ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

October 2023 Poison Center Hotline: 1-800-222-1222

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

Rivastigmine for Anticholinergic Delirium

As of February 2023, Akorn, the single-source manufacturer of physostigmine, has declared bankruptcy. While physostigmine has been on shortage prior to this announcement, physostigmine is not expected to be available in the future. Physostigmine is a reversible acetylcholinesterase inhibitor that has been used to manage central anticholinergic toxicity effects such as agitation, hallucinations, and delirium. Use of physostigmine in the past several decades has been controversial due to case reports of asystole in two patients who were exposed to tricyclic antidepressants (*Ann Emerg Med*. 1980;9(11):588-590); however, it has been shown to be safe and effective and have superior outcomes for the management of delirium compared to benzodiazepines alone (*Clin Toxicol*. 2019;57(1):50-55).

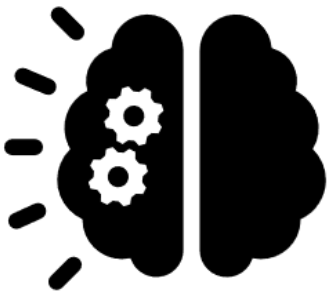
Shortage of physostigmine has driven investigations for alternatives to treat anticholinergic delirium. Rivastigmine has been a drug of interest because, like physostigmine, it is a tertiary amine that can cross the blood brain barrier, while quaternary amines within the same class (e.g., neostigmine and pyridostigmine) cannot. It is FDA approved to treat Alzheimer's disease, dementia, and Parkinson disease and is well tolerated in therapeutic use. It is available in oral capsules and 24-hour transdermal patches.

One Poison Center performed a retrospective review of patients with anticholinergic toxicity that were treated with rivastigmine. They described 30 patients who all received oral rivastigmine. Two patients received a transdermal rivastigmine patch in addition to oral doses, and two patients received oral rivastigmine after receiving doses of physostigmine. Anticholinergic symptoms improved in 20 patients, no change in 2 patients, and unclear benefit in 8 patients. Initial oral doses were 3 mg on average with an average duration of treatment with rivastigmine of 12.3 hours. Thirteen patients received more than one dose of rivastigmine. One patient had an episode of asymptomatic bradycardia that resolved spontaneously after removing the rivastigmine patch (*Clin Toxicol*. 61(2):22-23; 2023).

In patients with anticholinergic delirium, it may be difficult to administer an oral medication, so the patch may be more feasible. Rivastigmine may produce cholinergic adverse effects like nausea, vomiting, diarrhea, and bradycardia.

Data for rivastigmine are still limited so benzodiazepines are still recommended as a first-line treatment for hypertension, tachycardia, agitation, and seizures. Rivastigmine may be useful to manage central anticholinergic effects not controlled by benzodiazepines or if increasing doses of benzodiazepines may not be tolerated (e.g., due to sedation). Rivastigmine is not recommended at this time in patients who have overdosed on a tricyclic antidepressant or have a prolonged QRS interval due to theoretical concern for the development of arrhythmias in the setting of acetylcholinesterase inhibitors used to treat anticholinergic toxicity. Use of rivastigmine in anticholinergic toxicity is increasing and updates to recommendations are expected to continue as there is further clinical experience and more data are gathered.

For treatment recommendations for anticholinergic toxicity or any other poisoning, call your local Poison Center at 1-800-222-1222.



Did you know?

Multiple medicines have been affected by the recent bankruptcy.

British Anti-Lewisite (BAL) was originally made as an antidote to Lewisite, a chemical weapon made during World War II. It was later found to be effective for chelating lead. Akorn was also the single-source manufacturer for BAL which, like physostigmine, is not available at this time. Other chelators such as succimer and calcium disodium EDTA are still available. Consult your local Poison Center for information about antidote availability.

Victoria Macdonald, PharmD

Clinical Toxicology Fellow

@MPCToxTidbits