Quinine (Quinate, Quinbisul, Quinsul) for muscle cramp

Summary

- Quinine tablets should not be used for muscle cramp.
- The efficacy of quinine in preventing cramp is limited and is outweighed by the risk of severe thrombocytopenia, which may be fatal.
- The PBS listing and approved indications for muscle cramp for all oral quinine products have been deleted.

PBS Listing

The PBS listing for quinine for muscle cramp has been deleted. Quinine is still PBS listed for the treatment of malaria.

Reason for PBS listing

The PBS listing was deleted because the indications for muscle cramp for all oral quinine products have been removed due to an unfavourable benefit–harm profile (see *Place in therapy*).

Place in therapy

Quinine should not be used for treating muscle cramp. The efficacy of quinine in preventing cramp is marginal at best, and is outweighed by the risk of severe thrombocytopenia. For more information about quinine-induced thrombocytopenia, see *Safety issues*.

The Adverse Drug Reactions Advisory Committee (ADRAC) recently reviewed the safety and efficacy of quinine for muscle cramp and decided that the risk of adverse effects outweighs the benefits.[1] Consequently, the musculoskeletal indications (muscle cramp, treatment of myotonica congenita and diagnosis of myasthenia gravis) for oral quinine preparations have been withdrawn by the Therapeutic Goods Administration. Quinine is now indicated only for the treatment of malaria.

Quinine has poor efficacy in preventing muscle cramp

The evidence for quinine in muscle cramp is limited because studies have produced conflicting results. A meta-analysis of seven crossover 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.[2] Cramp severity was reduced only slightly, and there was no evidence of a reduction in cramp duration.[2]

Alternative therapies for muscle cramp

Consider underlying causes of cramp, such as electrolyte disturbances (particularly sodium deficiency due to heavy sweating), peripheral vascular disease or motor neurone disease. Possible drug causes of cramp include calcium-channel blockers, beta$_2$-agonists and diuretics.

No drugs are known to be effective for preventing muscle cramp. Verapamil, vitamin E and magnesium citrate have all been assessed for preventing muscle cramp but current evidence does not support their use.[3–6]

Passive stretch and massage of the affected muscle may relieve cramp. Stretching the calf muscles daily has been recommended to prevent cramp.[7] Although there is no clinical trial evidence to support these measures, anecdotal evidence suggests they may be effective and the risk of adverse effects is very low.

Safety issues

Quinine can cause severe thrombocytopenia, which is unpredictable and may be fatal.

Quinine-induced thrombocytopenia

Since 1972, ADRAC has received 214 reports of thrombocytopenia involving quinine, four of which resulted in death.[1] Quinine-induced thrombocytopenia is often severe (with bleeding, or risk of bleeding) and can require hospitalisation, monitoring and blood product support.[8]

Most cases occur within a few weeks of starting quinine, although thrombocytopenia has been reported months after initiation. Intermittent dosing may result in a longer time to onset.[8,9]

Quinine-induced thrombocytopenia is mediated by an immune mechanism so patients who experience it should subsequently avoid all quinine-containing products, including drinks such as bitter lemon and tonic water.

Dosing issues

There are no specific dosing issues.

Information for patients

Advise patients that the benefit of quinine in muscle cramp is small and uncertain, but that there is a risk of serious adverse effects. Discuss other ways to manage muscle cramp, such as passive stretching and massage.

Advise patients who have had quinine-induced thrombocytopenia to avoid all quinine-containing products, including bitter lemon and tonic water.

References

1. Therapeutic Goods Administration: Adverse Drug Reactions Unit. Personal communication.
2. Man-Son-Hing M, Wells G, Lau A. J Gen Intern Med 1998;13:600–6.
3. Roffe C, Sills S, Crome P, et al. Med Sci Monit 2002;8:CR326–30.
4. Baltodano N, Gallo BV, Weidler DJ. Arch Intern Med 1988;148:1969–70.
5. Connolly PS, Shirley EA, Wasson JH, et al. Arch Intern Med 1992;152:1877–80.
6. Frusso R, Zarate M, Augustovski F, et al. J Fam Pract 1999;48:868–71.
7. Daniell HW. N Engl J Med 1979;301:216.
8. Adverse Drug Reactions Advisory Committee. Adverse Drug React Bull 2002;21:10.
9. Brinker AD, Beitz J. Am J Hematol 2002;70:313–17.

Date prepared: October 2004