

Physostigmine (Antilirium[®])

Hundreds of commonly used prescription and over-the-counter medications and numerous plants have unintentional or advantageous anticholinergic effects, and when not used with caution, anticholinergic poisoning is likely. It is important to quickly recognize the clinical presentation of anticholinergic poisoning in order to choose the most appropriate care. The anticholinergic toxidrome includes dry skin, flushing, hyperthermia, thirst, dry mouth, mydriasis, tachycardia, urinary retention, decreased bowel sounds, and delirium/hallucinations.

Mechanism/Indications: Physostigmine is used as an antidote to reverse the toxicity of anticholinergic effects. Its primary mechanism of action is to reversibly inhibit acetylcholinesterase by competitively binding to the enzyme in order to prevent it from degrading acetylcholine. This temporary inhibition of acetylcholinesterase thereby temporarily boosts acetylcholine levels to overcome the anticholinergic toxicity. Structurally, physostigmine is a tertiary amine and is able to cross the blood-brain barrier to reverse both central and peripheral acetylcholine antagonism. Other stigmine class products are available (neostigmine, pyridostigmine, etc.); however, they are not indicated for anticholinergic toxicity due to poor CNS penetration. Although physostigmine is not intended for use as a first-line agent for anticholinergic toxicity and there are significant contraindications to be aware of, it is indicated for treatment of anticholinergic toxicity particularly when patients manifest both peripheral toxicity and moderate to severe agitation/delirium.

Adverse Effects/Contraindications: In addition to hypersensitivity to the drug or any component of the formulation, contraindications include GI/GU obstruction, diabetes mellitus, gangrene, severe asthma or COPD, severe cardiovascular disease or arrhythmias, overdose of any agent known to cause QRS prolongation (e.g. cyclic antidepressants, procainamide, disopyramide, quinine) and overdose of other cholinesterase inhibitors (e.g. neostigmine, pyridostigmine, edrophonium, some pesticides). The patient should be evaluated with an ECG and should have a normal QRS interval in order to minimize adverse effects. Excessive dosing of physostigmine will produce cholinergic toxicity. This includes diaphoresis, diarrhea, excessive salivation, bradycardia, vomiting, miosis, cardiac arrhythmias, and bronchospasm. Atropine at ½ the physostigmine dose should be at the bedside to reverse cholinergic symptoms should they occur. Seizures may occur if physostigmine is infused too quickly.

Dosing: In adults (>12 y.o.), the recommended dose of physostigmine is 1.0-2.0 mg. In children (≤ 12 y.o.) the recommendation is 0.02 mg/kg/dose (max single dose 0.5 mg). The drug should be given slowly over 3-5 mins via IV push. The dose can be repeated every 5-15 minutes until normal mental status is achieved or a maximum of 4 mg is administered in adults or 2 mg is administered in pediatrics.

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For more on physostigmine:

- Burns MJ, et al. A comparison of physostigmine and benzodiazepines for the treatment of anticholinergic poisoning. *Ann Emerg Med* 2000; 35:374.
- O'Donnell, SJ et al. Safety of Physostigmine Use for Anticholinergic Toxicity. *J Toxicol Clin Toxicol*. 2002. 40(5):684.