Brace for Chloroquine Poisonings Because of the Coronavirus Pandemic

BY LEON GUSSOW, MD

President Trump voiced enthusiasm in a March 19 press conference for using the drug chloroquine against the coronavirus, saying, “It’s been around a long time, so if things don’t go well, we know it won’t kill anyone.”

The antimalarial drug chloroquine has indeed been around for a long time, almost a century. It was discovered at Bayer Laboratories in Germany in 1934, where it was called Resochin, but it was not immediately introduced into clinical use because it was thought to be too toxic for human consumption. In retrospect, this failure to deploy the drug against malaria quickly was considered an enormous blunder. U.S. clinical studies carried out during World War II clearly demonstrated that the drug was a valuable anti-malaria agent, and it was approved for clinical use in 1947.

Today, chloroquine is also commonly used for treating rheumatoid arthritis and lupus erythematosus, but it is far from a safe drug. In fact, it is often included on the list of drugs that can kill a toddler in a single dose or pill. Its therapeutic index is narrow, which means that the space between the therapeutic dose and the potentially lethal dose is quite small.

To be sure, there is a small amount of (so far very) anecdotal evidence from China and France suggesting chloroquine might have some effect against the coronavirus, and a large clinical trial addressing this question is scheduled to start in New York State at the end of March. But with all the talk on social media and in presidential news conferences that chloroquine might be a magic bullet against the coronavirus, it’s inevitable that some individuals have started hoarding and self-treating without medical supervision, using lord knows what doses.

The New York Times already reported a run on the drug at local pharmacies. An Arizona man died within days of the president’s press conference after ingesting a home aquarium additive containing chloroquine phosphate thinking it would protect him against the coronavirus. His wife, who drank the same solution, recovered. She reported that their symptoms—dizziness, vomiting, and respiratory difficulties—began 30 minutes after exposure.

Now seems as good a time as any to review some key things to know about chloroquine and its toxicity. We should be prepared to see more cases.

Basic Pharmacology: Chloroquine is readily and rapidly absorbed from the GI tract, leading to a transient peak blood level shortly after ingestion. After the peak, the drug is quickly distributed to tissues in the heart, lungs, and other organs, as well as to erythrocytes. The volume of distribution is more than 100 L/kg (huge!), which means that little remains in the central blood compartment after the early peak.

In the heart, chloroquine blocks sodium and potassium channels, leading to prolongation of QRS and QT intervals, predisposing those who take the drug to ventricular tachycardia and other life-threatening cardiac arrhythmias. Chloroquine poisoning also causes severe hypokalemia, also predisposing those who take the drug to arrhythmias. This hypokalemia does not represent a total body potassium deficit but rather sequestration of the ion in cells. Chloroquine is also a myocardial depressant and a vasodilator.

Clinical Presentation: Onset of severe chloroquine toxicity can occur suddenly, usually within an hour or two of ingestion. Hypotension, seizures, respiratory compromise, and cardiovascular collapse can be precipitous after overdose.

Markers of Potential Lethal Toxicity: The reported potential lethal dose of chloroquine is 30-50 mg/kg, which means that ingestion of a single 250 mg or 500 mg tablet can be fatal for a toddler. Ingestion of more than 5 g, a systolic blood pressure higher than 80 mm Hg, a QRS greater than 120 msec, and significant hypokalemia in adults are all poor prognostic indicators.

Treatment: As with all cases of toxic ingestions, potential treatment modalities include supportive care, gastroin-
testinal decontamination, enhanced elimination (if possible), and specific antidotes.  

Supportive care: This always starts with the ABCs—secure the airway, ensure adequate ventilation and oxygenation, and support circulation with IV access, cardiac monitoring, fluids, and vasopressors as needed. Seizure activity can be treated initially with benzodiazepines.

Poison-induced widening of the QRS interval is often treated with sodium bicarbonate, but physicians must be careful because bicarb can further decrease already dangerously low potassium levels. Likewise, hypokalemia in chloroquine poisoning usually does not result from true deficit, and overly aggressive potassium replacement can lead to dangerous hyperkalemia. Levels should be checked frequently if the hypokalemia is severe enough to require potassium replacement.

Gastrointestinal decontamination: Gastric lavage has no proven efficacy in these cases, and it would probably delay or interfere with aggressive supportive care. A small study found that giving 25 g activated charcoal to three volunteers reduced the absorption of chloroquine by up to 95 percent, but it is not clear if this finding has any clinical relevance because the charcoal was administered within five minutes of ingestion and the amount of chloroquine (500 mg) was far below the usual lethal adult dose. Again, supportive measures should take priority.

Enhanced elimination: Chloroquine has an enormous volume of distribution and rapidly distributes out of the central blood compartment, so there is no evidence that hemodialysis could be initiated in time to be beneficial.

Specific treatment: A prospective French study looked at patients who had ingested more than 5 g chloroquine, comparing those treated using an experimental regimen with historical controls. (N Engl J Med. 1988;318[1]:1.) The experimental protocol included immediate intubation (in the field by a mobile medical unit) plus high-dose epinephrine and high-dose diazepam. Survival to hospital discharge was markedly greater in the experimental group (91%) than in the controls (9%).

Hydroxychloroquine tends to produce less severe overdoses than chloroquine, but the presentation and basic management are similar.

Unfortunately, poison control centers in the United States and worldwide will probably be getting much more experience with chloroquine poisoning in the coming months than we’ve had in the past, and that will probably change treatment protocols. As always with potentially severe toxic exposures, the key interventions are aggressive basic supportive care and contacting the local poison center for further recommendations.

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