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#### [Intervention Review]

# **Quinine for muscle cramps**

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#### **ABSTRACT**

# **Background**

Muscle cramps can occur anywhere and for many reasons. Quinine has been used to treat cramps of all causes. However, controversy continues about its efficacy and safety.

#### **Objectives**

To assess the efficacy and safety of quinine in treating muscle cramps.

## **Search methods**

We searched The Cochrane Neuromuscular Disease Group Register, The Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 3, 2010), MEDLINE, EMBASE and reference lists of articles up to July 2010.

#### **Selection criteria**

Randomised controlled trials of people of all ages with muscle cramps in any location and of any cause, treated with quinine or its derivatives.

### **Data collection and analysis**

Three authors independently selected trials for inclusion, assessed risk of bias and extracted data. We contacted study authors for additional information.

#### **Main results**

We identified 23 trials with a total of 1586 participants. Fifty-eight per cent of these participants were from five unpublished studies. Quinine was compared to placebo (20 trials, n = 1140), vitamin E (four trials, n = 543), a quinine-vitamin E combination (three trials, n = 510), a quinine-theophylline combination (one trial, n = 77), and xylocaine injections into the gastrocnemius muscle (one trial, n = 24). The most commonly used quinine dosage was 300 mg/day (range 200 to 500 mg).

Compared to placebo, quinine significantly reduced cramp number over two weeks by 28%, cramp intensity by 10%, and cramp days by 20%. Cramp duration was not significantly affected.



A significantly greater number of people suffered minor adverse events on quinine than placebo (risk difference +3%, 95% confidence intervals 0% to 6%), mainly gastrointestinal symptoms. Overdoses of quinine have been reported elsewhere to cause potentially fatal adverse effects, but in the included trials there was no significant difference in major adverse events compared with placebo (risk difference 0%, 95% confidence intervals -1% to 2%). One participant suffered from thrombocytopenia (0.12% risk) on quinine.

A quinine-vitamin E combination, vitamin E alone, and xylocaine injections into gastrocnemius were not significantly different to quinine across all outcomes, including adverse effects. Based on a single trial comparison, quinine alone was significantly less effective than a quinine-theophylline combination but with no significant differences in adverse events.

#### **Authors' conclusions**

There is moderate quality evidence that quinine significantly reduces cramp frequency, intensity and cramp days in dosages between 200 and 500 mg/day. There is moderate quality evidence that with use up to 60 days, the incidence of serious adverse events is not significantly greater than for placebo in the identified trials. Further research is required on the optimal dose and duration of use, and also on alternative treatments.

# PLAIN LANGUAGE SUMMARY

#### Quinine for muscle cramps

Muscle cramps can occur anywhere and in anyone; however, leg cramps are especially common in older people. Quinine is a medication which has been used to treat cramps for many years. There is conflicting evidence for its ability to reduce cramps. It can cause serious, even fatal adverse events, especially in overdosage. Twenty-three trials including 1586 participants were included in this review, comparing quinine or quinine derivatives against placebo or other interventions. There is moderate quality evidence that quinine significantly reduces cramp frequency, intensity and cramp days more than placebo. There is moderate quality evidence that there is a significant increase in minor adverse events with quinine compared to placebo but not in major adverse events. Overdosage however is well documented to cause serious harm including death. There is low quality evidence from one trial that theophylline combined with quinine improves cramps more than quinine alone. Low quality evidence shows there is no significant difference between quinine and vitamin E, quinine-vitamin E mixture, or xylocaine injections. More research is needed to clarify the optimum dose and duration of treatment, as well as alternatives to quinine.