Physostigmine is the Antidote for Anticholinergic Syndrome

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Recently, we read the observation by Walker et al. [1] published in the *Journal of Medical Toxicology* and commend the authors for their recognition of anticholinergic syndrome. However, we are distressed that a 13-year-old pediatric patient was treated with a novel drug without first having received the known antidote for anticholinergic delirium, physostigmine. The statement “the currently recommended therapies for anticholinergic toxidrome are largely supportive” is inaccurate. Physostigmine has been recommended by a consensus panel for hospitals providing emergency care for treatment of anticholinergic syndrome [2]. If there is an available antidote, the standard of care should never be “largely supportive.” Treating the underlying cause of patients’ symptoms, rather than simply managing clinical situations is central to the practice of medicine. Between 2003 and 2010, our center treated nearly 1200 patients with physostigmine, 80 % of whom experienced neurobehavioral improvement with appropriately dosed antidote [3]. Adverse effects were minimal and primarily consisted of short-lived peripheral cholinergic effects.

Physostigmine is available as an injection solution in 2 mg vials (\$8.21) available for use as packaged. Dexmedetomidine requires mixing in a controlled environment; according to Micromedex, “dilute 200 mcg (2 mL, \$65.28) with 48 ml of normal saline and then shake[n] gently to mix.” It is difficult to fathom that any pharmacy cannot readily provide physostigmine after its being ordered. The cost difference between dexmedetomidine and physostigmine is also significant.

Physostigmine was discovered over a century ago with its targeted clinical effects well-documented since that time [4]; to choose a much newer drug without an indication for anticholinergic toxidrome represents clinician-driven

experimentation. Was consent obtained from the parents before using this novel therapy? What would be the implications of an adverse event when the known antidote had not been used first?

For this patient, we would have recommended 0.02 mg/kg physostigmine (range 0.5–2 mg) over 2 min using peripheral intravenous access. At 8–10 min, we would have instructed the administering clinician to reassess the neurologic exam (we typically use Riker Sedation Analgesia Score [5] or ask the patient for presidents in reverse order before and after physostigmine (or other age/developmental marker)) as a simple way to assess change in cognition. If improvement is noted, we place an order for repeating physostigmine q1 h prn. The adverse effects of physostigmine are cholinergic in nature and occur 10–20 min after administration, or when CNS peak effect occurs [6]. In our experience, with the dosing as recommended above, this would amount to diaphoresis, emesis, diarrhea, and/or urinary incontinence [7]. With proper intermittent, weight-based dosing, more robust cholinergic effects of bronchorrhea and bradycardia are not observed. Seizures are rare, and often cannot be attributed to the antidote use [3]. Cholinergic symptoms would not be anticipated in such a case as the one described due to the classical history and physical findings. When they do emerge in the absence of improvement in mentation, central anticholinergia is ruled out, and the therapy should be abandoned. In such a circumstance, adjunctive treatments for managing an undifferentiated toxicologic delirium might then logically be considered.

References

1. Walker A, Delle Donne A, Douglas E, Spicer K, Pluim T. Novel use of dexmedetomidine for the treatment of anticholinergic toxidrome. *J Med Toxicol* 2014.

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2. Dart RC, Borron SW, Caravati EM, Cobaugh DJ, Curry SC, Falk JL, et al. Expert consensus guidelines for stocking of antidotes in hospitals that provide emergency care. *Ann Emerg Med* 2009;54:386–94 e1.
3. Rasimas JJ, Smolcic EE, Cressell A, Sachdeva K, Donovan JW. Bedside toxicologic experience with physostigmine and flumazenil. *Clinical Toxicology Abstract* 2010
4. Proudfoot A (2006) The early toxicology of physostigmine: a tale of beans, great men and egos. *Toxicol Rev* 25:99–138
5. Riker RR, Fraser GL (2001) Monitoring sedation, agitation, analgesia, neuromuscular blockade, and delirium in adult ICU patients. *Seminars in respiratory and critical care medicine* 22:189–98
6. Somani SM, Khaliq A (1987) Pharmacokinetics and pharmacodynamics of physostigmine in the rat after intravenous administration. *Drug metabolism and disposition: the biological fate of chemicals* 15:627–33
7. Walker WE, Levy RC, Hanenson IB (1976) Physostigmine—its use and abuse. *JACEP* 5:436–9