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Antimicrobial dressings: Comparison of the ability of a panel of dressings to prevent biofilm formation by key burn wound pathogens☆

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ABSTRACT

Antimicrobial medicated dressings (AMD) are often used to reduce bacterial infection of burns and other wounds. However, there is limited literature regarding comparative efficacies to inform effective clinical decision making.

Objectives: Following on from a previous study where we demonstrated good antibiofilm properties of acetic acid (AA), we assessed and compared the *in vitro* anti-biofilm activity of a range of AMDs and non-AMDs to AA.

Methods: Laboratory experiments determined the ability of a range of eleven commercial AMD, two nAMD, and AA, to prevent the formation of biofilms of a panel of four isolates of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.

Results: There is a large variation in ability of different dressings to inhibit biofilm formation, seen between dressings that contain the same, and those that contain other antimicrobial agents. The best performing AMD were Mepilex® Ag and Acticoat. AA consistently prevented biofilm formation.

Conclusions: Large variation exists in the ability of AMD to prevent biofilm formation and colonisation of wounds. A standardised *in vitro* methodology should be developed for

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Abbreviations: AMD, antimicrobial dressing; nAMD, non-antimicrobial dressing; AA, acetic acid; ICU, intensive care unit; AM, antimicrobial; RCTs, randomised controlled trials; MH, Muller–Hinton; CV, crystal violet.

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external parties to examine and compare the efficacies of commercially available AMDs, along with robust clinical randomised controlled trials. This is essential for informed clinical decision-making and optimal patient management.

1. Introduction

Infection is a significant concern in patients who survive an initial burn insult. This complication of burn recovery impacts on morbidity, mortality and healthcare costs [1], and in some centres has been estimated to account for over 75% of the mortality [2].

Burns patients are especially susceptible to infection owing to the injury removing the protective barrier provided by the skin, combined with general immunosuppression, the presence of endogenous microflora, prolonged hospital stays, and invasive diagnostic and therapeutic procedures [3]. Consequently despite careful treatment and infection control practices, burn wounds are readily colonised with a range of pathogenic micro-organisms, significantly delaying wound healing, and increasing risks of systemic infection, and graft failure [4].

The most frequently implicated bacteria are *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter* spp [5,6]. Of these, *P. aeruginosa* and *A. baumannii* are most prevalent [7], with Lawrence [8] finding *P. aeruginosa* in one-third of burn wounds, and in 59% of those patients with extensive burns. Yali et al. [9] took clinical samples from burns patients in burn intensive care units (ICU) and common burn wards and identified the organisms causing infection. 1621 pathogens were isolated from 2395 clinical samples of the burn ICU, and of these 74.2% were Gram-negative. *A. baumannii* was the most prevalent representing 34.4% of all pathogens present in this setting. Additionally, there is also concern that patients may acquire bacteria with resistance to multiple systemic antimicrobials, such as the carbapenem resistant *Enterobacteriaceae* (CRE), for which there are very limited treatment options.

Colonisation of burn wounds typically occurs as biofilms (communities of bacteria), which are harder to treat and eradicate owing to reduced rates of metabolism and protection (against antimicrobial agents and the immune response) afforded by the polysaccharide matrix [10]. Consequently the presence of biofilms is associated with persistence of colonisation and increased risk of systemic infection [1]. Hence, general principles of wound management include appropriate systemic care (e.g. in terms of pain control, nutrition and control of serum glucose levels in those with diabetes mellitus), combined with local wound care (especially in terms of preventing colonisation). For burn wounds, the standard of care worldwide is early excision of necrotic tissues followed by covering the wound with a medical dressing. Prevention and treatment of bacterial colonisation are key parts of wound care [11].

There is a large array of dressings and a range of factors that govern the choice of dressing that is most appropriate for wound management (e.g. type of wound, stage of healing process, and volume of exudate). However, for burns and other wounds where infection is a high risk, antimicrobial dressings (AMD) may be used. Typically the antimicrobial agent (AM) is contained within a commercially marketed wound dressing, which can be used both prophylactically (to prevent colonisation of the wound and subsequent biofilm formation), and in the treatment of established infection. Systemic administration of antimicrobials is not thought to be necessary nor useful for the management of local wound infections, since the drugs (i) may not penetrate well into the wounds (due to poor blood flow and the presence of dead tissue) [10], (ii) would need to be used in very high doses (to treat organisms growing in sessile biofilms) [12], and (iii) systemic administration has not been shown to prevent bacterial colonisation [13]. Furthermore, inappropriate use of systemic antibiotics can be associated with problems of allergy, toxicity and the development of resistance in non-target organisms.

AMD account for approximately a quarter of all dressings prescribed in primary care in England [14], and may contain a range of antimicrobial agents (e.g. silver, iodine, honey, and chlorhexidine). The use of AMD and silver-dressings (which are classed as 'advanced' dressings) has risen in recent years, with £25 million spent on silver dressings in 2006/2007 [10]. Indeed, one in every seven wound dressing items prescribed by the NHS contain silver as an active agent [10].

Silver (Ag) has been used extensively in burn wound management [15] and is a potent antimicrobial. Silver-containing dressings vary in their composition and act by a combination of (i) absorbing wound exudates and killing the microorganisms drawn into the dressings, and/or (ii) releasing active silver onto the wound bed. These biologically active ions then bind to negatively charged proteins, RNA, and DNA and damage bacterial cell walls, inhibit replication and reduce metabolism and growth [16]. Broad antimicrobial activity has been reported against Gram-positive and Gram-negative organisms [17], protozoa, viruses [18], and fungi [19].

AMD are marketed as effective against a broad range of bacteria (growing as biofilms) over multiple days, and are indicated for a variety of serious wounds (e.g. partial thickness burns, ulcers, donor and graft sites, traumatic, and surgical wounds). Provided that the agent is considered to only provide an ancillary action on the wound, the majority of dressings (including AMD) are classified as medical devices [20]. This means there are lesser requirements in terms of robust data from randomised controlled trials (RCTs) to support safety and efficacy, and literature reviews and commercial company-led research are often deemed acceptable for licensing. Consequently, there is little data available in peer-reviewed literature concerning their activity [11]. Unsurprisingly in clinical practice, opinions on the use of silver dressings are divided, with some clinicians believing that they have a role to