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Effects of the Medicines and Healthcare products Regulatory Agency's safety update on the frequency and characteristics of quinine toxicity in the UK

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INTRODUCTION:

Quinine is commonly prescribed for leg cramps although available evidence indicates limited clinical benefit, and substantial placebo effect has been observed in clinical trials (1, 2). Quinine may cause severe toxic effects especially in overdose (3). Because of concerns about the benefit-risk balance for quinine use in leg cramps, the UK Medicines and Healthcare products Regulatory Agency (MHRA) issued a safety update in June 2010 advising restricted use (4). In a separate report, we have demonstrated that this has led to a reversal in growth of quinine prescribing. In this study, the impact on quinine toxicity, especially in overdose, is examined.

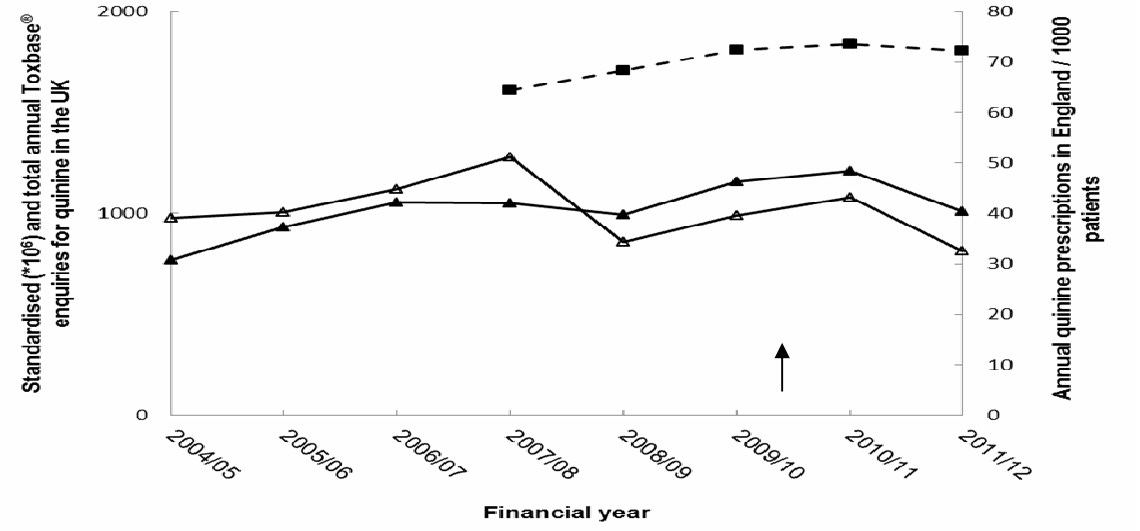
METHOD:

Data on telephone enquiries and accesses to the Toxbase® website relating to quinine from 2008/9 to 2011/12 were obtained from the National Poisons Information Service (NPIS). Characteristics of quinine toxicity from telephone enquiries and the frequency of Toxbase® quinine user sessions were analysed. Pearson's correlation and joinpoint regression tests were used to test for associations and changes in trends respectively.

RESULTS:

Before the MHRA update, Toxbase® quinine accesses were increasing but this has since shown a reversal in trend (difference in slopes -19.76 [95% CI -39.28 to -9.20], p value = 0.0575). These changes correlate with changes in the volume of quinine prescribing in England (correlation coefficient=0.5594; p value=0.0103) (Figure 1).

Figure 1: Trends of Toxbase® enquiries and quinine prescribing



Quinine prescribing in England (■). Total (▲) and standardised [ratio of total quinine to total product] (Δ) annual Toxbase® quinine accesses. MHRA quinine safety update publication (↑).

In the fiscal years 2008/9 to 2011/12, NPIS received 510 telephone enquiries involving quinine. Of these, 259 (51%) related to cases of accidental use or therapeutic error who ingested doses commonly between 0.2 and 0.9g, and remained mostly asymptomatic. Deliberate self-harm accounted for nearly 40% of all cases with a median ingested dose (range) of 4.4 (0.9–19.0)g and was responsible for most symptomatic reports. The incidences of deliberate self-harm and serious toxic features associated with quinine overdose are shown in Table 1. Other serious clinical features over the 4 year period included acidosis (28), stupor or coma (18), hypoglycaemia (8), convulsions (4) and death (2). Telephone enquiry numbers were not large enough for detailed statistical analysis of time trends.

Table 1: Characteristics of telephone enquiries to NPIS relating to quinine

	2008/9	2009/10	2010/11	2011/12
Self-harm, n (%)	53(39%)	63(43%)	34(32%)	46(38%)
Cardiac toxicity, n (%)*	18(13%)	33(22%)	29(28%)	26(21%)
Visual impairment, n (%)	17(13%)	26(18%)	16(15%)	14(11%)
Hearing impairment, n (%)	10(7%)	6(4%)	3(3%)	13(11%)
Cardiac toxicity, visual or hearing impairment, n (%)	45(33%)	65(44%)	48(46%)	53(43%)
Total number of cases (n)	136	147	105	122

*Defined as bundle branch block, bradycardia, tachyarrhythmia, QT prolongation and/or cardiac arrests.

CONCLUSION:

The MHRA safety update and subsequent reductions in prescribing have been associated with reduced Toxbase® accesses. Reductions in telephone enquiries, especially those involving

serious toxicity, cannot be demonstrated due to low numbers. Further gains may be realised by encouraging more substantial reductions in quinine prescribing.

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