Letter to the Editor

Fatal Chloroquine Poisoning: A Rare Cause of Sudden Cardiac Arrest

Dear Editor,

Chloroquine is a widely available drug, used for the treatment of malaria and as prophylaxis for travellers to endemic countries.

Chloroquine has a narrow therapeutic index. Large overdoses are highly fatal and there are no known antidotes. Its terminal elimination half-life is long (1 to 2 months) – a property that has made it a popular and effective anti-malarial, as well as an effective suicidal agent, with severe and sustained cardiotoxicity after an overdose. Such is the potency of chloroquine as a suicidal agent that it is presented in a critical overview of ways to commit suicide in the French book 'Suicide Mode D'Emploi'.

However, chloroquine poisoning is rare in developed countries and as such, is not easily recognised. We report, herein, a case of fatal and unsuspected chloroquine poisoning in a 37-year-old female who suffered a sudden cardiac arrest.

Case report

This was a 37-year-old female who presented to the clinic complaining of nausea. She appeared restless and agitated. After 20 minutes, she lost consciousness, became pulseless and apnoeic. The initial rhythm recorded was ventricular tachycardia (VT). Advanced cardiac life support was initiated with intubation, chest compressions and administration of a total of 10 mg of IV adrenaline, IV atropine 2.4 mg and IV sodium bicarbonate (8.4%) 50 mmol/L. During the resuscitation, her cardiac rhythm alternated between ventricular fibrillation (VF) and asystole. Return of spontaneous circulation (ROSC) was achieved after 45 minutes.

She had a background of depression, was on fluvoxamine and zolpidem and had no previous suicide attempts or deliberate self harm. She was otherwise well, with no history of cardiovascular disease. She was an active person and had a history of overseas trips for missionary work and recreational scuba diving.

Initial investigations were remarkable for hypokalemia of 1.9 mmol/L and hypernatremia of 150 mmol/L. Cardiac enzymes were normal. She was managed with mechanical ventilation and therapeutic hypothermia. Her initial electrocardiogram (ECG) showed sinus tachycardia of 102 beats/minute with a QT interval (QTC) of 372 ms. Potassium levels were corrected overnight with 120 mmol/L of IV potassium.

Her progress in intensive care unit (ICU) was poor. Neurological exam post-arrest showed fixed and dilated pupils, negative corneal and oculocephalic reflexes and Glasgow Coma Scale (GCS) of 3. She remained haemodynamically unstable and suffered another cardiac arrest from torsades de pointes. There was ROSC after 30 minutes of resuscitation. Electrolytes were normal by that time.

Blood toxicology the next day showed toxic levels of chloroquine (71.9 umol/L) and low levels of naproxen. We commenced IV diazepam (2 mg/kg loading followed by 1mg/kg/h infusion) and IV adrenaline and she stabilised with no further episodes of cardiac arrhythmias. At 96-hours, chloroquine levels remained high at 50 umol/L. She remained ill and developed nosocomial pneumonia and eventually died 10 days after admission to the ICU.

The post-mortem revealed pus in the airways and extensive consolidation in both lungs. No structural cardiac abnormalities were detected and coronary arteries were patent. High levels of chloroquine were detected on post-mortem toxicology (50 umol/L). Her death was certified as "pneumonia following chloroquine toxicity". A police investigation concluded that the patient had attempted suicide by chloroquine ingestion. How she obtained chloroquine was speculative, although we postulated that she had obtained the drug as prophylaxis for her overseas trips.

Discussion

In a young patient who has collapsed unexpectedly, poisoning and overdoses should always be part of the working diagnosis. In this case, chloroquine was an unexpected culprit as its use in our local setting is extremely limited.

This patient's nausea, vomiting and pulseless VT are common in massive chloroquine poisoning. The cardiotoxicity from chloroquine overdose is related to the development of atrioventricular block and widening of the

QRS interval. It also causes arteriolar dilation and has a negative inotropic effect, both of which contribute to shock. Patients may also develop severe hypokalaemia, which can occur within 3 hours of ingestion, and is strongly related to the severity of toxicity.[1] The hypokalemia is thought to be from potassium-channel blockade causing excess intracellular potassium distribution. Chloroquine toxicity may also present with drowsiness, irritability, vertigo, visual disturbances, convulsions, QRS widening, abdominal cramps, vomiting and apnoea.

The management of severe chloroquine intoxication involves control of airway, breathing and circulation, prevention of further absorption, stabilizing the cardiovascular system and aggressively managing hypokalemia. Activated charcoal absorbs chloroquine very effectively from the gastrointestinal tract (GIT), and should be administered as soon as possible in known or suspected chloroquine poisoning.[2] Other treatments of proven benefit include, use of intravenous sodium bicarbonate (8.4%) 1 to 2 mL/kg when there is QRS complex widening or prolonged QTC interval (aiming for a pH of 7.45 to 7.5), and overdrive pacing for ventricular tachycardia or torsades de pointes. Haemoperfusion is ineffective as chloroquine has a large volume of distribution in the blood and is highly concentrated in the red blood cells. Both chloroquine and its metabolites have elimination half-lives of 20 to 60 days, and can be detected in the urine months after a single dose.[3]

There are no known antidotes for chloroquine.

Intravenous diazepam use is contentious and the mechanisms underlying its antiarrhythmic properties are not fully defined, but could be related to a decrease in sympathetic output in the central nervous system and peripheral benzodiazepine receptor mediated regulation of the cardiac calcium channels.[4] Epinephrine reduces the cardiotoxic effects of chloroquine by reducing intraventricular conduction time.[5]

Poor prognostic factors include high concentrations of chloroquine in the blood and severe hypokalaemia. The reported lethal range of chloroquine lies between 9.3 to 309 umol/L. When epinephrine, mechanical ventilation and diazepam are instituted early, mortality is limited to about 10%.

There exist a few observations associating fluvoxamine to impaired membrane potential repolarisation resulting in QTC prolongation and ventricular arrhythmias. The chloroquine toxicity here may have been potentiated by her chronic fluvoxamine ingestion, even at therapeutic doses.

Conclusion

Acute chloroquine intoxication remains a serious illness, with high fatality rates. Although uncommon in countries where malaria is not endemic, it must be recognised as a potential cause of sudden cardiac arrest, recurrent arrhythmias and profound hypokalaemia in an individual with no prior cardiovascular history.

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