Ohio Poison Control System
1-800-222-1222
Poisoning Fact Sheet for Health Care Providers
Hydroxychloroquine & Chloroquine

Hydroxychloroquine sulfate (Plaquenil®) and chloroquine phosphate (Aralen®) belong to the aminoquinoline drug class. They are FDA-approved for the treatment and relapse prevention of uncomplicated malaria in children and adults. Additionally, hydroxychloroquine is FDA-approved for maintenance treatment of systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) in adults. Hydroxychloroquine and chloroquine are now used off-label in selected cases of respiratory illness caused by coronavirus disease 2019 (COVID-19). Studies are in process. The limited data available is conflicting.

Due to the narrow therapeutic index of these drugs, particularly chloroquine, we anticipate an increased incidence of drug overdose and toxicity. A death due to chloroquine toxicity in a patient attempting to treat symptoms of suspected COVID-19 has already been reported.[10]

Mechanism of Action for COVID-19: Unknown, however they demonstrate in-vitro anti-viral activity by blocking DNA and RNA synthesis of SARS-CoV, SARS-CoV-2 and other coronaviruses. Hydroxychloroquine displayed higher potency against SARS-CoV-2 in-vitro.

Mechanism of Toxicity: These medications display quinidine like cardiotoxicity. They also block DNA and RNA synthesis. Hydroxychloroquine demonstrates less toxicity and potency than chloroquine.

Toxic Dose: 250 mg chloroquine phosphate=150 mg chloroquine base. Lethal oral dose of chloroquine (children) is 300 mg chloroquine base. It is commercially available as chloroquine phosphate in 250 and 500 mg tablets, therefore, an ingestion of a couple tablets can be lethal. Lethal oral dose range of chloroquine (adults) 30-50 mg/kg of chloroquine base (~2.25-3 g). Oral ingestion of 8-22 g of hydroxychloroquine in adults can cause severe symptoms.

Symptoms of Toxicity:
Mild to moderate:
- GI symptoms: abdominal pain, nausea, vomiting
  CNS symptoms: Headache, visual disturbances resulting in permanent blindness (chronic use), hearing disturbances resulting in deafness
- Neuromuscular excitability

Severe (Develops within 1-2 hours; bolded symptom triad is suggestive of chloroquine overdose):
- Depressed myocardial contractility, varying degrees of heart block, **hypotension**, ventricular dysrhythmias, cardiac arrest
- Seizures
- Respiratory arrest
- QT and **QRS prolongation** (increased risk when combined with azithromycin; monitor EKG carefully)
- **Hypokalemia**
- Coma

Treatment:

- Discontinue offending medication and **call poison control center at 1-800-222-1222**
- Benzodiazepines are recommended first line treatment for agitation, seizures, and neuropsychiatric adverse effects. Large doses may be needed.
- Antiemetics as needed for GI symptoms. Avoid agents that can prolong QTc, if possible. Consider using isopropyl alcohol wipes as a non-pharmacologic treatment option.
- Analgesics as needed for headache
- Early intubation may improve outcomes in patients with respiratory depression and loss of airway protective reflexes.
- Administration of high-dose diazepam to augment dysrhythmia and hypotension management has been shown to improve survival in some studies. Dose recommendation: diazepam 2 mg/kg IV over 30 minutes, followed by an infusion of 1 – 2 mg/kg/day for 2 – 4 days.
- Activated charcoal if patient is intubated or orogastric lavage if ingestion < 1 hour ago
- Circulatory support with IV fluids and epinephrine 0.25 mcg/kg/min, increasing by 0.25 mcg/kg/min until adequate blood pressure is reached.
- 20% lipid emulsion (for CV disturbances) 1.5 mL/kg bolus over 2-3 min, then 0.25 mL/kg/min infusion, evaluate after 3 min then decrease rate to 0.025 mL/kg/min in patients with significant response.
- Use of sodium bicarbonate for QRS/QTc prolongation and potassium supplementation is controversial. Consultation with poison control is recommended in these cases.

References:

1. Olson KR, Anderson IB, Benowitz NL, et al. Poisoning & drug overdose, 7th ed. New York (NY): McGraw Hill Education; 2018. Chloroquine and other aminoquinolines; p. 194-7.
2. Lexicomp. Hudson (OH): Wolters Kluwer. 2019.
3. Micromedex. Greenwood Village (CO): Thomson Reuters Inc. 2020.
4. Information for clinicians on therapeutic options for COVID-19 patients. Centers for Disease Control and Prevention. 2020.
5. Gautret P, Lagier J, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *International Journal of Antimicrobial Agents.* 2020.
6. Cortegiani A, Ingoglia G, Ippolito M, et al. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. *J Crit Care*. 2020;S0883-9441(20):30390-7.
7. Liu J, Cao R, Xu M, et al. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. *Cell Discovery.* 2020;6(16):1-4.
8. Lu H. Efficacy and safety of hydroxychloroquine for treatment of pneumonia caused by 2019-nCoV (HC-nCoV): phase 3 clinical trial. Shanghai Public Health Clinical Center. 2020. NCT04261517.
9. Kim SH. Comparison of lopinavir/ritonavir or hydroxychloroquine in patients with mild coronavirus disease (COVID-19): phase 2 clinical trial. Asan Medical Center. 2020. NCT04307693.
10. Banner Health Newsroom. Banner Health experts warn against self-medicating to prevent or treat COVID-19. http://bannerhealth.mediaroom.com/chloroquinephosphate