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CASE REPORT: A Patient With Quinine Sulphate Intoxication

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ABSTRACT

Background: *Cinchonism* is classic symptoms from quinine overdose, include vomiting, tinnitus, deafness, headache, and visual disturbance. Quinine overdose may lead to serious side effects

Case report: We report a rare case a patient with tentamen suicide. Patient was consumed 24 tablets quinine 300mg quinine, and showed sign and symptoms of quinine sulphate intoxication. Patient had chinchonism, abnormal ECG and anemia, and sudden blindness and deafness. Patient was given fluid resuscitation, supportive therapy: anti emetic, anti-depressant, blood transfusion, and high dose steroid for 3 days. Patient was observed for laboratory, ECG and visual acuity, after 7 days patient got improvement, patient was discharged.

Conclusion: The ultimate predictor of outcome from quinine poisoning appears to be the cardiovascular response. Mortality rates vary from 0 to 6.25%. The majority of deaths occur from cardiotoxicity. The effect of quinine on hearing is considered reversible and auditory symptoms usually resolve within a few days

KEYWORDS: *intoxication, quinine sulphate, quinine intoxication,*

INTRODUCTION

Intoxication is impaired condition caused by use of drug or other chemical substance. Intoxication is highly dependent on the type and dose of drug and is influenced by an individual's level of tolerance and other factors. Exceptions to this may occur in individuals with certain underlying organic conditions, renal or hepatic insufficiency, in which small doses of a substance may produce a disproportionately severe intoxicating effect ⁽¹⁾ Quinine sulfate belongs to a class of drugs known as anti-malarial. Acute intoxication can be seen after ingestion of doses of 4-12g, but a dose of 8g can prove lethal. The average fatal dose for an adult is about 8g although deaths have been reported from as little as 1.5g in an adult and 900mg in a child. ⁽²⁾ We report a rare case, a patient with severe depression and had quinine sulfate intoxication. We will discuss about pharmacokinetic and pharmacodynamics quinine sulfate, sign and symptoms, how to diagnose and management quinine intoxication.

CASE

Miss A, 21 y.o, unmarried, Javanese, lived in Surabaya. On 1st of January 2019, admitted in the emergency unit at Dr. Soetomo hospital, after a tentamen suicide. He consumed 24 tablets quinine 300mg, (~to 7200 milligrams quinine) at 03.00 PM 31st of December 2018, 3 hours later she felt cold, freeze, headache, and tinnitus. She was vomiting more than 5 times. At 01.00 AM, patient was awakening and she noticed decrease in her visual acuity, being able identify shape and few colors like black and white. Approximately 5 minutes later, she could not identify shape or colors, she developed sudden blindness. Then she was brought into Dr. Soetomo hospital.

Patient felt palpitation, but did not have chest pain, difficulty breathing, she did not cough, she was not fever. She was cold and had tingling sensation both her legs and arms.

Patient was had severe nausea and vomiting yellowish liquid, but there was no blood. She complained abdominal pain, especially at epigastric. She had difficulty of eating, but still could drink water. Patient had no weight loss, and no excessive sweating, there was no bleeding manifestation. She did not complain of any urinary symptoms. Defecation within normal limits with a frequency is once a day.

Physical Examination

Patient was weak, GCS 456, BP 120/80 mmHg, pulse 108x/minute, RR24 x/minute, axillary body temperature 36.7°C. On examination of the head and neck there were conjunctiva anemic, no sclera jaundice, no cyanosis and no shortness of breath. Both pupils were fixed and dilated and there was no light perception in either eye. In patient there were also no tumor and no enlarged lymph nodes in the neck. On chest examination it appears symmetrical, no retraction and no use of breathing muscles. Cor, normal sounds, regular, and no additional heart sounds. Pulmo, vesicular breath sounds in lungs, no ronchi and no wheezing. On abdominal examination, there was epigastric pain, tenderness. On examination the extremities were found that the acral felt cold, dry, pale and no edema. Status ophthalmology Table 1.

