



Quinine associated blindness



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BACKGROUND

Quinine is commonly prescribed to the elderly for the treatment of benign nocturnal cramps, yet its use is not without complications.

OBJECTIVE

This article presents a case of quinine toxicity producing bilateral blindness, followed by a review of the adverse reactions associated with quinine use and its efficacy in treating benign nocturnal muscular cramps.

DISCUSSION

Visual loss has been associated with quinine serum concentrations above 10 µg/mL (therapeutic range 2–5 µg/mL). Other adverse reactions include neurological symptoms, haemolysis, acute renal failure and arrhythmia. There is conflicting evidence for the efficacy of quinine for leg cramps in randomised controlled studies, however, meta-analysis of these studies suggests some benefit. Although severe side effects are rare at therapeutic doses, the possibility of overdose needs to be considered when prescribing and an individual risk benefit analysis needs to be made. Benefits and adverse reactions should be closely monitored and medication ceased if appropriate.

Case history

Mr DB, 51 years of age with a history of medicated depression, attempted suicide by taking an overdose of quinine (13.5 g) and diazepam (150 mg) resulting in a decreased level of consciousness and agitation on presentation to an emergency department. Initially his pupils were equal but sluggish in their reaction to light. Computerised tomography (CT) scan of his head and lumbar puncture were normal, and aside from a K⁺ level of 3.1 mmol/L and a quinine level of 5.51 µg/mL (taken 24 hours postpresentation, therapeutic range 2–5 µg/mL) blood investigations were normal. Electrocardiogram (ECG) showed a prolonged QT interval of 0.47s and urinalysis revealed proteinuria and a trace of blood. The patient was placed on a cardiac monitor and given intravenous hydration. The

morning following admission the Glasgow Coma Score had returned to a score of 15/15 and the patient complained of a complete loss of sight. On further examination he was found to have no light perception and no pupillary light reflex. Fundoscopy demonstrated significant narrowing of retinal arterioles and macular oedema (*Figure 1*). After 4 days there was an extremely small central visual field allowing acuity in both eyes to reach 6/9 within this minute field area. After 4 weeks, signs of optic atrophy had developed and vision had not improved. A referral was made to the Royal Blind Society.

Adverse reactions including blindness are well documented with quinine intoxication and some of these have been noted in the context of therapeutic dosages.¹ Adverse reactions include:

- cinchonism (tinnitus, headache, nausea, abdominal pain and hypotension)
- haemolysis and haemolytic uraemic syndrome, disseminated intravascular coagulation, thrombocytopenic purpura,

agranulocytosis, hypoprothrombinaemia

- acute renal failure
- arrhythmia (QT prolongation, ventricular tachycardia and ventricular fibrillation), and
- visual disturbances including blurred vision, scotomata, photophobia, diplopia, fixed and dilated pupils, constricted visual fields, disturbed colour perception and blindness.

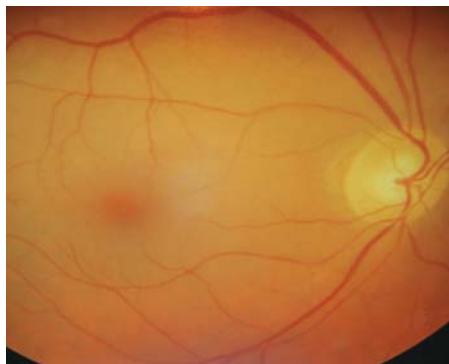


Figure 1. Retinoscopy 4 days after presentation demonstrating pallor, oedema and a cherry red spot in the macula. There is also arteriolar constriction with AV nipping just below the optic disc. Marked optic atrophy was apparent at 6 weeks

Numerous fatalities from quinine overdose have also been reported. If toxic amounts of quinine are ingested, blindness generally occurs after 9 hours.

The natural history following blindness from quinine retinal toxicity is for some vision to return to the point where the pupillary reflex is patent and colour vision is reasonable. There is usually some residual constriction of the visual field and frequently only a small central island of vision returns.² Visual loss has been associated with quinine serum concentrations above 10 µg/mL.³ The peak serum quinine concentration is not known for this case as the level was not taken until the following day. Retinal toxicity is thought to occur through arterial vasoconstriction causing ischaemia and eventually optic atrophy. It has been noted in the literature however, that the onset of vasoconstriction can occur after the onset of blindness and a direct toxicity to the neuroretina has also been proposed as a possible mechanism.⁴⁻⁶

Quinine is a commonly prescribed drug (especially in the elderly) for the treatment of benign nocturnal leg cramps. Data from the Health Insurance Commission (HIC) in Australia revealed that for the financial year 2002–2003 there was a total of 652 552 scripts written for quinine sulphate and quinine bisulphate through the PBS and RPBS at a cost of \$4.9 million. While some of these scripts would have been used for

the treatment of chloroquine resistant malaria, the majority is likely to be for nocturnal cramps. Given this level of prescription and the possible severe adverse reactions associated with quinine, the efficacy of the drug for prevention and treatment of nocturnal cramps should be considered. As it is known that quinine has a curare-like effect on skeletal muscle, decreasing the excitability of the motor end-plate and increasing the refractory period of muscle, there is a theoretical role for it in the treatment of leg cramp.

Results from double blind, randomised, placebo controlled studies are conflicting with some showing quinine to be significantly effective in reducing the frequency and severity of leg cramps compared with placebo or vitamin E, while others have shown no significant effect.^{8,9} Meta-analysis suggests there is some value in prescribing quinine for leg cramps.¹⁰ A risk-benefit analysis of quinine use should also acknowledge that while the regular quinine dosage of 300 mg has been associated with adverse reactions, severe side effects with this dose are rare. Patients using the drug in overdose quantities are far more likely to encounter problems. Nevertheless, caution should be used with any quinine prescription and the following recommendations are made concerning its use in general practice:

- consider nondrug interventions for cramp (eg. muscle stretching)
- reduce the dose in the elderly and those with renal or hepatic impairment
- ensure the patient understands the dosage regimen and use dosette packs if necessary
- consider the mental state of the patient and assess suicide risk
- consider undertaking baseline visual field and acuity assessment before commencing treatment
- use a 4 week therapeutic trial initially, closely monitoring benefits and side effects
- cease medication if no obvious benefit has been found or if adverse effects are noted.

Conflict of interest: none declared.

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