Systematic reviews of wound care management: (2) dressings and topical agents used in the healing of chronic wounds

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Authors' objectives
To evaluate the evidence for effectiveness and cost-effectiveness of dressings and topical preparations in pressure sores, leg ulcers and surgical wounds healing by secondary intention.

Searching
The following nineteen electronic databases were searched until October 1997: MEDLINE, CINAHL, ISI Science Citation Index, BIOSIS Previews, the British Diabetic Association Database, CISCOM, the Cochrane Database of Systematic Reviews, the Cochrane Wounds Group register of trials, Current Research in Britain (CRIB), DARE, Dissertation Abstracts, DH-Data, EconLit, EMBASE, Index to Scientific and Technical Proceedings, National Research Register, NHS EED, the Royal College of Nursing Database, and SIGLE. The electronic search was supplemented by a handsearch of 5 specialist wound care journals, 12 conference proceedings, and a search of systematic reviews held on DARE. Additional trials were identified by searching the bibliographies of all retrieved and relevant publications, and by asking an advisory panel of experts in wound management; companies with an interest in wound care were approached for unreported trials. Relevant economic evaluations were identified by adding economic related search terms to those used in the search for clinical trials. Authors of trials published after 1985 were contacted and asked to provide details of any associated economic evaluations.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), published or unpublished. Where a particular dressing was not evaluated by an RCT, prospective controlled trials were included.

Specific interventions included in the review
Dressings and topical agents in relation to wound healing.

Participants included in the review
Individuals with pressure sores, leg ulcers, sinuses, surgical wounds and wounds healing by secondary intention.

Outcomes assessed in the review
The proportion of wounds healed within a time period and the percentage or absolute change in wound area. Studies were only included if they had an outcome measure that was considered an objective measure of healing.

How were decisions on the relevance of primary studies made?
The retrieved studies were assessed for relevance by a single reviewer and decisions on final inclusion were checked by a second reviewer. Any disagreements were resolved by discussion with a third reviewer.

Assessment of study quality
The validity criteria used to assess primary studies were as follows: inclusion and exclusion criteria stated, overall sample size (arms), a priori sample size calculation, randomisation procedure stated, appropriate baseline characteristics reported, blinded outcome assessment reported, withdrawals stated, intention to treat (ITT) analysis. The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
Data from the included trials were extracted by a single reviewer into data extraction tables and then checked independently by a second reviewer. The following categories of data were extracted from each study: study and design (including wound type, and where appropriate, method of randomisation, objective outcome, and setting and length of treatment), inclusion and exclusion criteria, intervention details, baseline characteristics, results and withdrawals.

**Methods of synthesis**

**How were the studies combined?**

The results from each study were calculated as odds ratios (ORs) and/or effect sizes (ESs) using 95% confidence intervals (CIs), and where appropriate, similar studies were pooled in a meta-analysis (fixed-effect and random-effects models). The results of both the ORs and mean differences in healing rates were presented in forest plots. Publication bias was assessed using 2 funnel plots; one of all studies comparing traditional treatments with modern dressings or topical agents for the treatment of leg ulcers and pressure sores, and a second of studies comparing traditional treatments with hydrocolloid dressings for the treatment of leg ulcers and pressure sores.

**How were differences between studies investigated?**

For those studies pooled in a meta-analysis, heterogeneity was assessed using chi-squared test.

**Results of the review**

Five studies in relation to surgical wounds healing by secondary intention, 28 trials evaluating 31 comparisons of treatments in relation to pressure sores, and 60 studies in relation to leg ulcers were included.

Treatments for surgical wounds healing by secondary intention: one study found a statistically-significant reduction in healing time with traditional wet-to-dry dressings, compared with topical applications of aloe vera, for all wound types (OR -30, 95% CI: -55.01, -4.99) and for vertical incisions (OR -37, 95% CI: -67.26, -6.74).

Treatments for pressure sores: a single report suggested that the topical application of insulin was of significant benefit for wound healing when compared with standard nursing care (p=0.05). A meta-analysis of 5 reports (chi-squared=5.76, d.f.=4, p=0.218) comparing a hydrocolloid dressing with a traditional treatment suggested that treatment with hydrocolloid resulted in a statistically-significant improvement in the rate of pressure sore healing (OR 2.57, 95% CI: 1.58, 4.18).

