The prevention and treatment of diabetic foot ulcers: a review of clinical effectiveness studies

Kaltenthaler E, Morrell C J, Booth A, Akehurst R L

Authors' objectives
To evaluate the effectiveness of interventions (including prevention) for diabetic foot ulcers.

Searching
CINAHL, the Cochrane Library, EMBASE, HealthSTAR, MEDLINE, PharmacoEconomics and Outcomes News, NHS EED and DataStar were searched from 1986 to 1996. In addition, the Internet was searched and handsearches were conducted (the focus of the handsearches were not reported). Only studies published in the English language were eligible. The subject terms used included 'Foot-Ulcer', 'Diabetic-Foot' and 'Diabetes Mellitis'. The textwords included 'Diabet*', 'foot', 'feet' and 'ulcer*'.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible. The follow-up periods, where stated, ranged from 14 days to 2 years.

Specific interventions included in the review
The following interventions for diabetic foot ulcers were eligible: prevention; multidisciplinary education and support; and treatments including topical applications, dressings, surgery, antibiosis, growth substances, hyperbaric oxygen, drug therapy, wound grafting, footwear, and contact casts. The actual interventions included:

dressings of various type (moist calcium alginate gel, dry fine mesh gauze, adhesive zinc oxide tape, adhesive occlusive hydrocolloid, polyurethane gel or foam, collagen-alginate, saline moistened);

topical treatment (RGD peptide matrix, topical saline, lyophilised collagen, hyaluronic acid medicated gauze);

drug therapy (selective serotonin);

total contact casting;

antibiotics (oral amoxicillin, clavulanic acid, cephalexin, clindamycin, and intravenous ampicillin/sulbactam or imipenem/cilastatin);

hyperbaric oxygen (including topical);

wound grafting (Dermagraft, non-adherent interface);

surgery (disarticulation one-stage technique versus disarticulation Wagner two-stage technique);

growth factor (bFGF, rhPDGF and CT-12);

therapeutic shoes versus patients' own shoes; and

preventative strategies (health education programme versus no education and placebo or no treatment control).

Participants included in the review
Diabetic patients with foot ulcers were eligible.
Outcomes assessed in the review
Studies assessing clinical effectiveness were eligible. The actual outcomes assessed included: healing rates; change in the size of the ulcers; healing time; bacterial culture; amputation rates; lower extremity abnormality; and ulcer relapse rates.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Validity was assessed and scored using the scale of Jadad et al. (see Other Publications of Related Interest). This scale evaluates the adequacy of randomisation method, double-blinding and adequacy of description of withdrawals. The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The information tabulated in the review included: author and year of publication; type of treatment; details of interventions; the number of patients per treatment arm; outcome measures and results; and follow-up period.

Methods of synthesis
How were the studies combined?
A narrative synthesis was undertaken.

How were differences between studies investigated?
Differences between the studies were discussed in the text of the review.

Results of the review
Twenty-three RCTs (at least 1,422 patients) were included. One RCT reported the sample size as 96 episodes.

The authors described the review as an overview rather than a comprehensive systematic review. The methodological deficiencies of the studies included: the use of small sample sizes, with only one RCT describing the sample size calculation; small sample size permitting confounding for uncontrolled variables; only 7 RCTs were double-blinded; the terms used as an outcome measure were often undefined; the length of follow-up, number of drop-outs and reasons for drop-outs were often not reported; and the use of short follow-up periods, which give a false impression of effectiveness.

Treatment.
Only 4 RCTs met all the Jadad quality criteria. Of these, one RCT (40 patients) found no significant difference in the rates of complete healing between serotonin antagonist and placebo at 3 months' follow-up. One RCT (96 episodes) found no significant difference in the rates of bacterial eradication between two different antibiotic regimens at the 1-year follow-up. Another RCT (44 patients) found no significant difference in the rates of complete healing between oral antibiotic and placebo at 20-days' follow-up. The fourth RCT (65 patients) showed a significantly improved healing rate (35% versus 8%) and number of patients with greater than 50% ulcer closure (75% versus 48%; p=0.03) for arginine-glycine-aspartic acid peptide matrix, compared with topical saline and standard treatment, after 10 weeks' follow-up.

Prevention strategies (2 RCTs, 599 patients).
Two good quality RCTs with large sample sizes reported significant benefit from the education programmes. Blinding was not possible. One RCT (396 patients) reported a 59% reduction (p=0.05) in the presence of a lower extremity abnormality in a group receiving a health education programme in comparison with a no education group. The other RCT (203 patients) reported a significantly lower amputation rate among those receiving a health education programme than among a no education group (4% versus 12% of limbs; p<0.005), and a significantly lower rate of ulcers in the education group (4.5% versus 15%; p<0.005). The results for 2 years' follow-up were reported.

Cost information
One RCT reported the costs and concluded that prevention programmes could prove more cost-effective than intervening after the development of foot ulcers. The authors stated that surgical techniques such as debridement, revascularisation and amputation were among the most expensive treatments for foot ulcer.

Authors' conclusions
Very few RCTs were identified and the overall quality of the research was poor. No cost-effectiveness studies alongside trials were identified. This shortage of rigorous trials highlights the need for more well-designed research in the prevention and treatment of diabetic foot ulcers, to determine clinical effectiveness as well as relative cost-effectiveness.

CRD commentary
The aims were stated, and the inclusion criteria were defined in terms of the study design, intervention, and participants. Many relevant sources were searched and details of the search strategy were given. However, the methods used to select the studies were not described. Restricting the literature search to studies in the English language may have resulted in the omission of other relevant studies, but the authors acknowledged this and noted that several papers were from non-English speaking countries. The validity of the primary studies was assessed using a validated scoring system, although the methods used to assess validity were not described. Relevant information was tabulated, with further information provided in the text. A narrative synthesis was appropriate given the lack of similarity among trials, and sources of higher quality evidence were highlighted. The authors considered the methodological deficiencies of the primary studies in detail, and made recommendations for future research based on the identified deficiencies.

The evidence presented supports the authors' conclusions.

Implications of the review for practice and research
Practice: The authors state that there is currently very little evidence upon which clinicians can base clinical decisions for the treatment of people with diabetic foot ulcers.

Research: The authors state that RCTs are needed alongside economic evaluations. They suggest that specific interventions requiring further research include total contact casting, growth factors, wound grafting and prevention. The authors recommend complete healing as the most appropriate outcome. They also recommend a follow-up period of 12 weeks, with a long-term follow-up of one year to monitor recurrence and enable calculation of wound-free time during the one year as a standard outcome. In addition, they consider that more attention should be paid to assessing the patients' health-related quality of life, acceptability, satisfaction, compliance, and tolerance of the treatment.

Bibliographic details

Other publications of related interest
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Subject indexing assigned by CRD

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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.