National Capital Poison Center ToxFacts
Chloroquine and Hydroxychloroquine

Background:

Chloroquine has been traditionally used for the prevention and treatment of malaria, but can also be found in aquarium products to treat parasites in fish. Hydroxychloroquine is used to treat autoimmune conditions, such as rheumatoid arthritis and lupus. More recently, these drugs have shown promise as treatments for patients with COVID-19 infection, which led to their addition to the National Stockpile by the Food and Drug Administration. Since these reports have surfaced, there has been an increase in overdoses involving chloroquine and its derivatives in an effort to prevent or self-treat COVID-19 infection. Chloroquine has a narrow margin of safety, and death from fatal dysrhythmias may occur rapidly, usually within 1-3 hours. This is due primarily to sodium and potassium blockade, as well as the profound intracellular shift of potassium.

Clinical Presentation:

CNS: altered mental status, coma, respiratory depression, dizziness, headache, seizures, dystonic reactions, Parkinson-like movements, visual disturbances
Cardiovascular: tachycardia, bradycardia, refractory ventricular dysrhythmias, hypotension
Endocrine: hypoglycemia
Gastrointestinal: abdominal pain, nausea, vomiting, diarrhea
Hematologic: hemolysis in patients with G6PD deficiency, methemoglobinemia, disseminated intravascular coagulation
Pulmonary: aspiration due to seizures/altered mental status
Renal/Electrolyte: severe hypokalemia, rhabdomyolysis

**Patients who have ingested a dose of 5 grams of chloroquine (30 mg/kg in children) or more, have a potassium of <2 mEq/L, a QRS duration of >120 ms, a systolic blood pressure of <80 mmHg, have a chloroquine concentration >8 mcg/mL, or present in ventricular fibrillation have a very poor prognosis.*

Diagnosis:

Based on history, physical exam, EKG, & laboratory findings:

- EKG: QRS and QTc prolongation, ST and T wave depression, U waves, AV block
- Arterial or venous blood gas in severely ill patients with concern for respiratory depression or methemoglobinemia
- Electrolytes, creatinine, & glucose
- Complete blood count
- G6PD testing in patients with evidence of hemolysis
- Creatinine phosphokinase if prolonged seizures or downtime
- ASA/APAP, other toxicology labs indicated by history
- Levels for chloroquine and hydroxychloroquine levels are not routinely available and do not change clinical care

- Head CT in patients with focal neurologic findings
- Chest x-ray if pulmonary symptoms
- HCG testing in women of child-bearing age

Treatment:

THERE IS NO EFFECTIVE ANTIDOTE FOR POISONING.
EARLY GASTROINTESTINAL DECONTAMINATION IS PARAMOUNT.

Decontamination:

- Activated charcoal 1 g/kg effectively binds chloroquine derivatives and should be administered to patients with an intact airway.
- Gastric lavage should be utilized in patients presenting early after a large chloroquine overdose, with airway protection as needed.

Supportive Therapy:

- Standard measures for airway, breathing, circulation; however, barbiturates should be avoided as induction agents as they have been associated with peri-intubation cardiac arrest.
- Cardiac monitoring due to the significant risk of dysrhythmias.
- Potassium levels should be monitored; however, hypokalemia may have a protective effect and redistribution of potassium may cause hyperkalemia as toxicity resolves; therefore, it is recommended to replete potassium if the level is less than 2 mEq/L or if sodium bicarbonate administration is required.
- QRS prolongation can be treated using sodium bicarbonate boluses 1 mEq/kg; however, this must be done cautiously as it may cause further intracellular shift of potassium. Potassium should be repleted prior to administering sodium bicarbonate and electrolytes should be monitored frequently.
- Lidocaine can be used for ventricular dysrhythmias. Avoid class IA (procainamide), IC (flecanide), and III (amiodarone) antidysrhythmics as these may potentiate cardiac toxicity.
- Magnesium sulfate, 2 g IV, should be used to treat dysrhythmias in the setting of QT prolongation (>500 ms). Magnesium sulfate, isoproterenol, and overdrive pacing can be used for Torsades de pointe.
- Administer isotonic saline for hypotension. If vasopressors are required, epinephrine is the preferred vasopressor. It should be noted that higher than usual doses may be required. The recommended starting dose is 0.25 mcg/kg/minute, titrated to maintain systolic blood pressure >90-100 mmHg. Note that epinephrine may exacerbate preexisting hypokalemia.
- High dose diazepam (2 mg/kg IV over 30 minutes, followed by 1-2 mg/kg/day for 2-4 days) in conjunction with epinephrine may mitigate chloroquine-associated cardiac toxicity and is recommended for patients with severe toxicity. It is unclear if other benzodiazepines have the same beneficial effect. Intravenous diazepam is 40% propylene glycol, which can lead to severe metabolic acidosis and clinical deterioration. Patients undergoing high dose diazepam treatment should be closely monitored and if this occurs, discontinue the diazepam. Midazolam 0.5 mg/kg may be useful in the setting of diazepam shortage. Intravenous midazolam does not contain propylene glycol.
- Seizures should be treated with benzodiazepines.

- Significant methemoglobinia can be treated with methylene blue (see separate ToxFacts).
- Due to their large volumes of distribution, hemodialysis and hemoperfusion are ineffective for chloroquine derivative overdose.
- Lipid emulsion therapy has been used in case reports in patients with refractory toxicity or cardiac arrest due to chloroquine derivatives; however, there are little data to support this practice.
- Extracorporeal life support (ECMO, cardiopulmonary bypass) should be considered for refractory hypotension when other measures have failed.

Disposition:

- Non-suicidal patients who have had decontamination with activated charcoal and have no symptoms, normal EKG/vital signs/labs may be discharged after a six-hour observation period.
- Patients that are suicidal, have symptoms of toxicity, EKG abnormalities, abnormal vital signs or laboratory findings, or significant co-ingestions should be admitted with telemetry; those with severe toxicity will require ICU admission.

Common Pitfalls:

- There is no effective antidote for chloroquine/hydroxychloroquine overdose. Early gastrointestinal decontamination is critical.
- Life-threatening cardiovascular collapse may occur rapidly after ingestion.
- Sodium bicarbonate and epinephrine may exacerbate hypokalemia.
- Avoid class IA, IC, and III antidysrhythmics, as they may worsen cardiac toxicity.
- Monitor patients receiving high-dose diazepam for evidence of propylene glycol toxicity.