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A systematic review and meta-analysis of clinical outcomes associated with nanocrystalline silver use compared to alternative silver delivery systems in the management of superficial and deep partial thickness burns

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ABSTRACT

Objective: The purpose of this systematic review and meta-analysis was to assess the clinical effectiveness of nanocrystalline silver compared to alternative silver delivery systems (silver sulphadiazine [SSD] and silver nitrate) in adults and children with superficial and deep partial thickness burns.

Methods: PubMed, EMBASE, Cochrane and other databases were searched to identify relevant randomised controlled trials and observational studies.

Results: Eight studies that assessed both nanocrystalline silver and SSD and one study that compared nanocrystalline silver vs. silver nitrate were identified. Nanocrystalline silver compared to SSD/silver nitrate was associated with a statistically significant reduction in infections (odds ratio [OR] 0.21, 95% CI 0.07–0.62, p=0.005), length of stay in hospital (mean difference −4.74 (95% CI −5.79 to −3.69, p=0.00001) and surgical procedures (OR 0.40, 95% CI 0.28–0.56, p=0.00001). Three studies that reported on pain had lower pain scores with nanocrystalline silver use than with SSD/silver nitrate; a high level of heterogeneity precluded pooling estimates.

Conclusion: This comprehensive systematic review and meta-analysis of the available evidence suggest that the use of nanocrystalline silver dressings results in shorter length of stay in hospital, less pain, fewer surgical procedures and reduced infection rates compared to silver sulphadiazine/silver nitrate.

1. Introduction

Burns are a serious health problem affecting adults and children globally [1]. In the United States alone, over 480,000 people require medical care for burns each year, leading to 40,000 hospitalisations [2]. The survival rate is a favourable 97% [2], however, burns are a cause of considerable morbidity.

Superficial burns affect the epidermal skin layer and superficial layer of dermis. Partial thickness burns may involve

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damage to deeper structures of the dermis and structures such as blood vessels and nerves [3]. Treatment of these burns is aimed at controlling infection and promoting healing with good aesthetic outcomes, and a wide variety of wound care products are currently available [3]. The process of burn management can often lead to infection resulting from local damage to the skin's protective barrier, together with supressed immune system function [4,5]. This high risk of infection often results in delayed wound healing and longer hospital stays, in addition to higher treatment costs [5]. Patient comfort on the potentially frequent application of dressings during wear and removal is also an important consideration in managing burn wounds [6] and there has been renewed focus on how antimicrobial delivery systems impact on pain control.

The antimicrobial properties of silver have been recognised since Roman times [7]. This heavy metal has a broad spectrum of activity against bacteria, yeasts and fungi and has been used in modern day wound healing since the early 1960s when 0.5% silver nitrate aqueous solution was used as an alternative to antibiotics in the management of major burns [8]. However, rapid inactivation by protein and chloride in the burn wound meant application frequencies could be up to 12 times per day to ensure that sufficient levels of silver ions were available to reduce the bacterial load [9]. Silver sulphadiazine (SSD) was introduced in the late 1960s, and this combination of silver linked to a sulphadiazine carrier reduced the frequency of application to once/twice daily as the effective release and replenishment of bactericidal levels of ionic silver were considerably improved [10]. SSD is still considered the standard antimicrobial treatment for burn wounds in many parts of the world. However, advances in technology have lead to newer silver dressings with improved forms of delivery systems, aimed at improving efficacy while minimising side effects [9]. The unique structure of the nanocrystalline silver dressing dictates activity and releases and replenishes bactericidal levels of positively charged silver ions to ensure fast and effective kill over extended time periods [11].

The management of burn wounds can take many forms. With the benefits of multiple treatment options come challenges for clinicians over which to choose. The purpose of this systematic review and meta-analysis was to assess the clinical effectiveness of nanocrystalline silver compared to two alternative silver delivery systems in adults and children with superficial and deep partial thickness burns in terms of infection control, length of stay (LOS) in hospital, surgical procedures and pain reduction.

2. Methods

2.1. Systematic review eligibility criteria

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [12]. It was based on the planned Population, Intervention, Comparator, and Outcomes (PICO) elements outlined in Table 1.

2.2. Search strategy

Studies were identified by searches of the following electronic databases: PubMed, EMBASE, Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment (HTA) Database, ClinicalTrials.gov, International Clinical Trials Registry Platform (ICTRP), and the European Trials Register. A search strategy was used to identify studies indexed on PubMed, and this was modified for searches of the other databases to account for differences in syntax and thesaurus headings. Search terms included both free text and MeSH terms. No limits were applied for language. The searches were run to include citations from 1990 (when most of the commonly used silvers became available) to May 2015. A pearl-growing technique (i.e. searching the references of relevant papers identified in the original search) was used to identify further publications of interest.

2.3. Study selection and data extraction

Two reviewers independently assessed the full text papers of the studies identified during the abstract assessment stage for inclusion, and any differences in opinion were arbitrated by a third reviewer. Initially, five papers were fully independently data extracted by two reviewers using a standardised data extraction form and then validated by one reviewer. Since agreement between the two reviewers was high the remaining papers were independently extracted by one reviewer and

Table 1 – Inclusion and exclusion criteria.

Criteria	Inclusion	Exclusion
Type of study	RCTs, retrospective and prospective comparative observational studies	Systematic reviews, conference abstracts, case series, case reports, narrative reviews, editorials, opinions; studies performed in animals
Population	Adults and children with deep partial and superficial partial thickness burns	Full thickness burns
Geographical location	Publications from any country	None
Interventions	Nanocrystalline silver (ACTICOAT), SSD, silver nitrate	Other silver dressings other than nanocrystalline silver (ACTICOAT), SSD and silver nitrate
Outcomes of interest	Infection, LOS, incidence of surgical procedures (defined as debridement & skin grafting) and pain	

LOS, length of stay [in hospital]; SSD, silver sulphadiazine; RCT, randomised controlled trial.