Treatments for leg ulcers: compared with a control preparation, both mononuclear cultured cells in culture medium and topical ketanserin significantly increased healing rates in one trial of arterial leg ulcers. Collagen sponges appeared to be effective in 2 trials of leg ulcers but there were insufficient data to determine the significance of these results.

Nine trials compared hydrocolloid dressings with traditional or control dressings for venous ulcers. The meta-analysis of the 8 studies (chi-squared=16.72, d.f.=7, p=0.019) providing data on the proportion of ulcers completely healed during the trial period, demonstrated no significant difference in this outcome (pooled OR 1.45, 95% CI: 0.83, 2.34). Two trials compared semi-permeable film dressings with traditional or control therapies: one found a larger reduction in wound area under the film dressing (ES 32.15, 95% CI: 10.18, 54.12) but the other found no significant difference in healing rates (OR 1.48, 95% CI: 0.3, 4.3). Two trials compared foam dressings with traditional or control therapies: one trial found a reduction in wound area with foam dressing (ES 144, 95% CI: 48.8, 239) but the other found no difference in the proportion of ulcers healed (OR 1.67, 95% CI: 0.8, 3.3). Woven zinc oxide paste bandage was more effective than either an alginate dressing (OR 3.6, 95% CI: 1.1, 6.14) or a zinc oxide-impregnated stockinette (OR 1.83, 95% CI: 0.78, 4.28) in one trial.

In 2 trials comparing different hydrocolloids, no significant difference in healing rates was found. Two trials comparing hydrocolloids with foam dressings found no statistically-significant difference in the proportion of ulcers healed over the trial period. Pooling the data from the two trials (chi-squared=0.00, d.f.=1, p=1) again showed no difference in healing rates (OR 1.0, 95% CI: 0.48, 2.07).

In trials of topical agents, one trial reported a higher proportion of ulcers that healed with allopurinol (OR 2.98, 95% CI: 1.28, 6.94) and with dimethyl sulfoxide (OR 3.28, 95% CI: 1.39, 7.71) than when compared with placebo. Of 2
trials comparing hyaluronic acid with control, one found a difference in daily healing rate that favoured the hyaluronic acid (ES 34), and the other found no difference in the proportion of ulcers healed over the trial period (OR 0.72, 95% CI: 0.2, 2.56).

Four trials compared biological dressings with traditional therapies. None found statistically-significant differences in results.

Two trials compared dressings with topical preparations. There was no difference in the proportion of ulcers healed between patients treated with cryopreserved cultured allografts or a hydrocolloid (OR 0.83, 95% CI: 0.21, 3.2), though the former-treated ulcers had a higher rate of epithelialisation. A collagen dressing healed a higher proportion of ulcers than treatment with daily antiseptic (OR 26.6, 95% CI: 2.3, 308).

A comparison of buffered acidifying ointment and ointment reported there was no difference in the proportion of ulcers healed, but there was a higher rate of epithelialisation with the buffered ointment group. In another trial there were higher healing rates with amino acid soaks than with saline soaks.

Quality assessment (treatments for surgical wounds healing by secondary intention and treatments for pressure sores): the majority of trials had methodological weaknesses. Fewer than 6% of studies reported an a priori estimate of the number of participants required to have sufficient power to detect a clinical effect as statistically significant, the median number of wounds recruited to a trial was 50 (range: 14 - 168). Blinding of investigators at outcome assessment was reported in fewer than 18% of trials. One or more patient characteristics were recorded by treatment group in 80% of studies, but wound size at baseline was reported in only 60%. Withdrawals occurred in most trials and were recorded by group and cause in 88% of trials where it was appropriate, but only 13% analysed the results on an ITT basis. Seventy-six per cent of trials described inclusion criteria, but information that indicated whether participants had been truly randomised to alternative treatments was given in only 20%.

