ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

June 2016 | Poison Center Hotline: 1-800-222-1222

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

Physostigmine for Anticholinergic Toxicity

Numerous pharmaceutical agents (e.g. antihistamines, select antidepressants, antipsychotics) possess anticholinergic properties. Anticholinergic toxicity, due to overdose or therapeutic misadventure, can result in a range of clinical signs and symptoms. The central nervous system (CNS) effects may be the most pronounced and include garbled speech, hallucinations, delirium, agitation and infrequently, seizures.

Physostigmine is a tertiary acetylcholinesterase inhibitor that was recommended in the past to treat the anticholinergic toxicity associated with tricyclic antidepressant (TCA) overdose, but it is now considered contraindicated.[1] In Pentel et al, two patients with TCA overdose and prolonged QRS intervals (120 and 240 msec) without tachycardia developed bradycardia and asystole after receiving physostigmine.[2] These cases and similar reports have significantly decreased the use of physostigmine in the clinical setting of anticholinergic overdoses, but lately there has been a resurgence in its use.

The CNS effects of anticholinergic toxicity can usually be managed with benzodiazepines. However, when appropriately used, physostigmine can decrease or resolve agitation and delirium associated with anticholinergic toxicity better than benzodiazepines.[3] In isolated, pure anticholinergic toxicity (e.g. jimsonweed, diphenhydramine without QRS or QTc prolongation), reversal of CNS effects with physostigmine may lead to avoidance of diagnostic procedures such as lumbar puncture and head CT.

Mad as a Hatter

Did you know?

The classic anticholinergic toxidrome is due to the competitive antagonism of acetylcholine at central and peripheral muscarinic receptors.

Central anticholinergic effects include agitation, delirium, auditory and visual hallucinations. Peripheral effects also may be noted: dry mouth, mydriasis, blurred vision, absent bowel sounds, urinary retention, dry and flushed skin, tachycardia, and hyperthermia. Collectively, the anticholinergic toxidrome signs and symptoms are commonly described as "*mad as a hatter, red as a beet, hot as a hare, blind as a bat, dry as a bone, and the heart runs alone*".

Pre Administration Checklist

- *History of exposure to anticholinergic agent*
- *Confirm anticholinergic toxicity by physical exam (including bladder scan)*
- *Review contraindications (QRS > 100 ms, HR < 100 bpm, TCA overdose)*
- *Place patient on cardiac monitor, pulse oximeter*
- *Atropine at the bedside for possible cholinergic adverse effects*

Administration

- *Physostigmine formulation: 2mg/2mL vials*
- *Adult dose: 0.5-2 mg IV over 5 min; repeat every 5 min PRN (max total dose: 2 mg total)*
- *Pediatric dose: 0.02 mg/kg (max 0.5 mg/dose) IV over 5 min, repeat every 5 min PRN (max total dose: 2 mg)*
- ***Clinical goal**: reversal of agitation or delirium*
- *Total dose required for reversal of agitation or delirium may vary*

continued on page 2

Physostigmine for Anticholinergic Toxicity

Inappropriate or excessive administration of physostigmine can result in cholinergic toxicity, particularly bradycardia, bronchospasm and bronchorrhea, which can be life-threatening. Seizures have been reported with rapid administration.[4] The presence of significant cardiac sodium channel blockade toxicity (QRS > 100 msec and terminal R wave at aVR), seen with TCA, bupropion, phenothiazine, and occasionally diphenhydramine overdoses, is a contraindication.

Physostigmine still has a role in the clinical management of isolated pure anticholinergic toxicity.[3,5,6] Clinicians must consider the risks and benefits of physostigmine and identify the appropriate patients who may benefit from physostigmine administration.

Physostigmine Tips

- *Physostigmine has been used in a variety of anticholinergic intoxications due to agents such as atropine, scopolamine, cyclobenzaprine, antihistamines, benztropine, antipsychotics and jimsonweed.*
- *Give doses over at least 5 minutes and in 0.5 mg increments to reduce risk of adverse effects.*
- *Onset is within minutes and duration is 1-2 hours. If needed, judicious use of additional doses may be considered.*
- *If no clinical response is noted, consider a diagnosis other than anticholinergic toxicity.*

Gina L Stassinos, PharmD
Clinical Toxicology Fellow
Maryland Poison Center
University of Maryland School of Pharmacy

References

1. Burks J, Walker J, Rumack B et al. Tricyclic antidepressant poisoning. JAMA 1974;230:1405-1407.
2. Pentel P, Peterson CD. Asystole complicating physostigmine treatment in tricyclic antidepressant overdose. Ann Emerg Med 1980; 9:588–590.
3. Burns MJ, Linden CH, Graudins A et al. A comparison of physostigmine and benzodiazepines for the treatment of anticholinergic poisoning. Annals of Emergency Medicine 2000;35:374-381.
4. Newton RW: Physostigmine salicylate in the treatment of tricyclic antidepressant overdosage. JAMA 1975;231:941-943.
5. Watkins J, Schwarz E, Arroyo-Plasencia et al. The use of physostigmine by toxicologists in anticholinergic toxicity. J Med Toxicol 2015;11:179-184
6. Dart R, Borron S, Caravati E, et al. Expert consensus guidelines for stocking of antidotes in hospitals that provide emergency care. Ann Emerg Med 2009;54:386-394.e1.