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Quinine intoxications reported to the Scottish Poisons Information Bureau 1997–2002: a continuing problem

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Quinine is widely prescribed in the UK for night cramps. Its potential toxicity in overdose is well known. We have reviewed the Scottish experience of enquiries regarding quinine overdose to the poisons information service responsible for Scotland over a 6-year period. Between 1997 and 2002 there were 96 reports of suspected quinine toxicity from Scotland (population 5.2 million), 19 of which were in children. The largest quantities of drug ingested were in patients between the ages of 11 and 30. In comparison with older studies the pattern of quinine poisoning does not appear to have changed in the UK over 20 years, despite recognition that it is a toxic agent in overdose, and particularly in children.

Keywords: quinine, poisoning, toxbase

Introduction

Quinine is widely used in the UK in the treatment of nocturnal cramps, despite limited evidence of efficacy [1]. In 2000–2001 2354 800 prescription items for quinine products were dispensed in the community for England alone, costing more than £4.1 million. The population of Scotland is 5.2 million, approximately 10% of England. Compared with this level of prescribing the overall incidence of self-poisoning is relatively low; however, the effects of quinine in overdose may be severe. Toxicologically quinine is important owing to its ability to impair vision permanently and cause death by cardiotoxicity. Auditory symptoms are also common, though rarely permanent. The smallest reported fatal dose is 1.5 g in an adult [2] and 900 mg in a child. There is a high risk of visual loss and cardiac complications when plasma concentrations of quinine exceed 15 mg l^{-1} at any stage after overdosage [3].

In 1985 Boland and colleagues working at the Poisons Unit in Guy's Hospital were consulted 225 times regarding quinine poisoning over a 5-year period [4]. Since then there have been few reports investigating how the situation has altered. The present report reviews consultations made to the Scottish Poisons Information Bureau following acute quinine ingestions in the period 1997–2002.

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Methods

The Scottish Poisons Information Bureau (NPIS Edinburgh) is part of the National Poisons Information Service. It is responsible for providing information on poisoning to health professionals in Scotland and for the web-based TOXBASE system, which is widely consulted in the UK for the treatment of acute intoxication [5]. Details of all telephone consultations received in the centre, of which over 90% originate in Scotland, are recorded and details entered into a database. This database was interrogated regarding sex and age of patient, dose taken, symptoms recorded and severity of event. Where clinically relevant all cases of quinine poisoning are followed up by letter. Follow-up data were reviewed where responses were available.

Results

Between 1997 and 2002 the Scottish Poisons Information Bureau received 32 353 telephone inquiries from Scotland, of which 119 concerned 96 cases of quinine poisoning in Scotland (95 ingestions, one infusion). There were, in addition, telephone enquiries concerning nine quinine ingestions from England and four from Northern Ireland. For the Scottish cases the ratio of quinine ingestions in males to females overall was 1 : 1.2 (45% : 55%) compared with 1 : 1 (49.9% : 50.1%) for all Scottish enquiries. The estimated amount of quinine ingested was available in 89 cases (see Table 1). The reported amount is often given as a range or the strength of tablets is not included, so broad categories have been used for analysis.

The doses reported to have been ingested appeared to correlate well with the poisoning severity score [6] and the patients' symptoms. Hence at doses <1 g taken in 24 h (33 cases), the poisoning severity score classified 52% as having no toxicity, 30% as having minor toxicity *and* only one each moderate and severe (therapeutic for 1 week and 600 mg day^{-1} for 1 week). However, in those that had reported ingestion of >10 g (six cases), 66% were classified as having serious toxicity with a further 33% being classified as having moderate toxicity at the time of the call. Follow-up was available in 13% of reports, usually in cases where ingestions were classified as moderate or severe. One death occurred in a 77-year-old woman who took 8–12 g. There were 29 reports of coingestion with other drugs; 13 of these reports included the ingestion of analgesics and nine reports included ingestion with alcohol (Table 2).

Paediatric ingestions

Nineteen of the reported ingestions occurred in the 0–10-year age group (with a mean age of 2 years 1 month; range 1 year to 3 years 9 months; 12 males, seven females). All these cases were classified as unintentional. Most had taken only one tablet, although one who might have taken up to 10 had no symptoms. There were two cases of vomiting, one associated with drowsiness; the rest showed no symptoms.

Adult ingestions

In the 11–30-year age group ($n = 18$), the amounts ingested ranged from 2 to 3 g to 150 tablets. All were classified as intentional. There was a female preponderance in this group of 11 : 7. In the 31–70 ($n = 36$) year age groups the amounts were between four and five tablets to 84 × 300 mg. The gender ratio was 1 : 1. Twenty-two of the 54 reports in the 11–70 groups were associated with coingestion of other drugs or alcohol.

More than half the reported low doses of quinine ingestion had symptoms. Most were minor, but in one case a therapeutic dose for 1 week produced hallucinations, confusion and darkened urine. In another case 600 mg day^{-1} for 7 days with mefloquine caused ventricular tachycardia, torsade de pointes and cardiac arrest.

