The effectiveness of non-surgical interventions in the treatment of Charcot foot

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CRD summary
The authors concluded that bisphosphonates may improve the healing of Charcot foot when added to standard interventions to control the position and shape of the foot. The review was generally well conducted but, given the small number of included studies, small sample sizes and variation between the studies, the authors’ conclusions should be treated with caution.

Authors' objectives
To determine the impact of nonsurgical interventions for Charcot foot on lesions, ulceration, rate of surgical interventions, rate of hospital admission, quality of life and clinical healing.

Searching
The following were searched from inception to November 2006 for articles in any language: Academic Search Elite, Australasian Medical Index, BioMed Central, the BMJ website, the Cochrane Library, Digital Dissertations, Health Source: Academiei/Nursing Edition, Ingenta Connect, MedlinePlus, PEDro, Social Services Abstracts, PsycINFO, Wiley Interscience, AMED, AUSThealth, Blackwell Synergy, CINAHL, Current Contents Connect, Health Source: Consumer Edition, HighWire Press, NLM Gateway, ScienceDirect, PsycARTICLES and Web of Science; the search terms were reported. The reviewers handsearched other literature including conference proceedings, journals and the reference lists of all retrieved articles. Postgraduate and doctoral dissertations were searched for using Dissertation Abstracts International and Proceedings First, and experts were contacted.

Study selection
Controlled trials of nonsurgical interventions in patients with an acute primary diagnosis of Charcot foot of neuropathic aetiology were eligible for inclusion. Studies of patients with Charcot-Marie-tooth disease, or other neurological or bony destructive disorders, were excluded. The included studies were of bisphosphonates (pamidronate or alendronate) in varying doses, radiotherapy, and a combined magnetic field bone growth simulator; all patients also received standard care (e.g. immobilisation, foot care, antibiotics). Control conditions were immobilisation treatment placebo or sham radiotherapy. The methods used to diagnose Charcot foot varied between studies. Some studies included only patients with type I or type II diabetes. The primary outcomes were incidence of foot ulceration, infection and amputation, callus development, number and duration of hospital admissions, acceptability of treatment, and quality-of-life measures. The secondary outcomes were disease activity, limb temperature or alkaline phosphatase levels. Other outcomes were also reported. Where stated, the follow-up period ranged from 2 weeks to 12 months. The included studies were carried out in the USA, UK, Germany and Italy.

Two reviewers independently selected the studies.

Assessment of study quality
Methodological quality was assessed using the Joanna Briggs Institute's (JBI) Critical Appraisal of Evidence Effectiveness tool. This tool contains 10 questions assessing randomisation, blinding, allocation concealment, information about withdrawals, comparability of the treatment and baseline groups, reliability of the outcome measures and standardised measurement of outcomes across treatment and control groups, adequate follow-up (greater than 80%) and appropriate statistical analysis. Each item was awarded a score of 1 or 0, giving a potential maximum score of 10.

Two reviewers independently assessed study quality, with the opinion of a third reviewer sought in the case of disagreement.

Data extraction
The data were extracted onto JBI data extraction sheets. Additional information was sought from the authors of individual studies.
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

**Methods of synthesis**
The results were combined in a narrative under separate sub-headings for each type of intervention.

**Results of the review**
Five studies (n=135) were included in the review: four randomised controlled trials (RCTs; n=102) and one controlled clinical trial (n=33).

The methodological quality of the included studies ranged from 5 to 10. There was one poor-quality study, three moderate-quality studies and one high-quality study. None of the included studies assessed reductions in lesions, ulceration, rate of surgical interventions, rate of hospital admission or quality of life.

Three studies (n=92) evaluated pharmacological interventions. One high-quality RCT (n=39) found that treatment with 90 mg pamidronate in saline over 4 hours resulted in significantly lower urinary deoxypyridinoline at 4 weeks compared with placebo (4.4 ± 0.4 nmol/mmol creatine versus 7.1 ± 1.0, p<0.01). Both groups also received standard foot care. In this trial, the reductions in overall symptoms (weighted mean difference, WMD -9.50, 95% confidence interval, CI: -14.9, -4.1) and bone-specific alkaline phosphatase (WMD -4.5, 95% CI: -5.4, -3.6) were greater at 4 weeks in the treatment group compared with placebo. There was no significant difference between the treatment and control groups in reduction of foot temperature. One moderate-quality RCT (n=20) found that treatment with 70 mg alendronate orally once weekly plus standard care of total contact cast and pneumatic walker was associated with significantly lower collagen COOH-terminal telopeptide of type I collagen than standard care alone (0.30 ± 0.03 versus 0.54 ± 0.05, p<0.05). In this trial, there was no significant difference between the treatment and control groups in reduction of foot temperature and bone alkaline phosphatase. One low-quality controlled trial (n=22) reported significantly greater reductions in limb temperature (WMD -5.10, 95% CI: -6.21, -3.99, p<0.001) and mean phosphatase levels (WMD -89.91, 95% CI: -104.87, -74.95, p<0.001) in a group treated with pamidronate compared to standard care with immobilisation treatment.

Magnetic field stimulation plus immobilisation was associated with significantly reduced deformity (one RCT, n=31; WMD -0.7, p<0.05) and significantly reduced healing time to consolidation (WMD -12.1, p<0.001) than mobilisation alone. Palliative radiotherapy was not associated with any significant difference in healing time when compared with patients receiving sham radiotherapy (one RCT, n=12).

**Authors’ conclusions**
Bisphosphonates may improve the healing of Charcot foot by reducing skin temperature and disease activity of Charcot foot when applied in addition to standard interventions to control the position and the shape of the foot.

**CRD commentary**
The review addressed a clear question that was well-defined in terms of the intervention, participants and study design. Some outcomes appear to have been included that were not predetermined inclusion criteria, leading to the possibility of bias in the review process. A wide range of sources were searched and appropriate steps were taken to minimise language and publication bias. A validity assessment was conducted and the results of this were reported and used to inform the results. Suitable steps were taken in the study selection and validity assessment processes to minimise reviewer error and bias. However, it is unclear whether similar steps were taken when extracting the data. The decision to combine the studies in a narrative analysis was appropriate given the clinical heterogeneity between the included studies. Indeed, the variation in patients, interventions and outcomes between the included studies limits the ability to draw meaningful conclusions about the efficacy of nonsurgical interventions in Charcot foot. The review was generally well conducted. However, given the small number of included studies, small sample sizes, lack of evidence on primary review outcomes and variation between the studies, the authors’ conclusions should be treated with caution.

**Implications of the review for practice and research**
Practice: The authors stated that the evidence tentatively suggests that bisphosphonates may improve healing of Charcot foot...
foot when delivered in addition to standard non-operative care.

Research: The authors stated that further well-designed RCTs evaluating standard nonsurgical care of Charcot foot, magnetic therapy and bisphosphonates are needed. Future trials should pay particular attention to blinding and randomisation, and should be adequately powered. Future research should include more short- and long-term clinical and patient-focused outcome measures.

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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.