Quality assessment (treatments for leg ulcers): the majority of trials had methodological weaknesses. Fewer than 9% of studies reported an a priori estimate of the number of participants required for the trial to have sufficient power to detect a clinical difference as statistically significant. The median number of wounds recruited to a trial was 48.5 (range: 9 - 233). Blinding of investigators at outcome assessment was reported in fewer than 7% of trials. One or more patient characteristics were recorded by treatment group in 36 out of 48 (75%) studies, but wound size at baseline (by group) was reported in only 30 of the 48 (62%) studies. Withdrawals occurred in most trials; the number and cause were recorded by group in 46% of trials where it was appropriate, but only 18% performed an ITT analysis. Sixty-two per cent described relevant inclusion criteria, but information that indicated that participants had been randomised with allocation concealment was given in only 10% of trials.

Publication bias assessment: the overall funnel plot of all studies comparing a traditional treatment with a modern therapy showed little evidence of asymmetry. However, for the subgroup of trials that compared a hydrocolloid dressing with a traditional treatment, asymmetry was clearly evident. Publication bias for studies favouring hydrocolloid treatment may be responsible for this result. Further analyses are reported in the paper.

Cost information
Yes. Nine trials provided sufficient data on costs of treatment to allow cost-effectiveness analysis: 6 evaluated cost-effectiveness in pressure sore treatments and 3 papers reported cost-effectiveness data in leg ulcer trials.

Authors' conclusions
There is insufficient evidence of effectiveness of any particular dressing or topical agent for surgical wounds healing by secondary intention; the few studies there are, are small and of poor quality. There is little evidence to indicate which dressings or topical agents are the most effective in the treatment of chronic wounds. However, there is evidence that hydrocolloid dressings are better than wet-to-dry dressings for the treatment of pressure sores. In the treatment of venous ulcers, low adherent dressings are as effective as hydrocolloid dressings beneath compression bandaging.
CRD commentary
This is a methodologically-sound review with a clearly-stated review question. The literature search was comprehensive and included both published and unpublished research. Publication bias was also assessed. Primary studies were assessed for validity, but details regarding the criteria by which the validity of primary studies were assessed and how judgements of validity were made, were not reported. Study details were well reported and the data analysis used suitable methods. Heterogeneity was investigated and the review process was well described. The authors’ conclusions appear to follow from the results presented.

Implications of the review for practice and research
Practice: The authors state that 'there is little evidence to indicate which dressings or topical agents are the most effective in the treatment of chronic wounds. However, there is evidence that hydrocolloid dressings are better than wet-to-dry dressings for the treatment of pressure sores. In the treatment of venous ulcers, low adherent dressings are as effective as hydrocolloid dressings beneath compression bandaging'.

Research: The authors state that 'research methodology could be significantly improved and commissioning groups may wish to consider the following aspects for future research: the number of patients in a trial should be based on an a priori sample size calculation; a truly objective outcome measure should be used or wound healing should be expressed as both percentage and absolute change in area; for each patient a single reference wound should be selected; experimental groups should be comparable at baseline; head-to-head comparisons of contemporary dressings are required and should use agents that are recommended for wounds of a similar nature; a complete and thorough description of concurrent treatments, including secondary dressings, should be given in trial reports; assessment of outcomes should ideally be blind to treatment, or completely objective; survival rate analysis should be adopted for all studies that assess wound healing; studies to determine the biological mechanisms involved in wound healing are needed; future trials should include cost-effectiveness and quality of life assessments, as well as objective measures of dressing performance; economic evaluations should be incorporated within trials that are sufficiently large to detect appropriate economic and clinical outcomes; to prevent publication bias and ensure the inclusion of unpublished trials in systematic reviews, those involved in primary research should make their data available to those undertaking systematic reviews'.

Funding
NHS R&D Health Technology Assessment (HTA) Programme, project number 93/29/01.

Bibliographic details

PubMedID
10683589

Original Paper URL
http://www.hta.ac.uk/project/9120086.asp

Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Topical; Anti-Infective Agents /therapeutic use; Bandages; Clinical Trials as Topic; Cost-Benefit Analysis; Dermatologic Agents /therapeutic use; Free Radical Scavengers /therapeutic use; Humans; Leg Ulcer /therapy; Platelet Aggregation Inhibitors /therapeutic use; Pressure Ulcer /therapy; Wound Healing /physiology; Wound Infection /prevention & control; Wounds and Injuries /drug therapy /therapy
AccessionNumber
12000008247

Date bibliographic record published
30/11/2001

Date abstract record published
30/11/2001

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.