

Massive Atropine Eye Drop Ingestion Treated with High-Dose Physostigmine to Avoid Intubation

Samuel J. Stellpflug, MD*†

Jon B. Cole, MD*†

Brian A. Isaacson, MD‡

Christian P. Lintner, DBAT†

Elisabeth F. Bilden, MD†

* Regions Hospital, Department of Emergency Medicine, Toxicology Education and Clinical Service, St Paul, Minnesota

† Hennepin Regional Poison Center, Minneapolis, Minnesota

‡ Fairview Ridges Medical Center, Department of Emergency Medicine, Burnsville, Minnesota

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Case: A 34-year-old male presented after ingesting 150 mg of atropine. He had altered mental status, sinus tachycardia, dry mucosa, flushed skin, and hyperthermia. Sequential doses of physostigmine, totaling 14 mg, were successful in reversing antimuscarinic toxicity and prevented the need to perform airway control with endotracheal intubation. At completion of treatment, heart rate and mental status had improved, and intubation was never performed.

Discussion: Atropine causes anticholinergic toxicity; physostigmine reverses this by inhibiting acetylcholinesterase. Atropine eye drop ingestions are rare. The 14 mg of physostigmine administered is much higher than typical dosing. It is likely the physostigmine prevented intubation. Atropine eye drops can be dangerous, and physostigmine should be considered in treatment. [West J Emerg Med. 2012;13(1):77–79.]

INTRODUCTION

Atropine, or hyoscyamine, is an alkaloid used commonly for its antimuscarinic properties.¹ It acts as a competitive antagonist of acetylcholine at muscarinic receptors. It can be administered by various routes, including the eye drop formulation of atropine sulfate, used to induce cycloplegia and mydriasis.² In overdose, atropine can cause tachycardia, agitation, delirium, dilated pupils, dry mucous membranes, dry skin, and hypoactive bowel sounds. These phenomena have been described even with attempted therapeutic ophthalmic use.^{1,3} Ingestion of as little as a few drops of atropine in eye drop formulation can cause anticholinergic, or more specifically antimuscarinic, toxicity.⁴ The antimuscarinic toxidrome results from blockade of the neurotransmitter acetylcholine at central and peripheral muscarinic receptors.⁵

Physostigmine is a carbamate that acts by reversibly inhibiting acetylcholinesterase. Unlike quaternary amine acetylcholinesterase inhibitors (such as neostigmine) that treat peripheral manifestations of the antimuscarinic toxidrome, physostigmine is a tertiary amine, and thus is able to cross the

blood-brain barrier to treat both central (eg, agitation and delirium) and peripheral (eg, tachycardia) antimuscarinic manifestations.⁵ The use of physostigmine began as early as the 19th century for its ability to reverse the signs and symptoms of anticholinergic poisonings. Its popularity grew in the 1960s and 1970s as a general antidote and diagnostic tool for altered mental status.⁶ A case series published in 1980 illustrated 2 cases of patients who developed asystolic cardiac arrests in the context of tricyclic antidepressant overdose where treatment included physostigmine.⁷ The frequency of use of this antidote declined after that report. However, recent literature has tempered some of the concern about the deleterious effects of physostigmine, and its use has again become more frequent.^{6,8} The usual dose of physostigmine is 0.5 to 2 mg administered by slow intravenous (IV) push, with repeat doses administered every 15 to 40 minutes as necessary.⁹ It is unusual for doses in the emergency department to exceed 2 to 4 mg.

We describe an adult male with a massive ingestion of atropine eye drops treated successfully with 11 mg IV physostigmine in the emergency department. Successful

treatment in this case is defined as improvement of altered mental status and avoidance of need for intubation.

CASE REPORT

A 34-year-old male presented to an urgent care center, where he collapsed on arrival in the triage area, per providers in that department. He stated that he had emptied a full bottle of atropine eye drop solution into a glass of water and ingested it in an attempt to harm himself. The atropine concentration was 10 mg/mL, making for a total ingestion of 150 mg. On initial presentation, he had altered mental status with waxing and waning coherence, and when awake, he was very combative. He was also tachycardic with a heart rate (HR) of 125 beats per minute. A fingerstick glucose was normal. He was given 2 mg IV lorazepam, 4 mg IV ondansetron, 50 gm oral activated charcoal, and quickly transferred to a larger local hospital for further care.

In the emergency department at the accepting facility, the patient continued to have altered mental status, varying between severe sedation and uncontrolled agitation. His HR was 150 beats per minute, blood pressure (BP) 150/90 mmHg, respiratory rate 24 breaths per minute, and oxygen saturation 95% on room air. He had flushed skin, dry oral mucosa, nonreactive mydriasis, and a rectal temperature of 100.2°F. He showed no signs of trauma and had a nonfocal neurologic examination other than the gross altered mental status. The remainder of his physical exam was unremarkable. Electrocardiogram revealed sinus tachycardia and no interval or segment abnormalities.

