ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

Oleandrin and Other Cardioactive Steroids

Recently, oleandrin has been suggested for the treatment or prevention of COVID-19 without any evidence. Oleandrin, one of multiple cardioactive steroid(s) (CAS), is derived from the *Nerium oleander* plant. Although use of CAS date back to the ancient Egyptians, the only therapeutically used CAS is digoxin from the foxglove plant (*Digitalis spp*). There are numerous CAS including thevetin from yellow oleander (*Thevetia peruviana*), convallatoxin from lily of the valley (*Convallaria majalis*), along with dogbane, red squill, and the bufadienolides from the secretions of *Bufo* toads. Poisoning from *N. oleander* has resulted in a mortality ranging from 3.1 – 10.9%, and ingestion of 5 – 15 leaves has been fatal *(JAMA 1982;247:1596–1597; Toxicon 2010;1;56(3):273-81)*. Generally, most CAS including oleander are not available outside of their natural plant forms or homeopathic products. Sometimes these are brewed into teas, concentrating the CAS.

CAS inhibit the Na^+/K^+–ATPase pump, increasing intracellular Ca^{++}. Increased intracellular Ca^{++} induces Ca^{++} release of from the sarcoplasmic reticulum, increasing inotropy *(Pharmacol 2005;25,35–52).* CAS also shift K^+ extracellularly, increase vagal tone, and decrease conduction through the sinoatrial and atrioventricular nodes. This causes numerous EKG abnormalities, but what is most often seen are increased automaticity, ST scooping (i.e. Salvador Dali's mustache), and an increased PR interval.

Following acute ingestion, patients will present with gastrointestinal symptoms such as nausea or vomiting (which may preclude use of activated charcoal); also hyperkalemia ($K^+ > 5.0$ mEq/L) which can be a marker of severe toxicity. Serum $K^+ > 5.5$ mEq/L has been associated with 100% mortality in acute digoxin ingestion. In chronic ingestion, the symptoms are more vague: abdominal pain, weight loss, headache, and visual disturbances including yellow halos *(Toxicon 2010;56(3):273-81).* Patients can develop significant hypotension, bradycardia, and dysrhythmias with acute or chronic poisoning.

The management of CAS poisoning is supportive for most cases. Serum digoxin levels can be obtained, but the results need to be interpreted with caution. The test is specific for digoxin; therefore, a positive level may indicate the presence of some CAS due to cross reactivity with the assay, but the number itself is not correlated with toxicity. Additionally, patients with certain diseases with increased inotropic need (ex. heart failure) may produce endogenous digoxin-like immunoreactive substances which can also interfere *(Crit Rev Clin Lab Sci 1986;23:177–200)*. This principle also applies to the use of digoxin immune Fab (DigiFab®). Digoxin Fab antibodies bind circulating digoxin, removing it from the site of toxicity, but it is not specific for other CAS. Therefore, if someone is acutely ill with a CAS other than digoxin, the recommended dosing calculation for digoxin immune Fab does not apply; giving a larger empiric dose should be considered. In a trial of digoxin immune Fab for oleander poisoning, a dose of 30 vials was found to be most effective, however a newer study suggests a titrated approach *(Lancet 2000;18;355(9208):967-72; Clin Toxicol. 2018;56(7):678–680*).

In summary, oleandrin and CAS toxicity can be severe with hypotension, bradycardia, and dysrhythmias. It is important to not rely on the level for most cases and instead treat the patient with digoxin immune Fab if they have significant symptoms (dysrhythmias, hyperkalemia) with a history suggestive of CAS ingestion.

Faisal Syed Minhaj, Pharm.D.
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Did you know?

The three largest toxicology societies have put out a joint statement addressing Oleandrin for COVID-19

The American College of Medical Toxicology, the American Academy of Clinical Toxicology, and the American Association of Poison Control Centers issued a position statement on August 20, 2020 that recommends "against the use of oleandrin outside of rigorous, medically-supervised clinical research with regulatory oversight". They go on to "implore consumers to not rush to use an untested remedy with potentially life-threatening toxicity". Read the full statement here: *https://www.acmt.net/_Library/Documents/08_20_20_Oleandrin_Toxicity.pdf*

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