Table 1. Status ophthalmology

	Dextra	Sinistra
Visus Ocular	Poor light perception	Poor light perception
Palpebra	Edema-/-	Edema-/-
Konjungtiva	Hiperemi-/-	Hiperemi-/-
Kornea	Clear +/+	Clear +/+
Iris	Radier +/+	Radier +/+
Pupil	Round+/, light reflex decreased, Ø9mm/9mm, RAPD -/-	Round+/, light reflex decreased, Ø9mm/9mm, RAPD -/-
Lens	Clear +/+	Clear +/+
Fundus reflex	+	+
Papil NII	Hiperemi+	Hiperemi+
Retina	Bleeding-	-
Makula reflex	+	+

Additional Examination

The laboratory results Blood sugar 63 mg/dL; BUN 10 mg/dl; SK 0.63 mg/d; SGOT/PT 29/9 U/L; albumin 4.11 g/dL; Na 144 mmol/L; K 3.5 mmol/L; Cl 108 mmol/L, Hb 7.7 g/d; WBC 11.670 /μL; PLT406.000; neutrophil 85.9%; lymphocytes 6.6%; monocytes 7.2%; PPT 11.1seconds; aPTT 25.8 seconds, HbsAg NR. CXR within normal limits. ECG SR 107x/minute, regular rhythms, normal axis, prolonged QT interval. QT interval 420 ms.

Cardiology: Prolonged QT interval without symptoms of arrhythmia

Oropharyngology

Sudden deafness caused by ototoxic

Neurology

Focal deficit, gloves stocking hyposthesia caused by drug induced polyneuropathy

Initial assessment: Quinine Intoxication + *Cinchonism* + ODS TON+ vomiting + anemia hypochromic microcytic+ hypoglycemia + severe depression. This patient was planned for audiometry, ECG serial, CBC, LFT, RFT serial and consult to psychiatry department. Tx: NaCl 0.9% 1000cc/day, D40 1 flash intravenous, maintenance Dextrosa 5% 1000cc/day. Injection metoclopramide every 8 hours/day. Injection ranitidine 2x1. Injection mecobalamine 2x1. Transfusion PRC 2 pack/day until Hb 10gr/dl. Monitor cardiac conduction and rhythm, serum electrolytes, blood glucose and visual acuity

Disease progression

Day 2nd: Patient complained blindness and nausea, but she had less vomiting. ECG: sinus 104x/minute. Blood sugar 133 mg/dL, bili D 0.3 bili tot 0.8. Psychiatry: Severe depression without psychotic + tentamen suicide. Advice: Sentraline 1x50mg p.o, klobazam 2x5mg p.o. Tx: Injection MP 1000mg/day. Injection metoclopramide 3x1. Injection mecobalamine 2x1. Transfusion PRC 2 pack/day until Hb 10gr/dl. Sukralfat syrup 3xCII p.o. Sentraline 1x50mg p.o, klobazam 2x5mg p.o.

Day 5th Patient had better vision, she could see, and differentiate colour Hb10,6 WBC16.940 PLT344.000 SGOT20 SGPT32 Bun9 Sk0,6 Blood sugar 126. Therapy: inj.metoclopramide 3x1. Inj.mecobalamine 2x1. Sukralfat syrup 3xCII. Methylprednisolone 3x16mg. Fe tablet 3x200mg. Sentraline 1x50mg, klobazam 2x5mg
Day 7th Patient had no complaints. Patient had BP 120/80mm Hg, heart rate 76 per minute and body temperature 37c. VOD:1/60 VOS: 1/60, Pupil: round, Ø3mm/3mm, Patient was discharged.

DISCUSSION

Quinine is rapidly and almost completely absorbed from the upper gastrointestinal tract when given orally. Peak plasma concentrations occur 1 to 3 hours after ingestion. Approximately 89% is bound to plasma proteins. The volume of distribution is 1.8 L/kg, and the elimination half-life is 9-15 hours. About 75% is metabolized by the liver, kidneys, and muscles. ⁽⁶⁾⁽⁷⁾

Acute intoxication can be seen after ingestion of doses of 4-12g, but a dose of 8g can prove lethal. The average fatal dose for an adult is about 8g although deaths have been reported from as little as 1.5g ⁽²⁾

Quinine can adversely affect almost every body system. The most common adverse events associated with called “cinchonism”, which occurs to some degree in almost all patients taking quinine.

