

Nanocrystalline silver dressings for wounds other than burns and donor sites

Update: 10 March 2014

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SUMMARY

QUESTION

What is the best available evidence regarding the use of nanocrystalline silver dressings for wounds (other than burns and donor sites)?

CLINICAL BOTTOM LINE

Slow-release nanocrystalline silver dressings play an important part in the treatment of infected wounds by reducing the bacterial burden and inflammation. Nanocrystalline silver has been found to be a broad-spectrum antimicrobial agent effective against gram-negative and gram-positive bacteria (including those that are multi-drug resistant), yeast, fungi and viruses^{1,2}.

Nanomaterials are often unique, differing in physical, chemical and biological ways from their macro counterparts. In the case of silver, the smaller the particle the larger the surface area that is available for interaction, resulting in an increased bactericidal effect. Nanocrystalline silver's ability to reduce bacterial burden is thought to be due to the capacity of silver ions to attach to and penetrate the surface of the cell membrane, permanently disturb cell respiratory function and interfere with the cell's ability to replicate³.

REDUCTION OF BACTERIA LEVELS

- A comparative laboratory study reported that nanocrystalline silver dressings reduced the pathogenic bacterial count for *Staphylococcus aureus* and *Pseudomonas aeruginosa* below the limit of detection (less than 10 cfu/ml) by 24 hours. This high efficacy was maintained with higher concentrations of bacteria at 48 hours⁴. (Level 5)
- An *in vitro* study compared six dressings — silver sulphate, silver alginate, silver collagen matrix, nanocrystalline silver and two types of silver foam. Only the nanocrystalline silver dressing was bactericidal within 30 minutes (i.e. capable of producing a log reduction greater than three) against *Staphylococcus aureus* ($p < 0.001$). Over the nine days of the study it continued to show an inhibitory effect, indicating its sustained release properties⁵. (Level 5)
- A small (N=10 MRSA colonised wounds) observational study found that nanocrystalline dressings had provided a complete or almost complete barrier to the spread/

penetration of MRSA in 95% of culture results over a 72-hour period. Sixty-seven per cent of all wound observations indicated a decrease in MRSA load, with an 11% eradication rate⁶. (Level 3)

- In studying the use of nanocrystalline dressings (in combination with compression bandages) in the treatment of chronic venous leg ulcers (median duration 17.3 weeks) in 15 patients over a 12-week period, there was a significant reduction in the log₁₀ total bacterial count ($p = 0.011$) from baseline⁷. (Level 3)

INFLAMMATION

The anti-inflammatory properties of nanocrystalline silver have been examined by a number of *in vivo* comparative studies, for example:

- Contact dermatitis induced in pigs was treated daily with nanocrystalline silver dressings, 0.5% silver nitrate, or saline. Those treated with nanocrystalline had near-normal skin after 72 hours, whilst other treatment groups remained clinically inflamed. The authors suggested that this result might be due to a highly discriminatory process linked to the type of silver released (e.g. Ago) that differs from the indiscriminate activity of Ag⁺⁸. (Level 5)
- A similar study of induced contact dermatitis in guinea pigs compared five daily applications to the affected area of one of the following: topical nanocrystalline silver cream, medium and high potency steroids, tacrolimus and pimecrolimus. Nanocrystalline silver was found to significantly reduce erythema within one day of treatment. After five days of treatment there were no signs of erythema in more than 50% of the animals. These results were comparable to the sample that received steroids and immunosuppressants. However, the effect of nanocrystalline silver appeared to be more rapid⁹. (Level 5)

WOUND HEALING

The following results need to be considered in the context that healing will only be facilitated by the use of nanocrystalline if no other impediments to healing are present, such as underlying disease (e.g. peripheral arterial disease, chronic venous insufficiency) or trauma.

- A porcine model was used to investigate the effect of nanocrystalline silver on wound healing. Full-thickness

porcine wounds were covered with either silver-containing dressings or control dressings which did not contain silver. Unlike the control dressings, nanocrystalline silver dressings were found to promote rapid wound healing. This was characterised by the rapid development of well vascularised granulation tissue that supported tissue grafting four days post-injury, and decreased wound oedema, particularly during the first days post-injury¹⁰. (Level 5)

- A randomised controlled trial (RCT) (n=266) comparing the effectiveness of nanocrystalline silver and cadexomer iodine dressings on leg ulcers compromised by bacterial burden produced comparable results in overall healing rates and the percentage of wounds healed, i.e. 100% epithelialisation within 12 weeks (64% vs 63%). However, nanocrystalline silver was associated with significantly more rapid healing rates during the first two weeks of treatment in all five sub-groups of wounds ($p < 0.01$). In ulcers unlikely to heal within the 12-week time frame — large, chronic ulcers which may also have moderate to high levels of exudate — nanocrystalline silver dressings also achieved more rapid healing¹¹. (Level 1)
- In the 12 patients who completed the study, Sibbald *et al.*⁷ found a mean reduction in ulcer surface of 83.5% (range 66.1–100%) at the end of 12 weeks, with four of the chronic ulcers healing completely. (Level 3)

Several earlier small studies on the use of nanocrystalline silver in chronic wounds supported these findings¹.

