The treatment of quinine poisoning with charcoal haemoperfusion

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Summary
Quinine poisoning is rare but serious. Attempts at treatment by active removal have proved unsuccessful because of its high degree of protein binding. We describe two cases of non-accidental overdose of quinine (19.5 g and 15 g) with potentially fatal serum quinine levels. Both patients were treated by 2 periods of charcoal haemoperfusion during which quinine clearances of up to 125 ml/min were obtained. Both patients recovered, though one had some residual visual disturbance. We suggest that in cases of quinine poisoning, charcoal haemoperfusion may be a safe and effective method of drug removal, to be used with stellate ganglion block.

KEY WORDS: quinine poisoning, haemoperfusion.

Introduction
Quinine poisoning is uncommon, but the results are often serious with a fatal or disabling outcome. The most characteristic abnormality is a toxic amblyopia which is often permanent but has been treated successfully with stellate ganglion block. Haemoperfusion over charcoal or resin has been used effectively to treat various poisonings. This is the first report to describe the clinical use of charcoal haemoperfusion in the removal of quinine, a drug which is highly protein-bound and has hitherto resisted active removal by other means.

Method
The serum quinine estimations were made with a devised assay of ultraviolet absorption after chloroform extraction. Standard or blank (1 ml) was mixed with 1 ml of 5 M sodium hydroxide and the quinine sulphate extracted into 10 ml of chloroform. After mixing and centrifuging, the aqueous layer was discarded and the chloroform layer filtered and acidified with 0.25 M sulphuric acid. The ultraviolet absorbance was then measured at 250 nm. A graph was constructed, plotting absorbance against concentration of standards (5, 10, 20, 30 and 40 mg quinine sulphate/litre) and a linear response was obtained over this range.

Case 1
A 37-year-old man presented in casualty 2 hr after ingestion of 19.5 g of quinine bisulphate (65 x 300 mg tabs) and 60 mg of flurazepam (4 x 15 mg tabs) as an act of deliberate self-poisoning. He was fully conscious and communicative with no visual disturbance, but, without warning, he vomited and stopped breathing. Following resuscitation, he had a nodal tachycardia, was deeply unconscious and slowly developed large, irregular pupils which responded poorly to light. After a short period of spontaneous respiration, he required mechanical ventilation. The chest X-ray showed extensive pulmonary shadowing compatible with aspiration. Supportive measures and traditional attempts at removal of quinine with gastric lavage and forced acid diuresis were undertaken, but, abandoned because of the possibility of pulmonary oedema. A serum quinine level of 17 mg/litre taken 4 hr after ingestion confirmed the severity of the poisoning and charcoal column haemoperfusion was started 9 hr after ingestion. He was perfused at a blood flow rate of 300 ml/min through a standard Haemocoll (Smith and Nephew)
charcoal column for 4 hr. The calculated quinine clearance was 109 ml/min.

There were no serious complications; hypotension, hypothermia or hypocalcaemia did not occur and, during the procedure, the platelet loss was only 36% (350 x 10⁶/litre to 225 x 10⁶/litre), returning to pre-perfusion levels with 6 hr. After 4 hr perfusion, he was easily rouseable, and spontaneous respiration returned. He could talk, but was totally deaf and blind, with fixed, dilated pupils and pale, ischaemic retinae. Bilateral stellate ganglion block was unsuccessful until 19 hr after admission. A single dose of acetazolamide was given but retrolbar vasodilators were not used.

Over the subsequent 24 hr, his respiratory function deteriorated and he was returned to the ventilator. Thirty-six hours after the first haemoperfusion, his serum quinine had again risen to dangerous levels (22 mg/litre) and a second 4 hr perfusion was performed. A calculated quinine clearance of 50 ml/min was obtained during the second treatment (blood flow rate 300 ml/min). Thereafter his condition improved and by the 6th day he could hear the whispered voice but could only see the brightest light. Two weeks after admission, he no longer required ventilation but was still hypoxic and had complete loss of colour vision and severely constricted visual fields. Colour vision was objectively normal to standard testing and perimetry showed a peripheral visual field constriction. He complained of profound perceptive difficulty with constrast, distance and with distinction between natural and artificial light.

He left hospital after 5 weeks and at follow-up one month later, his visual symptoms were unchanged. He had bitemporal scotomata to red vision (Amsler chart), the retinal vessels showed marked attenuation and narrowing and there was pallor of the right disc.

**Case 2**

A 23-year-old male was admitted a few hours after taking an overdose of approximately 15 g of quinine sulphate and a lesser, unknown, quantity of paracetamol and betaistine. He was rational but drowsy, complaining of slight bilateral hearing loss but no visual disturbance. The serum paracetamol level was 29 mg/litre and serum quinine 20 mg/litre. Over the next few hours he developed cinchonism with agitation, tremor, tinnitus and deafness. His pupils became dilated but continued to respond to light and his retinae became pale. Immediate bilateral stellate ganglion block was performed. A 6 hr haemoperfusion was begun some 12 hr after ingestion when the serum quinine level was 31 mg/litre (Fig. 1). Quinine clearance obtained during the perfusion was 105 ml/min measured in the first hour (flow rate 300 ml/min). There was a brisk rebound rise in serum quinine to 17 mg/litre from 9 mg/litre at the end of the first session. The stellate ganglion block produced only temporary meiosis but the appearance of the fundus was reversed. The following day his general condition was improved and there were no signs of toxicity in spite of a persisting high serum quinine level of 12 mg/litre. After a second 4 hr perfusion (clearance 125 ml/min), the level had fallen to 3 mg/litre. On discharge from hospital he had no visual symptoms and his acuity and colour vision were normal and have remained so.

**Fig. 1.** Serum quinine levels during treatment (Case 1).

**Discussion**

The medicinal use of quinine is currently limited to the treatment of malaria and the doubtful prevention of night cramps. As oral quinine sulphate, it is 95% absorbed from the small intestine, with peak blood levels occurring 1-3 hr after a therapeutic dose. It is 70% protein-bound and mainly distributed in the extracellular fluid. Hepatic hydroxylation of available quinine occurs rapidly and excretion is mainly in the urine, being twice as great when the urine is acidic (Goodman and Gilman, 1975; Taggart et al., 1948). The fatal dose is approximately 8 g, but the range is wide with reports of a fatality after 3 g (Markham, Dodson and Eckberg, 1967), and survival after 31 g (Glick and Mumford, 1955). Specific measures for the active treatment of quinine poisoning have included forced acid diuresis, peritoneal dialysis (Donadio, 1968), haemodialysis (Floyd et al., 1974) and exchange transfusion (Burrows et al., 1972); all with only limited success. The clearance of quinine during haemodialysis is 35 ml/min and during peritoneal dialysis only 8-13 ml/min, which is less than the urinary clearance under optimum conditions (13-5-18 ml/min). The failure of these membrane dependent systems to remove the drug is
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Quinine poisoning treated with charcoal haemoperfusion (105–125 ml/min) compare favourably with in vitro studies and are considerably better than results obtained by other methods of active quinine removal. We therefore suggest that in quinine poisoning with high serum levels, active removal of the drug by charcoal column haemoperfusion should be considered in anticipation of symptoms.

References


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The treatment of quinine poisoning with charcoal haemoperfusion.

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