



# TOXTALKS

A BULLETIN FOR HEALTHCARE PROFESSIONALS WHO MANAGE POISONED PATIENTS

Blue Ridge Poison Center

University of Virginia Health

March 2022

## CHANGING OUR PERCEPTION OF DIPHENHYDRAMINE

### Case report:

A 57 year old female presents to the Emergency Department (ED) after ingesting 3 bottles of Motrin PM (ibuprofen with diphenhydramine). EMS reports that there were no other drugs or medications found on scene. The patient is not on any prescription medications. She has a 45 second seizure prehospital and arrives to the ED unresponsive to sternal rub. Vital signs show HR 123, BP 80/50, RR 16, SpO2 100%, 98.6 degrees F. On exam the patient is somnolent and not arousable to sternal rub, has dry axilla and flushed skin, dilated pupils, and exhibits no hyperreflexia or ankle clonus. She is intubated and started on a norepinephrine infusion. An EKG shows a wide complex tachycardia with a QRS interval of 130 ms and a Qtc of 600 ms. She is given 100 mEq of sodium bicarb and 2 gm of magnesium. Her Qtc is unchanged but her QRS narrows to 100 ms and her norepinephrine dosing requirement decreases. She is started on a sodium bicarbonate infusion and admitted to the ICU. Labs are unremarkable. The patient becomes more alert over the next 36 hours and is extubated. Serial EKGs show an improvement of the intervals with a QRS of 80 ms and a Qtc of 460 ms. Norepinephrine no longer required and the sodium bicarb drip is discontinued. With resolution of clinical effects, the patient is transferred to psychiatric unit for further care.

### The dangers of diphenhydramine

Diphenhydramine is a widely used over the counter allergy medication. The most common brand name is Benadryl though it is also marketed as a sleep aid under the name ZzzQuil or in combination products such as Tylenol PM

[Next page]

## NEWS AND NOTES:



Welcome to Katerina Deasy, BSN, a new Poison Information Specialist at the BRPC! Ms. Deasy received her

nursing degree from VCU. She brings a wealth of experience caring for ICU patients at her former job with Mary Washington Hospital in Fredericksburg, VA. She is one of five children: all "air force brats," says Deasy.

*Did you know?* Only licensed nurses and pharmacists may be hired to become Poison Information Specialists (SPI) at U.S. poison centers. Upon hire, new SPIs must undergo a 6 months' orientation process and 2 years of on-the-job training in managing toxic exposures of all kinds. Then they must pass a stringent national certification exam.

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or Motrin PM. Over the counter medications may be thought of as safe by consumers because no prescription is required to obtain them. This perception is misleading in the case of diphenhydramine as it shares a similar chemical structure and thus many mechanisms of action with tricyclic antidepressants (TCAs), which are notoriously dangerous in overdose.

TCAs are not prescribed as widely as they once were in part due to their dangers in overdose. Unfortunately, because diphenhydramine is easy to purchase over the counter, it is easy to abuse. Intentional overdoses, misuse and abuse of diphenhydramine reported to US Poison Centers has increased since 2005 according to a recent article. In 2020, the Benadryl Challenge emerged on TikTok, a social media platform, and encouraged teens to take Benadryl until they started hallucinating. Because hallucinations do not occur in isolation, teens were experiencing other symptoms of toxicity and reports of hospitalizations and one death as a result of the Benadryl Challenge reached the news. The FDA issued a warning about the dangers of diphenhydramine in September of 2020 in response to these reports but the misuse continues to be a concern today.

### **Diphenhydramine mechanism of action of and symptoms of toxicity**

Diphenhydramine is commonly known to be a first generation antihistamine and an anticholinergic agent, however it also works to block cardiac fast sodium channels and potassium efflux channels which cause EKG changes and potentially life threatening cardiac toxicity. Table 1 illustrates the fact that diphenhydramine shares four of the seven TCA mechanisms of action and can therefore cause similar symptoms in overdose.

**Symptoms of diphenhydramine in overdose** can include CNS depression, agitation, delirium, hallucinations, picking behavior, mumbling speech, mydriasis, flushed dry skin, hyperthermia, tachycardia and seizures. The cardiac sodium channel blockade and corresponding wide QRS can lead to decreased inotropy and hypotension. The prolonged Qtc interval can lead to torsade de pointes, however this is less common due to the protective effect of the tachycardia.

The severity of symptoms is dose dependent with moderate symptoms including EKG changes, tachycardia, agitation, and confusion occurring with ingestions > 0.3 g. Seizure risk is significantly increased with ingestions > 1.5 g.

[Next page]

**Table 1: Comparison of the mechanisms of action of tricyclic antidepressants vs diphenhydramine and corresponding symptoms in overdose**

Mechanism of action	Tricyclic antidepressant	Diphenhydramine	Symptoms
Sodium channel blocker	+	+	Wide QRS
Potassium efflux blocker	+	+	Prolonged Qtc
Anticholinergic	+	+	Anticholinergic toxidrome
Antihistamine	+	+	CNS depression, seizures
GABA antagonist	+	-	Seizures
Biogenic amine reuptake inhibitor	+	-	Hypotension
Alpha 1 antagonist	+	-	Hypotension

#### **Treatment of diphenhydramine overdose**

Treatment of diphenhydramine toxicity depends on the symptoms present. Seizures should be treated with benzodiazepines. EKG changes are treated similarly to TCA toxicity, with sodium bicarbonate for a prolonged QRS and magnesium for a prolonged QTc. Other treatments, such as physostigmine, may be considered in select cases. Please call the Blue Ridge Poison Center to discuss management of diphenhydramine exposures.

Resources available upon request.

The Blue Ridge Poison Center receives funding from University of Virginia Health, the Virginia Department of Health, and the U.S. Health Resources Services Administration (HRSA). We are accredited by the American Association of Poison Control Centers. We've been proudly serving the Commonwealth since 1978.

Poison safety tips, free materials, & more:

