Treating intermittent claudication with Tibetan medicine Padma 28: does it work?

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CRD summary
The authors concluded that Padma 28 provides significant relief from peripheral arterial occlusive disease-related symptoms (e.g. walking distance). However, given the methodological limitations of this review, the reliability of the authors' conclusions is questionable.

Authors' objectives
To evaluate the efficacy and safety of Padma 28 in the treatment of peripheral arterial occlusive disease (PAOD).

Searching
MEDLINE, PubMed, EMBASE, TOXLINE, AMED, AIDSLINE, HealthSTAR, Cancerlit and the Cochrane Library were searched from inception to June 2004; the search terms were reported. The reference lists of relevant publications were also checked. Experts and the manufacturer of Padma 28 were contacted for additional relevant publications.

Study selection
To be eligible, patients had to have intermittent claudication due to PAOD (Fontaine stage II disease). The mean age of the participants ranged from 55 to 74 years.

Studies that evaluated Padma 28 compared with placebo were included in the review. The dosage ranged from 309 to 382 mg per capsule, two capsules taken twice or three times per day. Eligible studies had to have a minimum duration of at least 12 weeks. All of the included studies had a duration of at least 16 weeks.

Eligible studies had to evaluate pain-free and/or maximum walking distance, as measured by a standardised treadmill test.

Randomised controlled trials (RCTs) with a minimum sample size of 30 were eligible for inclusion. Non-randomised controlled studies were also included in the review.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors stated that raw data were partially or fully obtained, and reanalysed in all studies. The data were extracted in an intention-to-treat format where possible. The last observation carried forward method was used for missing values.

One reviewer extracted the data, which were checked by other reviewers.

Methods of synthesis
For dichotomous data, a meta-analysis examining pooled odds ratios (ORs) was performed; for continuous data, a pooled weighted mean difference (WMD) was calculated. The data were pooled using fixed-effect methods (Mantel-Haenszel and Peto). Sensitivity analyses were conducted by randomly eliminating trials from the analyses. Potential sources of heterogeneity (e.g. age, gender, hypertension, hypercholesterolaemia, hyperlipidaemia, walking distance on admission, concomitant treatment) were explored using regression analysis.

Results of the review
Six trials (n=414), presented in seven publications, were included in the review: 4 RCTs and 2 controlled trials. The sample sizes ranged from 30 to 100 participants.
One study demonstrated significant differences between the intervention and control groups at baseline and was not included in the meta-analyses.

Padma 28 treatment significantly improved maximum treadmill walking distance after 16 weeks compared with placebo (5 trials; WMD 63.51, 95% confidence interval, CI: 27.11, 99.91, p<0.001). In addition, a significantly greater proportion of individuals in the treatment group increased their walking distance by 100 metres or more (5 trials; OR 10, 95% CI: 3.03, 33.33, p<0.001). There was significant heterogeneity between the studies (p=0.002). It is noted that one of the included studies included a sample of participants from another study.

Sensitivity analyses did not alter the direction of the results. None of the variables analysed in the regression analyses demonstrated a significant correlation with the outcome.

Safety data were obtained from 19 studies (information on 13 of these studies was not reported). The results suggest that treatment with Padma 28 is well tolerated.

**Authors' conclusions**
Padma 28 provides significant relief from PAOD-related symptoms (e.g. walking distance).

**CRD commentary**
The review addressed a clear question and was supported by appropriate inclusion criteria. However, the criteria were not strictly adhered to. While reasons for nonadherence were provided, the protocol of systematic review methodology will have been undermined. A number of databases were searched and non-English studies were included in the review, thereby limiting language bias. The validity of the included studies was not reported, thus the results from the studies, and any synthesis of them, may not be reliable. The authors reported that more than one reviewer was involved in the data extraction, thus reducing the potential of reviewer bias in some stages of the review process. Given the heterogeneity between the studies, it may not have been appropriate to pool the results. Data from one study involved a sub-sample of participants from an earlier study and should probably have not been pooled with the other studies. Given the methodological limitations of this review, and the small sample sizes of the included studies, the reliability of the authors' conclusions is questionable.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated that larger RCTs investigating the efficacy of Padma 28 are needed.

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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.