Tinnitus and other auditory symptoms occurred in 31% of patients and appeared to be dose related, occurring in only 17% of patients who had reportedly ingested <1 g of quinine compared with 80% who had reportedly ingested >5 g. Visual toxicity was present in only one patient whose stated ingested dose was <1 g but in 80% of the patients who had ingested >5 g of quinine. Auditory symptoms usually resolve within a few days of the overdose. Evidence of cardiological dysfunction was only initially present as minor ECG changes. However, when reported dose exceeded 5 g around a third of patients had cardiac effects. Such observations support previous reports where quinine toxicity is related to plasma concentrations and hence to dose ingested.

Elderly ingestions

In those aged ≥71 years ($n = 16$) the M : F gender ratio was 1 : 3. Fifty percent had ingested <1 g in 24 h (range 200 mg to 80 tablets) and 63% were accidental; 69% had no or minor symptoms.

Table 1 Percentage incidence of quinine poisoning with respect to age and dose reported to be taken.

Age group (years)	n	*<1 g, %*	*1–5 g, %*	*5–10 g, %*	*>10 g, %*	*Unknown, %*
0–10	19	68	11	0	0	21
11–30	18	11	28	22	17	22
31–70	36	31	25	6	8	30
> 70	16	50	25	13	6	6
Unknown	7	43	14	0	0	43

Discussion

This series of cases provides further information on the pattern of quinine exposure in the UK following concerns expressed in publication in the 1980s. Studies examining the epidemiology of poisoning in children concluded that quinine, along with digoxin, had the highest case fatality rate in those under the age of 4, with an estimated mortality of 1 in 25 intoxications [7].

Table 2 Percentage of commonly reported symptoms by reported dose of quinine taken (where known in g), and in all cases about which an enquiry was made.

Dose	*None*	*Gastrointestinal symptoms*	*Hearing*	*Visual*	*Cardiac*	*Decreased GCS*
< 1 g, $n = 37$	51	14	5	3	5	8
1–5 g, $n = 21$	43	14	19	29	14	5
5.1–10 g, $n = 8$	0	13	63	75	38	25
> 10 g, $n = 7$	0	43	57	57	29	14
All enquiries, $N = 96$	38	14	19	23	15	11

GCS, Glasgow Coma Score.

Overall our data suggest toxicity is often not serious in children because only one or two tablets are taken before the container is discarded. One potential confounder is that the poisons information services may receive a disproportionately large number of paediatric enquiries following parental concern, and emergency staff being more apprehensive about paediatric ingestions regardless of the amount taken compared with adults. However, it remains a major concern that in this series nearly a fifth of the enquiries were about children. Child-resistant containers have been shown to decrease the incidence of childhood poisoning [8], nevertheless there is continuing need to educate family members about simple safety issues and storage of quinine tablets which are often not perceived as being particularly toxic.

In adults quinine poisoning almost always follows intentional ingestion, perhaps apart from the elderly in whom in this series toxic symptoms arose because of medication error in at least one individual. Auditory symptoms resolve as plasma levels fall, visual toxicity, which is well known, may be persistent. Although the literature reports three patients developing visual toxicity with ingestions of <1 g, lack of confirmatory plasma level monitoring casts doubt on their veracity. This and other larger series indicate these effects are associated with larger overdoses, normally associated with plasma concentrations >10 mg l^{-1} [3] indicating that this is likely to be a dose-related effect in all individuals exposed.

Cardiological dysfunction is the usual reason for death, and is manifest initially as ECG changes. These are common in doses >5 g in adults, and our series confirms this cut-off with >30% of patients reporting ingestion of these amounts having ECG changes.

Poisons information services are occasionally called about medication errors, and in the elderly this was a factor. Two cases may have developed symptoms of overdose following a therapeutic dose, but we have no plasma concentration monitoring to confirm this. Although the NPIS is not the prime agency for adverse drug reaction reports, low-dose quinine has the potential to cause severe drug toxicity by causing autoimmune thrombocytopenia.

Treatment of quinine overdose has changed little over the last 15 years. The principles remain based around supportive care. A volunteer study has shown that repeated dose-activated charcoal increases quinine clearance [10] and a case report has also indicated the potential usefulness of this approach in managing poisoning [10]. Ocular changes are secondary to direct retinal toxicity of quinine and hence stellate ganglion blockade, previously advocated, is not effective [11]. Management of arrhythmias and other cardiovascular complications is based on correction of acidosis with sodium bicarbonate and management of torsade with magnesium sulphate or overdrive cardiac pacing. There is generally no role for anti-arrhythmic drugs.

In summary, quinine remains a potentially extremely toxic agent in children. The patterns of exposure as reported to a poisons information service do not seem to have changed dramatically over a period of 20 years, and, more worryingly, we continue to have a significant number of enquiries in potentially susceptible age groups. In adults intentional overdose is the main reason for ingestion, but the age group presenting most frequently with highest doses (11–30 years) is one in which quinine would almost never be prescribed for therapeutic indications in the UK.

There is a concern that despite the documented toxicity of this agent and its questionable efficacy, large numbers of prescriptions continue to be available in the community. Children appear to be at highest risk from inadvertent ingestion, whilst the 11–30-year age group take the largest overdoses, which are often intentional. Treatment remains largely supportive.

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