Quinine overdose may lead to serious side effects including irreversible visual loss, and can be fatal. Symptoms include vomiting, tinnitus, deafness, headache, vasodilation and visual disturbance. Features of a significant overdose include convulsions, impairment of consciousness, respiratory depression, QT prolongation, ventricular arrhythmia, cardiogenic shock and renal failure. High doses of quinine are teratogenic and may cause miscarriage. Hypokalemia and hypoglycemia may also occur ⁽²⁾

The cardio-toxicity of quinine is due to its negative inotropic action, and to its effect on cardiac conduction, resulting in decreased rates of depolarization and conduction, and increased action potential and effective refractory period. Quinine’s alpha-blocking properties may result in hypotension and further exacerbate myocardial depression by decreasing coronary perfusion. Quinine overdose has been associated with circulatory collapse and ventricular arrhythmias⁽⁹⁾

Ophthalmic impairment and deafness may occur with severe poisoning. ⁽⁸⁾Hematologic abnormalities are rare and include Coombs’ positive hemolytic anemia, neutropenia, disseminated intravascular coagulation, hypofibrinogenemia, and thrombocytopenia with quinine-dependent, platelet-specific antibodies demonstrated. Renal tubular obstruction, acute renal failure, and granulomatous hepatitis have also been reported. Inappropriate beta cell secretion of insulin can be stimulated by quinine, and hypoglycemia has occurred. In skeletal muscle, quinine decreases the excitability of the motor-end plate, which may explain its use in treating nocturnal leg cramps. Quinine has direct irritant effects on the gastrointestinal (GI) tract and stimulates the brainstem center responsible for nausea and emesis ⁽⁸⁾

Adults should be referred to hospital if more than 30 mg/kg of quinine base has been taken.. ⁽⁸⁾. Oxygen, hemodynamic monitoring, IV fluid resuscitation, ECG and blood glucose measurements. If patient is coma, urgent intubation and ventilation are needed ⁽⁸⁾

Treatment of the gastrointestinal usually not required, but antiemetics may and intravenous fluids are necessary in clinical profuse vomiting or diarrhoea self-limited. Quinine is rapidly absorbed and emesis usually occurs with large ingestions, gastric emptying is often unnecessary. If a patient ingests a toxic dose, arrives within 3 to 6 hours after ingestion, and has not vomited, gastric emptying should be considered. Consider activated charcoal if the patient presents within 1 hour. Multiple dose activated charcoal will enhance quinine elimination. Activated charcoal effectively adsorbs quinine and may additionally decrease serum concentrations by altering enteroenteric circulation ⁽⁸⁾.

Toxic optic neuropathy is caused by the damage to the optic nerve through different toxins.. High dose methyl prednisolone intravenously at 1 g/day for 3 days, followed by oral prednisolone at 1 mg/kg, significant visual improvement inhibition of the retinal and macular atrophy was also observed ^(10,11,12)

In this patient, activated charcoal was not given because patient came to the hospital after 12 hours ingestion of quinine. Patient was given supportive therapy . Nacl 0,9% 1000cc/day, Dextrosa 5% 1000cc/day. Injection methylprednisolone 1000mg/ day for 3 days. Injection metoclopramide 3x1. Injection mecobalamine 2x1. Transfusion PRC 2 pack/day until Hb 10gr/dl. Sucralfate syrup 3xCII p.o. Sentraline 1x50mg p.o, klobazam 2x5mg p.o.

Observe patients for at least 12 hours after ingestion. Monitor cardiac, electrolytes, blood glucose and visual acuity. Other treatment is symptomatic ⁽⁸⁾ Predictor of outcome from quinine poisoning appears to be the cardiovascular response. Mortality rates vary from 0 to 6.25%. The majority of deaths occur from cardiotoxicity. ⁽⁷⁾

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