OTHER ASPECTS OF WOUND MANAGEMENT

A survey¹² of 44 community nurses rated nanocrystalline silver dressings as significantly more effective than cadexomer iodine in managing wound exudate ($p < 0.01$), maintaining the integrity of peri-wound skin ($p < 0.05$), and managing wound odour ($p < 0.05$). (Level 4) Both Miller *et al.*'s¹¹ study and a small case series¹³ (n=4) supported these findings in relation to wound exudate. In the latter study, reduction of exudate fluid occurred in the four cases of decubitus ulcers treated with nanocrystalline silver dressings. (Level 4)

SAFETY

Concerns have been raised in regard to the possible toxic effects of nanocrystalline silver on viable wound tissue. *In vitro* studies^{1,14} have reported that nanocrystalline silver is cytotoxic to fibroblasts and keratinocytes, and impedes epithelialisation. A study¹⁵ comparing the use of nanocrystalline silver with another silver-coated dressing in 16 paired donor sites in 15 patients concluded nanocrystalline silver delays re-epithelialisation. Donor sites dressed with nanocrystalline silver required a mean of 14.5 ± 6.7 days to achieve >90% re-epithelialisation compared to a mean of 9.1 ± 1.6 days for the comparator ($p = 0.004$). The comparator sites achieved significantly greater estimated re-epithelialisation on days 6, 8, 10 and 12 than the nanocrystalline silver dressed sites.

(Level 3) Although there is no *in vivo* evidence to suggest that nanocrystalline silver is toxic when used to treat other types of wounds it is recommended that these dressings be used with caution in epithelialising wounds¹

The possibility of dermal and systemic absorption has also been studied to a limited extent:

- An *in vitro* study examined the penetration of silver nanoparticles through intact and damaged skin. The absorption was very low but detectable in both cases, with penetration being detected in the stratum corneum and the outermost surface of the epidermis¹⁶. (Level 5)
- Nanocrystalline silver dressings were applied to a sample of 16 healthy patients with normal, intact skin approximately five days prior to surgery. The treated skin samples, which were removed as surgical waste, were analysed to determine silver concentration. Additionally, silver serum levels were analysed before and after dressing application. There was no demonstrable rise in serum silver levels post-treatment. The results suggested that silver nanoparticles are able to penetrate intact human skin beyond the stratum corneum and deep into the reticular dermis *in vivo* and may form clusters. However, the silver nanoparticles did not reach systemic circulation. On the basis of this finding, the authors suggested nanocrystalline silver applied to the skin should not negatively affect end organs¹⁷. (Level 3)
- Sibbald *et al.*⁷ found that there was a slight but significant increase ($p = 0.05$) in silver concentration in the serum of study participants during the 12 weeks of their study, but this increase was within the normal range (zero–14.9ng/mL). (Level 3)

The use of silver nanoparticles is contraindicated in silver-sensitive individuals¹⁸.

LEVEL OF EVIDENCE

This evidence summary is based on a structured literature and database search combining search terms that describe nanocrystalline silver, wound healing, wound inflammation and infection. The evidence in this summary comes from:

- One RCT comparing nanocrystalline silver and cadexomer iodine¹¹.
- A prospective, controlled, matched pair study comparing rate of re-epithelialisation of donor sites using nanocrystalline silver versus another silver-coated dressing¹⁵.
- A review of *in vitro*, animal and human studies of the effectiveness of nanocrystalline silver dressings in wound management¹.
- Three clinical studies, all with small sample sizes, examining the effectiveness of various characteristics of nanocrystalline silver^{6,7,17}.
- A small case series reporting the effectiveness of nanocrystalline silver on healing decubitus ulcers¹³.

- A survey of nurses comparing nanocrystalline silver and cadexomer iodine on aspects of wound management¹².
- A review of the methods used in the preparation of silver nanoparticles³.
- Three *in vivo* animal studies, two on the anti-inflammatory effect^{8,9} and one on the wound healing properties of nanocrystalline silver¹⁰.
- Four *in vitro* studies, two on the antimicrobial efficacy^{4,5} and two on the toxicology of nanocrystalline silver^{4,16}.
- A review of *in vitro* studies of the bactericidal effectiveness of silver nanoparticles on multi-drug resistant bacteria².
- Manufacturer's instructions^{18,19}.

BEST PRACTICE RECOMMENDATIONS

- Nanocrystalline silver dressings should be used selectively for infected wounds, particularly in diabetics or patients with peripheral arterial occlusion disease in which systemic antibiotics often do not reach peripheral infection. (Grade A)
- The effectiveness of a nanocrystalline dressing should be evaluated at two weeks. Extension of use beyond this time period should be based on expert clinical judgement. (Grade B)
- Nanocrystalline silver dressings should be used with caution in re-epithelising wounds. (Grade B)
- To activate the release of silver ions on to the wound surface, it is recommended that some types of nanocrystalline dressings require dampening with water. (1) Do not use saline¹⁹. (Grade B)
- Wounds with moderate to high levels of exudate may require a secondary absorbent dressing, which should be changed on a regular basis as required. (Grade B)

RELATED TOPICS

ES 1710 Management of burn wounds: clinical efficacy and safety of Acticoat™.

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