Clinical Toxicology

Massive chloroquine overdose – a survivor

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Summary: Large chloroquine overdoses are almost inevitably fatal. We describe the presentation and management of a patient with such an overdose who survived, due to general supportive care and new specific treatment.

Introduction

Large overdoses of chloroquine are usually fatal, with death occurring rapidly due to a direct effect of the drug on the myocardium. Patients with such an overdose may present with nausea, diplopia, convulsions, respiratory and cardiac arrest. We report the survival of a patient whose intravascular chloroquine level is probably one of the highest ever recorded.

Case report

A 30 year old Asian woman presented following a grand mal seizure in the street. No other history was available. On arrival she was unresponsive with a Glasgow Coma Scale of 6, constricted but reacting pupils, minimal respiratory effort, a heart rate of 50 and a blood pressure of 95/70 mmHg. Immediate standard resuscitation was instigated; the patient was intubated, mechanically ventilated, and an electrocardiogram performed which showed a sinus bradycardia with QRS interval of 0.16 seconds. Naloxone and atropine were given, resulting in an initial improvement in heart rate, but subsequently she had an asystolic cardiac arrest. She was resuscitated with external cardiac compression and intravenous adrenaline 1 mg which established a regular rhythm with a rate of 60/min and a blood pressure of 70/50 mmHg. Supportive therapy with a dopamine infusion (5–20 μg/kg/min) was started.

All routine blood results were normal, with the exception of the potassium level which was 1.4 mmol/l (normal range 3.5–5.0 mmol/l). Potassium supplementation was added. A toxicology screen was requested and revealed a plasma chloroquine level of 47 μmol/l. Following the recommendations of recent studies, a continuous diazepam infusion (2 mg/kg/24 h) was instituted. Over the next 24 hours the patient had episodes of ventricular tachycardia which were treated with cardioversion. On the third day the infusions of dopamine and diazepam were gradually stopped. The patient was extubated 66 hours after admission, at which time her plasma chloroquine level was 2.4 μmol/l. Although unwilling to discuss the circumstances and amount of her overdose, the patient made an uneventful medical recovery.

Discussion

Therapeutic chloroquine levels during treatment for rheumatoid diseases are of the order of 0.8 μmol/l blood. In chronically treated patients side effects are common above 2.5 μmol/l. Riou et al. have described the survival of a group of patients in whom the highest measured blood chloroquine level was 80 μmol/l.2

The patient described in this case report had a plasma concentration of 47 μmol/l. It is difficult to make direct comparisons between blood and plasma concentrations, especially in acute dosage, but an estimate would put the blood concentration as being 4–8 times the plasma concentration. Such an estimate would make this the highest ever recorded concentration of chloroquine in a surviving overdose patient. It is certainly the highest recorded concentration in the United Kingdom.

Chloroquine is rapidly absorbed from the gastrointestinal tract, resulting in transiently high intravascular concentrations which are potentially cardiotoxic. Redistribution from this central com-
partment, with extensive tissue binding, means that toxic effects rarely last more than 24 hours, despite an elimination half life of 6–14 days. Providing adequate support is given until the intravascular chloroquine concentration has fallen, no permanent myocardial or cerebral damage should result.

Riou et al.² have identified certain prognostic parameters in chloroquine overdose (Table I) and recommended the use of diazepam infusions to treat severe cases in whom a fatal outcome would previously have been expected. Chloroquine causes a vasodilatation and myocardial depression,¹ and the use of inotropic agents in chloroquine poisoning can be easily understood. The protective role of diazepam is not so readily explained. Following reports that administration of diazepam reduced the mortality rate for patients with chloroquine poisoning,⁷ experimental studies were initiated. These showed that diazepam decreased mortality in rats,⁸ and improved haemodynamic function and electrocardiography features and increased urine output, and hence urinary chloroquine excretion in pigs³ with chloroquine poisoning. In Riou’s series, no patient had demonstrable cardiac problems. This may have been because the diagnosis was known at the outset in all cases.

Hence, treatment consisting of mechanical ventilation, inotropic support and diazepam infusion was instigated early – in some cases even in the patients’ homes. Our patient, in whom the diagnosis was initially unknown, received mechanical ventilation and inotropic support in the Accident and Emergency Department as part of our standard resuscitation procedure. The diazepam infusion was delayed for 5 hours whilst the diagnosis was established from the drug screen. Ventricular tachycardia was controlled by cardioversion, but it is possible that this might have been unnecessary if diazepam therapy had been started earlier.

The Paris society, which promotes voluntary suicide, recommends chloroquine to its members as a potentially toxic drug which is easily obtainable over the counter.⁹ Although this is not in itself a reason to make it a prescription only medication, it is imperative that doctors are aware of its ready availability, and of its potentially fatal effects when taken in large doses.

Acknowledgements

We thank the Guy's Hospital Poisons Unit for the toxicology screen and the serial plasma chloroquine assays, and Dr J. Henry for his help and guidance in the preparation of this paper.

Table I Details of this case compared with predictors of a fatal outcome

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Present case</th>
<th>Predictors of a fatal outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>95 mmHg</td>
<td>&lt;85 mmHg</td>
</tr>
<tr>
<td>QRS complex duration</td>
<td>0.16 sec</td>
<td>&gt;0.12 sec</td>
</tr>
<tr>
<td>Dose</td>
<td>Unknown</td>
<td>&gt;5 g</td>
</tr>
<tr>
<td>Chloroquine concentration</td>
<td>47.5 μmol/l</td>
<td>&gt;25 μmol/l</td>
</tr>
</tbody>
</table>

References

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doi: 10.1136/pgmj.67.789.678

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