From: Ron Kirschner, MD, Medical Director

To: ALL HEALTH CARE PROFESSIONALS

Subject: Rivastigmine is an “Antidote” to the Physostigmine Shortage

Date: 6/29/21

* For over a decade, the incidence of diphenhydramine (DPH) ingestions reported to poison centers, both for self-harm and abuse, has been increasing (1), so you are likely to see more anticholinergic delirium.
* Treatment with a benzodiazepine is a reasonable first line therapy, since large DPH ingestions can be associated with seizures.
* More definitive treatment of anticholinergic delirium involves slow IV administration of the reversible cholinesterase inhibitor physostigmine (physo), but this is currently on nationwide shortage.
* The physo analogs neostigmine and pyridostigmine are quaternary amines with poor CNS penetration, so are unlikely to be effective in treating mental status changes.
* Hughes recently reported successful treatment of anticholinergic delirium with rivastigmine (2).
* Rivastigmine is a tertiary amine that readily enters the CNS. It is available as a 3 mg pill with peak absorption in 1 hour and duration of action ~10 h, but there is no IV formulation.
* A transdermal rivastigmine preparation is available, but absorption is slower (peak thought to be ~ 8 hours).
* In adults or adolescents with agitation thought due to anticholinergic toxicity, we recommend a parenteral benzodiazepine followed by consideration of oral rivastigmine 3 mg if able to take po. This dose could possibly be repeated in 60-90 minutes. Topical administration could be considered if unable to take po.
* After rivastigmine administration, consider 10-12 h observation for delirium recurrence.
* We encourage you to call and discuss your patients so that we can provide more case-specific individualized recommendations.

References

1. Nemanich A. Increased rates of diphenhydramine overdose, abuse, and misuse in the United States, 2005–2016. *Clin Toxicol* 2021 <https://doi.org/10.1080/15563650.2021.1892716>
2. Hughes AR. Letter in response to rivastigmine for the treatment of anticholinergic delirium. *Clin Toxicol* 2021 <https://doi.org/10.1080/15563650.2020.1869757>

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