Due to the intermittent somnolence and uncontrolled agitation, the emergency physicians at the accepting facility were concerned for the patient's ability to protect his airway enough to maintain oxygenation and ventilation. This, in combination with the recently administered charcoal and the possibility of emesis with subsequent aspiration, was enough cause for them to move towards rapid sequence induction (RSI) and endotracheal intubation. While preparing for the intubation, a medical toxicologist was consulted by the treating physicians. In an attempt to avoid the morbidity of the RSI, intubation, sedation, and mechanical ventilation, the decision was made to administer physostigmine to reverse the anticholinergic effects of the atropine.

Over the subsequent 75 minutes, physostigmine was titrated in 1 mg increments, each given over 3 to 5 minutes to a total dose of 11 mg. There was minimal change with the initial few doses, but after the fifth dose had been administered each 1 mg dose improved the patient's mental status along with normalizing the heart rate from the tachycardia listed above. Each of these signs would slowly worsen again over the ensuing 5 to 15 minutes, necessitating another dose. At the completion of treatment in the emergency department, the patient's HR had declined into the 90s beats per minute, and BP to 125/80 mmHg. His mental status was normalizing to the

point where he was relatively calm and could provide a little bit of subjective history.

Laboratory evaluation at the second hospital included a negative serum ethanol, negative acetaminophen, normal basic metabolic panel, normal complete blood count, and negative urine drugs of abuse immunoassay for amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, opiates, and phencyclidine. A serum atropine level later returned at 240 ng/mL (this was performed using the initial blood draw at the accepting facility).

He was admitted to the intensive care unit (ICU) for further observation and treatment. During the night in the ICU, he required 3 additional 1 mg doses of physostigmine for agitation that recurred. Endotracheal intubation was never performed. The remainder of the medical portion of his hospital stay was uneventful.

DISCUSSION

Atropine ingestions are common. In 2008, poison centers received 1,040 calls regarding plants containing anticholinergic toxins and 435 calls regarding atropine or diphenoxylate containing antidiarrheal medications.¹⁰ Ophthalmic preparation exposures are also a common poison center call with 3,481 calls occurring in 2008.¹⁰ Despite this, a paucity of atropine eye drop ingestion cases exist in the literature.

Atropine toxicity and lethality are not predictable by dose. Fatalities have been reported with exposures of less than 100 mg, and survival has been described with doses greater than 1 g orally.¹ The amount of atropine ingested by the patient in the case presented above falls into this potentially lethal range. To put the serum level of 240 ng/mL into perspective, an adult patient with a reported 1-g ingestion of atropine had a serum level of 129 ng/mL.¹¹ A study of 248 cases of accidental injections with personal autoinjectors demonstrated levels of 7.5 to 69 ng/mL.¹²

Making this case more remarkable was the liberal use of physostigmine. Standard dosing of physostigmine is 0.5 to 2 mg (0.02 mg/kg in children) given intravenously over at least 5 minutes with repeat dosing as needed 15 to 40 minutes later.⁹ When repeat dosing is needed, 4 mg total is usually sufficient.⁹ Our case is also unique in that physostigmine was administered in more rapid succession, and a total dose of 14 mg was required to control agitation and reverse delirium. The large amount of physostigmine required to treat this patient was likely due to the massive amount of atropine ingested, confirmed by the serum level of 240 ng/mL.

This case illustrates one of the most beneficial aspects of physostigmine use: the ability to control agitation and reverse delirium, thereby reducing the need for invasive interventions. Physostigmine administration, in this case, prevented the need for intubation, thus preventing patient exposure to the potential complications of this invasive procedure. This may be understated at first glance, but the morbidity of RSI, intubation, and mechanical ventilation are serious and well established.^{13,14}

It should be noted that along with potentially eliminating the need for intubation and potentially lowering the level of observation needed for a patient in the hospital, there are some concerns about the safety of the antidote itself. As mentioned earlier, much of this concern is likely unfounded and is based on a case series with questionable causality between the physostigmine and the negative outcomes.⁷ The most recent look in the literature on this topic is a retrospective case series including hundreds of patients that received the antidote. There was a seizure rate of less than 1% (all were self-limited) and there were no cardiac arrhythmias.¹⁵ The above benefits and risks of both physostigmine and intubation need to be weighed when deciding whether or not to use this treatment in this clinical scenario.

CONCLUSION

An oral overdose of atropine sulfate eye drops with severe altered mental status reversed with physostigmine is unique to the literature. Additionally, the dose of physostigmine administered was much higher than what is usually recommended or necessary. It is highly likely that the physostigmine administration prevented the potential morbidity of intubation and mechanical ventilation for the patient. Eye drops should be considered a potentially dangerous means of atropine exposure, and physostigmine should be considered in cases similar to this one with the goal of improving patient care and use of hospital resources. While the authors are not advocating a blanket use of high dose physostigmine for known antimuscarinic overdoses such as the one in this case, this treatment method may be considered if the likely benefit appears to outweigh a potential morbidity-inducing alternative.

Address for Correspondence: Samuel J. Stellpflug, MD, Regions Hospital, Department of Emergency Medicine, Toxicology Education and Clinical Service, 640 Jackson St, St Paul, MN 55101. E-mail: samuel.j.stellpflug@healthpartners.com.

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