A systematic review of the effectiveness of interventions to enhance the healing of chronic ulcers of the foot in diabetes


CRD summary
This generally well-conducted review concluded that some evidence existed to support the effectiveness of hydrogels, systemic hyperbaric oxygen, topical negative pressure and resection in the healing of chronic foot ulcers in diabetic patients, but further research is needed. Given the variable quality in available evidence and the small number of available studies, these conclusions should be treated with caution.

Authors' objectives
To evaluate the effectiveness of interventions on the healing of chronic foot ulcers in patients with diabetes.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Database of Systematic Reviews were searched for articles published in any language. Search terms were reported. Search dates varied across sources, spanning 1966 to December 2006. Previous high quality systematic reviews and Cochrane reviews were searched.

Study selection
Prospective and retrospective controlled studies of treatments for chronic foot ulcers in patients aged 18 or over with type I or type II diabetes, were eligible for inclusion. Studies had to include assessing of interventions on healing, time to healing, reduction in ulcer area or amputation.

Included studies were of a range of interventions in the areas of: sharp debridement and wound bed preparation with larvae; wound bed preparation using antiseptics, applications and dressing products; resection of the chronic wound; hyperbaric oxygen; reduction of tissue oedema; application of products designed to correct wound biochemistry and cell biology; stem cell therapy; bioengineered skin and skin grafts; and electrical, electromagnetic, lasers and ultrasounds. The ulcers treated ranged in severity across the included studies; some studies included patients with ulcers in areas other than the foot. One study included some patients who did not have diabetes.

Studies were screened at the title and abstracts stage by one reviewer. Identified full text articles were independently assessed for inclusion by two reviewers with agreement reached by discussion.

Assessment of study quality
Methodological quality of the included studies was assessed using the Dutch Cochrane Criteria with scoring specific to each study design. Randomised controlled trials (RCT) scored a maximum of 9 points, cohort studies a maximum of 8 points and case-control studies a maximum of 7 points. Each study was also rated as: high quality with low risk of bias; well conducted with low risk of bias; or as low quality with higher risk of bias. The studies were also assigned a level of evidence according to study design in accordance with the SIGN (Scottish Intercollegiate Guidelines Network) instrument.

Methodological quality was independently assessed by two reviewers with agreement reached by discussion.

Data extraction
Data were independently extracted by two reviewers, with agreement reached through discussion, and the evidence included in the tables was agreed following a discussion by the working party.

Methods of synthesis
The results were combined in a narrative synthesis.
Results of the review
Sixty studies were included for the review (n=24,747): 48 RCTS (n=3,684), one prospective cohort study (n=28), seven cohort studies (n=538) three retrospective cohort studies (n=20, 437) and one case-control study (n=60). Fifteen RCTs scored 3 or less on the quality criteria, 25 RCTs scored between 4 and 6 and eight RCTs scored 7 or more on the quality criteria. Eight cohort studies scored 3 or less, and three scored 4 or 5 on the validity assessment; the case control study scored 1 out of a possible 7 points.

Hydrogel (three studies, n=108 patients): Hydrogel dressings were associated with a significant improvement in ulcer healing compared to compared to saline-moistened gauze (one RCT) and ‘more rapid’ ulcer healing compared to gauze (one prospective cohort). The retrospective cohort study reported that amorphous hydrogel was associated with a reduced time to heal compared to wet or dry gauze but there was no difference in wound healing.

Resection of the wound (four studies, n=286 patients): Excision of the ulcer was associated with significantly shorter time to healing in three low to moderate quality studies and with significantly fewer recurrences in one cohort study. Early excision of infected tissue was associated with a significantly decreased rate of major amputation in one low quality cohort study.

Systemic hyperbaric oxygen (four studies, n=144 patients): Systemic hyperbaric oxygen was associated with significant reductions in the number of amputations (two studies), reduction of wound area (two studies) and healing (one study).

Topical negative pressure (four studies, n=297 patients): Results of topical negative pressure are limited by small sample sizes in two of the studies (both including only 10 patients). The largest RCT reported significantly increased healing rates.

The authors stated that ‘no data were found to justify the use of any other topically applies product or dressing’. Full results were reported for all of the included studies.

Authors’ conclusions
Some evidence existed to support the effectiveness of hydrogels, systemic hyperbaric oxygen, topical negative pressure and resection of neuropathic plantar ulcers, but more research is required to confirm these findings. No evidence was found to support the use of other topically applied products or dressings.

CRD commentary
The review addressed a clear question with well-defined inclusion criteria for participants and outcomes. Inclusion criteria for interventions and study design were broad. Several relevant databases were searched for articles in any language, reducing the risk of language bias. However, it was unclear whether a search was conducted for unpublished material, so publication bias cannot be ruled out. Appropriate steps were taken throughout the review process to minimise reviewer error and bias. A suitable validity assessment was carried out.

The quality of included studies varied widely, so the data presented in some studies may be unreliable. The decision to combine the studies in a narrative synthesis was appropriate given considerable clinical heterogeneity between included studies. Given this heterogeneity, only one or two studies were available for many of the included interventions, making it difficult to draw clear conclusions about the efficacy of such treatments. The synthesis may have benefited from a greater emphasis being placed on the high quality evidence.

This was a generally well-conducted review, but given the variable quality in available evidence and the small number of available studies, the authors’ conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The authors stated that extended resection of ulcers beneath the hallux may be considered and that the use of systemic hyperbaric oxygen is justified, particularly when revascularisation is not possible.

Research: The authors stated that further research is needed into sharp debridement, debriding agents, larvae, topical antiseptics, dressing products, hydrogels and epidermal growth factor. They also stated that larger, blinded, more robust
studies of systemic hyperbaric oxygen are needed, along with further research on the effectiveness and cost-effectiveness of topical negative pressure after surgery. The use of becaplermin in patients with ulcers that are resistant to simpler interventions needs to be evaluated.

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