Royal Soc Med 1982; 75: 268–273

Furno F, Morley KS, Wong B et al. Silver nanoparticles and polymeric medical devices: a new approach to prevention of infection. J Antimicrob Chemother 1994; 2004; 54: 1019–1024

Gardner SE, Frantz RA and Doebbeling BN. The validity of the clinical signs and symptoms used to identify localised wound infection. Wound Repair Regen 2001; 9: 178–186

Hancock RE, Sahl HG. Antimicrobial and host defense peptides as new antiinfective therapeutic strategies. Nature Biotechnology 2006; 24(12): 1551–1557

Kamat N. Use of sugar in infected wounds. Tropical Doctor 1993; 23(4): 185

Kaufman T, Eichenlaub EH, Angel MF (1985) Topical acidification promotes healing of experimental deep partial thickness skin burns: A randomized double blind preliminary study. Burns 12: 84–90

Lansdown ABG, Williams A (2004) How safe is silver in wound care? J Wound Care 13: 131–136

Lansdown AB, Williams A, Chandler S and Benfield S. Silver absorption and antibacterial efficacy of silver dressings. J Wound Care 2005; 14: 155–160

Mavric E, Wittmann S, Barth G, Henle T. Identification and quantification of methylglyoxal as the dominant antibacterial constituent of Manuka (Leptospermum scoparium) honeys from New Zealand. Molecular Nutrition and Food Research 2008; 52: 483–489

Molan PC. The role of honey in the management of wounds. J Wound Care 1999; 8(8): 415–418

Ovington LG. The value of silver in wound management. Podiatry Toda 1999; 12: 59–62

White JW. Inhibine and glucose oxidase in honey: A review. American Bee Journal 1966; 106: 214–216

White JW, Stubers MH and Shepartz AI. The identification of inhibine, the antibacterial factor in honey, as hydrogen peroxide and its origin in a honey glucose-oxidase system. Biochimica et Biophysica Acta 1963; 73: 57-70

Winter GD (1962) Formation of scab and the rate of epithelialisation of superficial wounds in the skin of the domestic pig. Nature 193: 293-294

Wright JB, Hansen DL, Burrell RE. The comparative efficacy of two antimicrobial barrier dressings: in vitro examination of two controlled-release silver dressings. Wounds 1998a; 10: 179–188

Wright JB, Lam K, Burrell RE. Wound management in an era of increasing bacterial resistance: a role for topical silver treatment. Am J Infect Control 1998b; 26: 572–577