Meta-analysis of efficacy of quinine for treatment of nocturnal leg cramps in elderly people

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Authors' objectives
To quantitatively assess the efficacy of quinine (as quinine sulphate) compared with a placebo in the treatment of nocturnal leg cramps in ambulatory people.

Searching
MEDLINE and EMBASE were searched from 1966 to 1994 and 1975 to 1994, respectively, using the keywords 'quinine', 'muscle cramps' and 'legs'. Current Contents was searched from January to April 1994, and the references of relevant articles and textbooks were checked. Authorities in the field were contacted for additional material. [A: Since publication of this study, we have located a number of unpublished studies pertaining to this subject. An updated meta-analysis including these studies is presently undergoing peer review.]

Study selection
Study designs of evaluations included in the review
Double-blind, randomised, placebo-controlled crossover trials were included.

Specific interventions included in the review
Quinine as quinine sulphate.

Participants included in the review
A general ambulatory population (non-dialysis patients) were included.

Outcomes assessed in the review
Reduction in nocturnal leg cramps for a 4-week period, severity and duration of nocturnal leg cramps, and cramp index (duration multiplied by severity of leg cramps).

How were decisions on the relevance of primary studies made?
Four independent people, blinded to the study, assessed the methods section of each paper for fulfilment of the inclusion criteria.

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

Data extraction
Two independent assessors extracted specified information. Any points of disagreement were settled by collaborative review.

Methods of synthesis
How were the studies combined?
Using data on individual patients, point estimates and 95% confidence intervals (CIs) were calculated using paired differences for the efficacy of quinine, compared with placebo. A hypothetical set of results was derived for one trial that did not give individual patient results and this was used in a sensitivity analysis.

How were differences between studies investigated?
Heterogeneity was tested using one-way analysis of variance; results identified one study was responsible for the heterogeneity. By removing the results of this study from the meta-analysis, the estimate of quinine efficacy was
reduced although the benefit remained significant.

**Results of the review**
Six randomised, placebo-controlled, crossover trials were included (107 patients).

Compared with the placebo, in a 4-week treatment period, the use of quinine significantly reduced the number of nocturnal cramps by 8.83 (95% CI: 4.16, 13.49), and reduced the number of nights by 27.5% (95% CI: -30.6, -24.4). There was no significant change in the mean severity of leg cramps with quinine (-0.048 units on a three-point visual analogue scale, 95% CI: -0.314, 0.218), compared with the placebo, or in cramp index (5.25 units, 95% CI: -10.43, 20.93). Of the small minority that reported any side-effects at all, only one person experienced serious side-effects.

**Authors' conclusions**
The results show that quinine sulphate is efficacious in the treatment of nocturnal leg cramps on ambulatory patients. As quinine may have serious side-effects, patients starting it for nocturnal leg cramps should undergo a therapeutic trial with close monitoring of its benefits and risks. The data suggest that patients should receive quinine on a regular basis for at least 4 weeks before conclusions about efficacy are drawn.

**CRD commentary**
This was a good systematic review. However, no details about any assessment of study validity other than the design inclusion criteria are given.

**Implications of the review for practice and research**
It may be appropriate to prescribe quinine for patients with nocturnal leg cramps, but given the possible serious side-effects patients taking this drug should be closely monitored.

**Bibliographic details**

**PubMedID**
7827545

**Original Paper URL**
http://www.bmj.com/content/310/6971/13

**Other publications of related interest**
This additional published commentary may also be of interest. Voon WC, Sheu SH. Diltiazem for nocturnal leg cramps. Age & Ageing 2001;30:91-92.

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Aged; Circadian Rhythm /physiology; Cross-Over Studies; Double-Blind Method; Female; Humans; Leg; Male; Muscle Cramp /drug therapy; Quinine /adverse effects /therapeutic use; Randomized Controlled Trials as Topic; Time Factors; Treatment Outcome

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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.