



## Pharmacy Friday



## Physostigmine for Anticholinergic Toxidrome

1. Medications that contain anticholinergic effects are abundant in prescription and over the counter (OTCs)
2. Their ease of access to anticholinergic drugs and lack of concern by most patients for serious adverse effects make them potentially dangerous drugs
3. Anticholinergic toxicity can lead to a complex toxidrome characterized in the CNS by hallucinations, delirium, agitation and seizures
4. Non-CNS effects can include dry mouth, mydriasis, blurred vision, decreased/absent bowel sounds, urinary retention, dry and flushed skin, tachycardia, and hyperthermia.
5. The earliest documented use of physostigmine to reverse anticholinergic delirium was in 1864 by Kleinwachter who treated prisoners who had mistakenly consumed atropine
6. Case reports from the 1980-90s showed an association between physostigmine use and worsened patient outcomes, which has led to a drastic decline in its use for anticholinergic toxicity
7. These case reports involved physostigmine administration in the setting of TCA toxicity with prolonged QRS have been the most common situation which displayed negatives outcomes and led to apprehensiveness to use physostigmine

Properties	Physostigmine
Dose	<ul style="list-style-type: none"><li>• IV: 0.5 to 2 mg</li><li>• Repeat every 5 min PRN to reverse agitation</li><li>• 2 mg cumulative MAX</li></ul>
Administration	<ul style="list-style-type: none"><li>• Slow IV Push ~3-5 min</li></ul>
Formulation	<ul style="list-style-type: none"><li>• IV: 2mg/2mL vials</li></ul>
PK/PD	<ul style="list-style-type: none"><li>• Onset ~1 min</li><li>• Duration 30-60 mins</li></ul>
Adverse Effect	<ul style="list-style-type: none"><li>• Bradycardia</li><li>• Bronchospasm</li><li>• Bronchorrhea</li><li>• Diaphoresis</li><li>• Muscle fasciculation</li></ul>
Warnings	<ul style="list-style-type: none"><li>• Convulsions may occur with overly rapid IV administration</li></ul>
Contraindication	<ul style="list-style-type: none"><li>• QRS &gt; 100 msec</li><li>• TCA toxicity</li></ul>

Author, Year	Design/ sample size	Offending Agents causing Toxicity	Outcome
<b>Boley SP, 2018</b>	Prospective observational analysis n=154	Antihistamines (68%), analgesics (19%), and antipsychotics (19%)	Delirium control in 79% of patients who received physostigmine versus 36% of those who did not (OR 6.6)  No difference in adverse events with physostigmine vs standard of care
<b>Arenas, 2018</b>	Retrospective cohort study n=191	Anticholinergic plant (35.1%), Diphenhydramine (29.3%), other antihistamines (7.3%), TCAs (1.6%), other agents (26.7%)	Patients exposed to non-diphenhydramine antihistamines, antipsychotics, and tricyclic antidepressants had 100% response to physostigmine  74.3% treated with physostigmine alone  One dose was effective in reversing or improving anticholinergic delirium in a majority (73.8%) of the patients
<b>Rosenbaum, 2010</b>	Retrospective study n=45	Undefined anticholinergic agents	31% received repeat dosing of physostigmine  45% of patient were d/c from ED  Patients are not likely to require repeat physostigmine dosing more than 6.5 h from their first dose
<b>Weizberg, 2006</b>	Case series n=2	Olanzapine overdose	1.5-2 mg of physostigmine led to regaining full consciousness
<b>Burns, 2000</b>	Retrospective study n=52	Undefined anticholinergic agents	Physostigmine controlled agitation and reversed delirium in 96% and 87% of patients vs Benzodiazepines controlled agitation in 24% and were ineffective in reversing delirium  Physostigmine had lower incidence of complications and shorter time to recovery
<b>Pentel, 1980</b>	Case Series n=2	TCA with prolonged QRS intervals (120 and 240 msec)	Both patients developed bradycardia and asystole after receiving physostigmine

**Conclusion:** Physostigmine at 0.5-2 mg is highly effective at reversing agitation and delirium in patients with anticholinergic toxidrome. Minimal adverse effects have been reported as long as there is no report of TCA ingestion and QRS < 100 msec. However, patient's delirium will return once the physostigmine wears off, so repeat dosing may be needed.

### References

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