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Nanocrystalline silver dressings as an efficient anti-MRSA barrier: a new solution to an increasing problem

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Summary The emergence of multi-drug-resistant strains of bacteria represents a particular challenge in the field of wound management. The aim of the current study was to investigate whether nanocrystalline silver dressings possess the physical properties to act as a barrier to the transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) in the laboratory setting and in a clinical setting. Initially, MRSA suspension and colony culture experiments were performed showing that nanocrystalline silver dressings act as potent and sustained antimicrobial agents, efficiently inhibiting MRSA penetration. Subsequently, a double-centre clinical trial was initiated using nanocrystalline silver dressings as a cover for 10 MRSA colonized wounds in a total of seven patients. By delineating the MRSA load on the upper side of the dressing and the wound bed each time the dressing was changed (i.e. after 1, 24, 48 and 72 h), nanocrystalline silver dressings were found to provide a complete, or almost complete, barrier to the penetration/spread of MRSA in 95% of readings. In addition, 67% of all wound observations showed a decrease in the MRSA load with an eradication rate of 11%. We believe that nanocrystalline silver dressings may become an important part of local MRSA management, with cost benefits to both patients and the healthcare system.

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Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) has become a pandemic problem. The Centers for Disease Control and Prevention's (CDC) National Nosocomial Infection Surveillance System reported that MRSA in US hospitals increased from 2.4% in 1975 to 35% in 1997,[1] with a higher incidence in intensive care units. Until recently, MRSA has been infrequently isolated from the community; however, publications suggest that the incidence of MRSA and other multi-resistant strains is increasing in the community setting,[2] and some deaths from community-acquired MRSA have been reported.[3,4]

Despite World Health Organization (WHO), CDC and national guidelines recommending isolation of MRSA patients, together with special nursing and treatment procedures to prevent and control MRSA infection and transmission, the growing pandemic places a substantial burden on the entire healthcare system. In the light of increasing death rates (in England and Wales, death records with a general diagnosis of *Staphylococcus aureus* infection showed that the proportion due to MRSA increased from 8% in 1993 to 44% in 1998[5]), 4.5-fold-longer periods of hospitalization[6] and increasing costs ($42–$59 million/year for Canadian hospitals[7]), there is an urgent need for new approaches to the management and containment of MRSA transmission/infection.

Acticoat® (Smith & Nephew, Hull, UK), a commercially available silver dressing, consists of silver nanocrystals organized in a coarse columnar structure. When used as a wound dressing, the small silver nanocrystals produce a very large surface area on the lower blue layer providing antimicrobial activity. The absorbent inner core maintains a moist wound environment necessary for the continuous release of silver[8] and advantageous wound-healing conditions.[9] Indications for use include protection against bacterial contamination in burns[10] and chronic wounds.[11]

The aim of the present study was to determine whether the properties of nanocrystalline silver dressings might be used as an active antimicrobial barrier to prevent MRSA transmission and cross-contamination from MRSA colonized wounds and lesions. For this purpose, an in vitro pilot study and a two-centre clinical trial were undertaken to test the potential MRSA barrier and microbial function of nanocrystalline silver dressings.

Patients and methods

Preclinical in vitro assessment

To test the potential MRSA barrier and lytic function of the dressing, a series of eight Columbia agar (bioMérieux, Paris, France) plates (diameter 90 mm/63.6 cm^2) were first inoculated with 0.1 ml MRSA suspensions (MacFarland: 0.5, Colorimeter, Vitek Inc., Loveland, Colorado, USA). A 4×4-cm nanocrystalline silver dressing, moistened with distilled water, was applied immediately to each plate, blue side down, for MRSA solution experiments [sMRSA, Figure 1(A)]. In addition, a series of eight MRSA inoculated plates were incubated at 37 °C to confluent colony growth for 24 h and were subsequently covered with wet dressings, blue side down (MRSA colony experiments, cMRSA). Both sets of plates (sMRSA and cMRSA) were incubated at 37 °C for 1, 24, 48 and 72 h. From the removed dressings, imprints of the upper and lower sides were applied on sterile Columbia agar plates. After 72 h of culture, the number of colonies/plate, representing the MRSA load on the upper and lower sides of the dressing, were directly counted. The area of each plate covered by a dressing (pA) was examined for MRSA growth directly after removal of the dressing. From the areas where no bacteria could be detected visually, smears were taken and cultured in 10 mL of brain heart infusion (bioMérieux) (24 h at 37 °C), and plated on Columbia agar.

As the blue lower side of a nanocrystalline silver dressing releases silver ions into the covered area, a further experiment was conducted to test whether the released silver ions inhibit MRSA by themselves (post-dressing effect). For this purpose, all test plates initially covered with dressing (1, 24, 48 and 72 h) were stored at 37 °C for a further 72 h without any dressing and MRSA regrowth was quantified. Where no regrowth of MRSA was observed, the areas previously covered with the dressing were re-inoculated with saturated MRSA suspensions in order to exclude the possibility that a lack of nutrients within the agar and/or dried-out bacteria were responsible for the lack of growth. Potential MRSA growth was quantified via direct colony determination after 1 h and every 24 h over a 72-h period. In total, three series of such MRSA re-infection experiments were performed.

Clinical assessment of MRSA-colonized external wounds

Between October 2002 and September 2003, seven patients with 10 wounds (Table I) colonized with MRSA were recruited from two centres (Department of Dermatology, Federal Academic Hospital Feldkirch, Feldkirch, Austria and Department of Dermatology, Wilheminenspital, Vienna, Austria) into an