

Quinine — poor efficacy in muscle cramp outweighed by risk of harm

SUMMARY

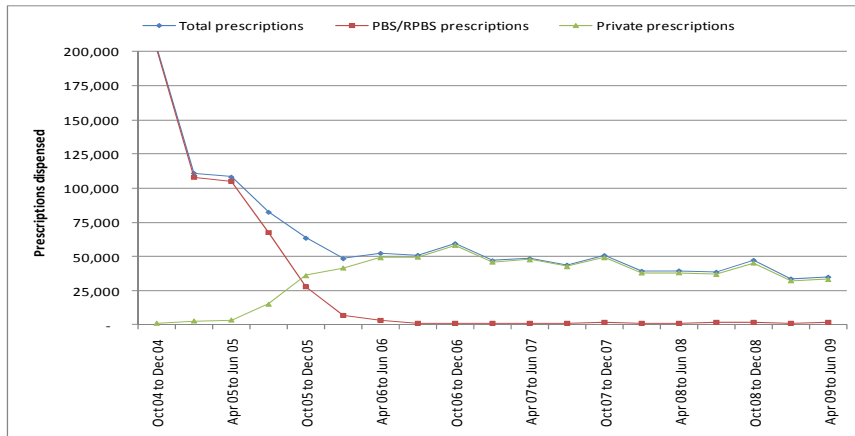
- Do not use quinine to prevent muscle cramp. The risk of thrombocytopenia outweighs quinine’s modest efficacy
- Safe, effective management of muscle cramp remains elusive: teaching stretching exercises may help provide relief
- Ask patients to stop taking quinine

Do not use quinine to prevent muscle cramp

Approval of quinine for the prevention of muscle cramp was withdrawn by the TGA in 2004 because of an unfavourable benefit:harm profile.¹ In 2005, quinine tablets became an authority PBS item subsidised only for use in malaria.²

Although quinine usage continues to decrease, more than 100,000 prescriptions are dispensed each year (Figure 1), far in excess of the quantity required to treat malaria cases.³

Figure 1 — Oral quinine prescriptions dispensed October 2004 – June 2009



Data provided by Drug Utilisation Sub-Committee (DUSC), Department of Health and Ageing, Canberra. © Commonwealth of Australia.

Quinine has poor efficacy in reducing muscle cramp

A meta-analysis of seven cross-over trials estimated that quinine prevented 3.6 cramps (95 % confidence interval 2.15 – 5.05) per person during a four week period — that is, less than one cramp per week.⁴ At baseline, trial participants experienced an average of 17 cramps over 4 weeks. Cramp severity was reduced only slightly, and there was no evidence of a reduction in cramp duration.

There is no evidence for the long-term efficacy or safety of quinine for preventing or treating leg cramp because clinical trials have been of short duration.



Quinine can cause severe thrombocytopenia

As of 2004, ADRAC had received 228 reports of thrombocytopenia involving quinine, six of which resulted in death.¹ Typically, cases occur within the first few weeks of starting quinine although intermittent dosing may result in a longer time to onset.^{5,6} Symptoms can be severe, requiring hospitalisation and platelet transfusion.^{5,7}

Drug sensitivity may persist, so patients with a history of quinine-induced thrombocytopenia should be advised to permanently avoid all quinine-containing products, including bitter lemon drinks and tonic water.

Alternatives to quinine

No treatments for idiopathic muscle cramp are supported by good quality evidence. Stretching exercises may provide relief for some patients.

Address the causes of cramp

Consider and address underlying causes of cramp, such as electrolyte disturbance (particularly sodium and calcium deficiency), peripheral vascular disease or motor neurone disease. Possible drug causes of cramp include calcium-channel blockers, beta₂-agonists and diuretics.

Other drugs, minerals and vitamins

There is insufficient evidence to support the use of agents that have been studied, including magnesium salts, vitamin E or verapamil.^{8,9}

Non-drug measures

Calf-stretching exercises can be recommended to prevent cramps. Although there is little evidence to support their efficacy in prevention, they encourage self care and are unlikely to cause adverse effects. A trial found that calf-stretching exercises were no more effective than non-stretching exercises in reducing the frequency or severity of muscle cramp.¹⁰ However, a benefit of non-stretching exercise cannot be excluded.

Ask patients to stop quinine

Patients may be reluctant to stop taking quinine for muscle cramp.

Explain that the benefit of quinine is small, but that there is a risk of serious adverse effects. Providing advice about stretching and massage may also help.

Information for patients^{9,11}

To prevent muscle cramp

- stretch your calf muscles several times a day. Stand approximately one metre in front of a wall, put your hands on the wall, and lean forward while keeping the soles of your feet flat on the floor. Your doctor or physiotherapist can provide further information about how often and how long you should stretch for
- sleep with loose covers or blankets, or hang your feet over the end of the bed, to reduce the likelihood of calf muscles contracting. If you sleep on your back, prop up your feet with a pillow



To ease muscle cramp

- stretch and massage the calf muscle. If the cramp happens when you are lying in bed, try to stretch the muscle by straightening your legs and flexing your feet towards your knees.
- Advise patients who have had quinine-induced thrombocytopenia to avoid all quinine-containing products, including bitter lemon and tonic water, because the condition occurs via an immune-based mechanism.

References

1. Adverse Drug Reactions Advisory Committee. Aust Adv Drug React Bull 2004;23:20.
2. Australian Government Department of Health and Ageing. March 2005 - Positive recommendations 2005. http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-general-outcomes_full.htm (accessed 3rd December 2009).
3. Australian Government Department of Health and Ageing. National Notifiable Diseases Surveillance System. 2009. <http://www9.health.gov.au/cda/Source/CDA-index.cfm> (accessed 3 December 2009).
4. Man-Son-Hing M, et al. J Gen Intern Med 1998;13:600-6.
5. Adverse Drug Reaction Advisory Committee. Aust Adv Drug React Bull 2002;21:10.
6. Brinker AD, Beitz J. Am J Hematol 2002;70:313-7.
7. Aster RH, Bougie DW. N Engl J Med 2007;357:580-7.
8. Young G. Clin Evid (Online) 2009;2009.
9. National Health Service Clinical Knowledge Summaries. Leg cramps - unknown cause. 2008. <http://www.cks.nhs.uk/home> (accessed 3rd December 2009).
10. Coppin RJ, et al. Br J Gen Pract 2005;55:186-91.
11. United States Department of Veterans Affairs. Quinine and Unapproved Use for Leg Cramps Due to Serious Side Effects. 2008. <http://www.pbm.va.gov/VACenterForMedicationSafety-BulletinsAndNewsAlerts.aspx> (accessed 3rd December 2009).

The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence.

Any treatment decision based on this information should be made in the context of the clinical circumstances of each patient.

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