



## Question: What is the evidence to support the use of quinine for the treatment of nocturnal leg cramps?

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### **Summary**

There is conflicting guidance available regarding the use of quinine to treat nocturnal leg cramps.<sup>1,2,3,4,5,6</sup> Quinine Sulphate tablets are licensed for the treatment and prevention of nocturnal leg cramps in adults and the elderly, when cramps cause regular disruption of sleep.<sup>7</sup> If Quinine is used to treat nocturnal leg cramps the advice outlined below should be taken into consideration.

### **Information**

Quinine (usually as quinine sulphate) has traditionally been used for nocturnal cramps.<sup>2</sup> There has been concern over its efficacy and potential for adverse effects, especially in the elderly.<sup>1,2,3,4</sup> The Food and Drug Administration (FDA) in the US ruled that quinine products should no longer be used for the management of nocturnal cramps.<sup>2,3</sup> A similar ban has been imposed in Australia.<sup>2</sup> In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) and the Commission on Human Medicines (CHM) Drug Safety Update in 2010 advised against routine use of quinine for nocturnal leg cramps.<sup>5</sup>

This Drug Safety Update outlined the following;

- Quinine is not a routine treatment for nocturnal leg cramps, and should only be used when cramps regularly disrupt sleep.<sup>5</sup>
- Before use of quinine for nocturnal leg cramps, the risks should be carefully considered relative to the potential benefits.<sup>5</sup>

Palliative Meds Info: Terms and Conditions

The information outlined above is intended for healthcare professionals only. The information outlined above is believed to accurately reflect the medical literature at the time of writing. Healthcare professionals must use their own judgment to determine the accuracy and relevance of the information. See [www.olh.ie](http://www.olh.ie) for full terms and conditions.

- After a trial of at least 4 weeks, treatment should be stopped if there is no benefit. If treatment continues, the benefits should be assessed around every 3 months.<sup>5</sup>
- Patients should be warned not to exceed the recommended dose.<sup>5</sup> Serious side effects including irreversible blindness and death may occur with overdose.<sup>5</sup>
- Thrombocytopenia is a rare but potentially life-threatening adverse reaction associated with quinine.<sup>5</sup> Patients should be instructed to stop treatment and consult a physician if signs of thrombocytopenia occur, such as unexplained petechiae, bruising or bleeding.<sup>5</sup>
- Quinine should not be prescribed or given to patients who have previously experienced any adverse reaction to quinine, including that found in beverages.<sup>5</sup>

In contrast, a 2015 Cochrane review concluded that there is:

- Low quality evidence that quinine (200mg - 500mg daily) significantly reduces cramp number and cramp days.<sup>6</sup>
- Moderate quality evidence that quinine reduces cramp intensity.<sup>6</sup>
- 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.<sup>6</sup>

The review identified 23 trials with a total of 1586 participants. However, concluded that further research is required to establish the optimal dose and duration of use.<sup>6</sup>

### **Medicines linked with Nocturnal Leg Cramps**

Although nocturnal leg cramps are idiopathic in most cases, Garrison et al found that treatment for legs cramps was substantially more likely in the year following introduction of inhaled long acting  $\beta_2$ -agonists, potassium-sparing diuretics, or thiazide-like diuretics.<sup>8</sup> In contrast, statin and loop diuretic associations were small.<sup>8</sup> Steroids, neuroleptics, antiretrovirals, morphine, acetylcholinesterase inhibitors and nifedipine have also been associated with leg cramps.<sup>9</sup>

### **Potential Drug Interactions**

Quinine has the potential to interact with other medications.<sup>7,9</sup> Quinine can result in increased plasma concentrations of digoxin and warfarin.<sup>9</sup> Increased toxicity is possible with potent CYP3A4 inhibitors i.e. azole antifungals, macrolide antibiotics, HIV protease

inhibitors and grapefruit juice.<sup>9</sup> The concomitant use of quinine with other QT prolonging medications can result in increased risk of ventricular arrhythmia.<sup>7,9</sup>

### **Alternative therapies**

Various pharmacologic treatments have been studied for nocturnal leg cramps, including magnesium, calcium channel blockers, sympathetic inhibitors, vitamin E, vitamin B complex, and antiepileptic medications.<sup>9,10</sup> Generally, these options were found to be well tolerated however the trials had substantial methodological flaws and a small sample size.<sup>9</sup>

### **References**

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