

MINNESOTA REGIONAL POISON CENTER

Guidance on Management of Physostigmine Shortage

Physostigmine, a reversible inhibitor of acetylcholinesterase, has historically been the antidote of choice for anticholinergic toxicity-associated delirium. A nationwide shortage of physostigmine calls for a closer look at potential alternative agents to use in addition to benzodiazepines for management of anticholinergic delirium:

Rivastigmine (Exelon)

- MOA: long-acting cholinesterase inhibitor
- Evidence:

Study	Dosing	Outcomes
Hughes, et al. Case Report (N=1)	Oral 3mg x3 over 75 min	RASS +3 to +1 at 2 hours after starting therapy
Van Kernebeek, et al. Case Report (N=1)	Oral 1.5mg BID x7 days	Rapid decline in agitation to normal within 24 hours of starting therapy
Sandia, et al. Case Report (N=6)	Transdermal Patch	Reduction in psychotic symptoms
Chiew, et al. Retrospective Review (N=50)	Transdermal Patch (N=22) Starting oral dose: 6 mg	Oral formulation appeared more effective than the patch
Lambson, et al. Retrospective Review (N=30)	Starting oral dose: 3 mg	Improvement in anticholinergic symptoms, no cholinergic adverse effects reported

- Dosing:
 - 3-6mg orally Q1h until resolution of CNS symptoms; maximum 12mg/24hr
 - Consider pharmacokinetic differences (see table below)
- MN Poison Center Recommendations for Indications:
 - Intubated anticholinergic patients to hopefully speed extubation
 - Anticholinergic patients who are awake but mildly agitated and are still able to take PO

Oral donepezil (Aricept)

- MOA: selective cholinesterase inhibitor in brain tissue & serum, without effects on heart & small intestine
- Evidence:

Study	Dosing	Outcomes
Noyan, et al. Case Report (N=1)	5mg orally daily x72hr	Dramatic improvement in mentation and verbal communication within 24hr

- Dosing Strategy: 5mg orally daily x 72hr
- MN Poison Center Recommendations for Indications:
 - Not recommended at this time

Comparison of Cholinesterase Inhibitors

	IV Physostigmine	Oral Rivastigmine	Transdermal Rivastigmine	Oral Donepezil
Usual Dose	0.5 - 2 mg IV over 5 mins Q10-30 min to response	1.5-6mg PO BID	9.5 – 13.3 mg/24-hour patch	5-10mg PO daily
Peak	2 minutes	1 hour	8-16 hours	3 hours
Duration	45 – 60 minutes	10 hours	Sustained over patch application, 3.4 hours once removed	T ½ ~72 hours
Efficacy	+++++	++	+	+
Safety Monitoring	Bradycardia, ventricular fibrillation, seizures	Bradycardia, syncope, N/V, abdominal pain	Bradycardia, syncope, N/V, abdominal pain	Bradycardia, syncope, N/V

References

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2. Van Kernebeek MW, Ghesquiere M, Vanderbruggen N, Verhoeven E, Hubloue I, Crunelle CL. Rivastigmine for the treatment of anticholinergic delirium following severe procyclidine intoxication. *Clin Toxicol (Phila)*. 2021;59(5):447-448.
3. Noyan MA, Elbi H, Aksu H. Donepezil for anticholinergic drug intoxication: a case report. *Prog Neuropsychopharmacol Biol Psychiatry*. 2003;27(5):885-887.
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