Silver treatments and silver-impregnated dressings for the healing of leg wounds and ulcers: a systematic review and meta-analysis

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CRD summary
This review found some evidence that silver-impregnated dressings improved the short-term healing of leg wounds and ulcers, but long-term effects remained unclear. The authors’ conclusions reflect the evidence presented but, given concerns about publication bias and included trial quality, the reliability of the conclusions is uncertain.

Authors’ objectives
To conduct a systematic review of silver dressings and treatments in wounds focusing on healing outcome parameters, and to attempt meta-analyses for these parameters.

Searching
MEDLINE, Scopus, and the Cochrane Library were searched for relevant studies published up to December 2008; no language restrictions were applied. Search terms were reported. Four relevant journals, the clinicaltrials.gov website and reviews were also searched. Experts were contacted to identify additional relevant studies. Only studies published in peer-reviewed journals were eligible.

Study selection
Eligible studies were randomised controlled trials (RCTs) of patients with any kind of leg ulcer or leg wound that used topical silver-based agents in the experimental arm and either placebo or any non-silver conservative wound treatment in the control group. Eligible trials had to report at least one of a range of wound-healing parameters including complete wound healing, wound size reduction, wound depth reduction, healing rate and time to heal. Trials of burns were excluded.

In included trials, the main wound type was venous ulcer; other wound types included arterial ulcers, diabetic foot ulcers, and surgical/traumatic wounds. Experimental dressings included silvadene, flamazine, contreet foam, aquacel Ag, restore contact layer silver, silvercel, and actisorb plus. Control dressings included tripeptide copper complex, placebo, non-adherent dressings, hydrocolloid dressing, allevyn hydrocellular foam, algosteril, povidone-iodine gauze, restore contact layer, algosteril, foam/alginate, hydrocolloid, gauze, silver dressing, and conventional dressing with granulating ointment/zinc paste.

Two reviewers selected studies independently. Disagreements resolved by discussion with a third reviewer.

Assessment of study quality
Trial quality was assessed using a modified version of a checklist devised by Downs and Black, which assigned trials a quality score ranging from zero and 29 points based on five domains: reporting, external validity, internal validity, bias, confounding, and power.

Two reviewers independently conducted the validity assessment. Discrepancies were resolved through discussion.

Data extraction
Data were extracted to calculate risk differences (RDs) and corresponding 95% confidence intervals (CIs) for dichotomous outcomes and mean differences and 95% CIs for continuous outcomes. Trial authors were contacted for missing data.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Risk differences (RDs) with 95% confidence intervals were pooled using Mantel-Haenszel fixed-effect model. Mean differences with 95% confidence intervals were pooled using inverse variance fixed-effect models. Heterogeneity was
assessed using $I^2$; where $I^2$ was more than 75%, a random-effects model was used.

Funnel plots were created and visually inspected for two outcomes to assess publication bias.

**Results of the review**

Ten RCTs were included in the review. Some trials reported number of participants (range 38 to 619); some trials reported number of ulcers. Analysis was conducted at a patient level. Total quality scores ranged from 9 to 23 points out of 29.

There was a significant reduction in wound size for silver-impregnated dressings compared with other dressings (WMD 10.29%, 95% CI 3.86 to 16.71; $I^2=$31%; five RCTs; n=1,000). There were no statistically significant differences between silver-impregnated dressings and other dressings for wound healing ($I^2=$33%; seven RCTs; n=1,118) or healing rate per day ($I^2 =$45%; three RCTs; n=320).

The authors stated there was some evidence of publication bias for the analysis of wound healing but not for wound size reduction.

**Authors’ conclusions**

The review provided some evidence that silver-impregnated dressings improved the short-term healing of wounds and ulcers, but long-term effects remained unclear.

**CRD commentary**

The search was thorough and without language restrictions, but only peer-reviewed journals were eligible, so the risk of publication bias could not be ruled out. Formal assessment of publication bias was carried out and some evidence for the analysis of wound healing was found. The study selection were clearly reported, appeared appropriate and was conducted by two reviewers independently. However, the number of reviewers extracting data was not reported, so the risk of reviewer error and bias at this stage could not be ruled out.

Trial quality was independently assessed and results were reported; quality was variable. A standard approach to synthesis was used and the results were clearly reported. The reporting of included trial details was thorough, improving review transparency; it indicated that one of the control groups used silver dressings.

The authors’ conclusions reflect the evidence presented but, given the potential for publication bias and the variable quality of the included trials, the reliability of the conclusions is uncertain.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that clinical trial data with long follow-up times are needed to determine longer-term effectiveness. They also stated that further research is needed to define the cost-effectiveness of silver-impregnated dressings and to quantify the precise benefits for patients with different comorbidities and wounds.

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