Ultrasound therapy in chronic leg ulceration: a meta-analysis

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Authors' objectives
To assess the evidence for the effect of ultrasound (US) therapy in the treatment of chronic leg ulcers.

Searching
Index Medicus (1950-66) and MEDLINE (1966-97) were searched using the following keywords: ultrasound therapy and ultrasonic therapy combined with physiotherapy. Only published articles were included. All articles in English, German, French, Swedish, Norwegian, and Danish were included if the title showed any relevance for US therapy. Additional articles were identified through reference lists of obtained articles. This was repeated until no new references were found, after which the search was considered finished.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) which compared interventions with either placebo, alternative treatment, or another control group.

The duration of treatment varied from 4 to 12 weeks.

Specific interventions included in the review
Therapeutic ultrasound therapy (various regimens) compared to placebo, alternative treatment, or another control group.

Participants included in the review
Participants with chronic leg ulcers (arterial, venous, rheumatoid, diabetic and post-traumatic). The mean age of participants ranged from 61 to 73 years, and the sex ratio (male:female) ranged from 10:12 to 4:22. This information was not available for one study.

Outcomes assessed in the review
Decrease in ulcer size, number of healed ulcers and healing time.

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 authors performed the selection.

Assessment of study quality
Although a formal validity assessment was not undertaken, information was extracted from the included clinical trials on: randomisation, comparison group treatment (i.e. placebo treatment, no treatment, non-US treatment), cross-over design, blinding of patient, physiotherapist, and evaluator. The three authors independently made decisions about the validity of included studies, and disagreements were discussed until an agreement was reached.

Data extraction
The three authors independently extracted data from the primary studies, and disagreements were discussed until an agreement was reached.

Although the number of drop-outs were recorded, there is no indication that data were extracted in an intention to treat format.
Methods of synthesis
How were the studies combined?
Effect sizes were calculated and the studies were combined (where appropriate) in a meta-analysis. Differences between US and control treatment were weighted by sample size, upon which the results were based (number of recruited patients minus withdrawals, drop-outs, exclusions and missing data). Mean differences in effect sizes were quoted with 95% confidence intervals.

The results of three studies which presented data on the number of healed ulcers were pooled and a Fisher's exact test was performed.

How were differences between studies investigated?
A test for heterogeneity is not reported. However, the authors state that the mean ulcer area was very different at inclusion, giving the impression of heterogeneity within and between studies.

Results of the review
Six randomised controlled trials were included in the analysis, comprising a total of 265 participants.

All six studies included data after 4 weeks of treatment and five studies included data after 8 weeks of treatment.

There was a significant effect of US treatment compared with control treatment with the effect size 16.9% (95% CI: 6.3%, 27.5%, p<0.05) after 4 weeks and 14.5% (95% CI: 6.6%, 22.3%, p<0.01) after 8 weeks of treatment.

Three studies which presented data on the number of healed ulcers showed that treatment was not significant at 4 or 8 weeks, although it approached significance after 8 weeks of treatment (therapeutic gain 15%, 95% CI: 1%, 30%, p=0.06). It was found that 197 participants would be necessary in each group for this therapeutic gain in number of healed ulcers to reach significance.

No severe side effects were registered in any of the studies. The sum of drop-outs from the US-treated groups was 23 and from the placebo treated groups 32. In no studies was a significant difference found.

It was not possible to do a dose-response relationship calculation because of insufficient information in the included articles concerning the treatment area and the size of the sound head.

Authors' conclusions
This analysis suggests that ultrasound has the best effect being delivered in low doses around the edge of the ulcer, but further studies are required to confirm this possible effect and to evaluate a possible dose-response relationship.

CRD commentary
The review focuses on a well defined question. Inclusion criteria are appropriate, and sufficient details of the included studies are provided.

The literature search was fairly narrow and could have been extended to include other databases, such as EMBASE and handsearching of relevant articles. The authors only include published material, and thus publication bias can not be ruled out.

Although the validity of included studies is not formally assessed, information on randomisation, comparison group treatment, cross-over design and blinding was extracted. It would have been useful if the authors had scored this information in some way, although there were probably too few studies to perform a sensitivity analysis. Tests for heterogeneity were not performed before the primary studies were combined.

The conclusions follow from the results, however, these should be interpreted with caution due to possible heterogeneity, insufficient blinding in included studies, and the small total number of participants involved.
Implications of the review for practice and research

The authors state that future research should confirm the effect indicated by this analysis, and focus on the dose-response relationship, especially as smaller doses seem to have higher response. They also suggest that future studies should compare delivery of US directly into the ulcer with delivery around the ulcer, because it appears that US delivered around the ulcer has the best effect.

They suggest that well-designed studies with comparable patient material are needed for this purpose. This includes an examination and a reliable diagnosis of the ulcer etiology including distal blood pressure measurements (ankle-arm pressure index). The US delivery mode, frequency, dose per treatment, treatment area, size of US probe, treatment time and number of treatments should also be described. A well-defined reproducible concomitant treatment (i.e. compression bandage) should also be included, and follow-up controls are needed to evaluate the quality of the healed ulcers.

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