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Rivastigmine for the treatment of anticholinergic delirium

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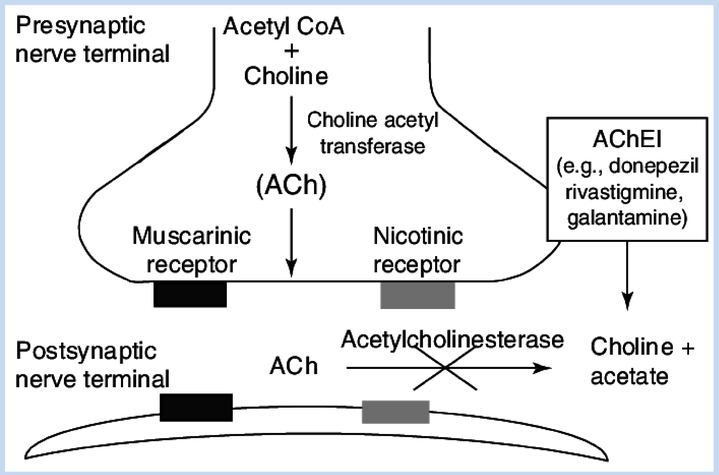
KEY WORDS
Anticholinergic delirium, rivastigmine, cholinesterase-inhibitor, physostigmine.

CASE REPORT

Massive procyclidine intoxication.
Anticholinergic toxidrome. Supportive treatment.
Agitated delirium in ICU.
Failure of standard therapy.
Ongoing anticholingergic delirium.
Start Rivastigmine 1,5mg twice daily.



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DISCUSSION

Anticholinergic drugs competitively inhibit binding of the neurotransmitter acetylcholine to muscarinic acetylcholine receptors, and are commonly referred to as antimuscarinic agents. These receptors are found on peripheral postganglionic cholinergic nerves in smooth muscle (intestinal, bronchial and cardiac), the secretory glands (salivary and sweath), the ciliary body of the eye, and the central nervous system (CNS). The expected clinical effects of these drugs are thus modulated through disturbances in the parasympathetic nervous system for the expected *peripheral effects*, and the brain for *central effects*. It is important to realize that these agents do not bind to nicotinic acetylcholine receptors, on the neuromuscular junction, unlike NMBA's(Neuro Muscular Blocking Agents). The clinical features of overdose are mostly remembered for its peripheral effects (red, dry, hot, blind, full), although a central symptomatology (delirium, hallucinations) is often, and sometimes uniquely, present. The central effects cause an agitated delirium that is characterized by restlessness, irritability, disorientation, confusion, agitation, auditory and visual hallucinations, and incoherent speech. Repetitive picking at the bed clothes or imaginary objects is also characteristic. Clinical presentation usually consists of both peripheral and central manifestations, but either of both can be absent. There is no specific or diagnostically relevant test for anticholinergic toxicity so diagnosis is solely based on clinical grounds.

Treatment of anticholinergic toxicity primarily includes observation, monitoring and supportive care. Despite its worldwide application over years, the use of *physostigmine* to reverse anticholinergic toxicity remains controversial. Physostigmine is a reversible acetylcholinerase inhibitor, that crosses the blood-brain-barrier. Acetylcholinesterase inhibition results in acetylcholine accumulation that reverses both central and peripheral anticholinergic effects. Its major adverse effects are dysrhythmias, profound bradycardia and seizures. Physostigmine is however broadly accepted as a treatment in cases of severe agitation and delirium, in patients not responsive to benzodiazepines, and with clear indications of anticholinergic toxicity.

From a pharmacological point of view, *central Ach-inhibitors* like rivastigmine, already commonly used but for different indications, seems to be a valuable alternative, and has been suggested in recent articles. It increases acetylcholine in the CNS through reversible inhibition of its hydrolysis by Acetylcholinesterase.

Rivastigmine has a rapid oral absorption, and a good penetration of the blood brain barrier. A single dose inhibits cholinesterase for approximately 10hours.

We considered rivastigmine an excellent choice for reversal of this massive single drug intoxication because of its long acting profile and its specificity for the central tissue, with presumed less peripheral toxicity.