Safety and Efficacy of Physostigmine: A 10-Year Retrospective Review

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Background
- Physostigmine, a reversible acetylcholinesterase inhibitor, is an effective antidote to reverse anti-muscarinic delirium.
- Safety of physostigmine administration came into question after 2 case reports of complications in the setting of tricyclic antidepressant poisoning.

Hypothesis
Physostigmine is a safe and effective antidote for the management of suspected anticholinergic agitated delirium.

Methods
Retrospective chart review of patients of all ages reported to CPCS who received physostigmine as an antidote to reverse anticholinergic delirium from 2002 – 2012.
- CPCS database was queried for all cases where 'physostigmine' was entered in the treatment field or reported in case notes.
- Data was reviewed by three separate reviewers.
- A fourth reviewer reviewed and adjudicated discrepancies.

Patient Information

<table>
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<tr>
<th>Gender</th>
<th>n (%)</th>
<th>Male</th>
<th>Female</th>
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<tr>
<td>71</td>
<td>37.1</td>
<td>120</td>
<td>62.9</td>
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| Age (years) | Average (range) | 25 (3–80) |

| Presenting Signs/Symptoms | n (%) | Tachycardia | 163 (85.3) | Agitated | 113 (59.1) | Mydriasis | 106 (55.0) | Advanced Mental Status | 95 (51.6) | Hallucinations | 97 (50.8) | Dry skin | 46 (25.7) | Hyperthermia (T > 38.0°C) | 31 (16.3) | Urinary Retention | 13 (6.8) | QTC prolongation | 8 (4.2) | QRS prolongation | 3 (1.6) | QRS and QTC prolongation | 1 (0.5) |

| Ingestion | n (%) | Anticholinergic Plant | 67 (35.1) | Diphenhydramine | 56 (29.3) | Unknown | 17 (8.9) | Antihistamine | 15 (7.9) | Combination products | 10 (5.2) | Other | 8 (4.2) | Other anticholinergic | 7 (3.6) | Muscle Relaxants | 4 (2.1) | Antipsychotics | 4 (2.1) | Tricyclic antidepressant | 3 (1.6) |

Table 1. Patient information including demographics, presenting signs and symptoms, and primary ingestion.

| Efficacy | n (%) | Clinical Response to Physostigmine | Improvement or normalization of mental status | 141 (73.8) | None | 30 (15.7) | Unknown | 26 (13.5) |

| Dose of physostigmine (mg) | n (%) | 0.25 – 0.5 | 64 (33.5) | 1 – 2 | 53 (27.7) | 2.1 – 4 | 5 (2.6) | 4 | 4 | Unknown | 66 (36.1) |

| Repeat Doses of physostigmine | n (%) | No repeat doses | 113 (59.1) | 1 repeat dose | 37 (19.4) | 2 repeat doses | 29 (15.2) | Unknown | 12 (6.3) |

Table 2. Improvement in signs or symptoms following physostigmine administration.

| Safety | n (%) | Adverse Events | None | 183 (96) | Vomiting | 3 (1.6) | EKG changes | 18 (1.8) | QRS prolongation | 2 (1.0) | PVCs | 1 (0.5) | Seizure | 2 (1.0) | Death | 1 (0.5) |

Table 3. Reported adverse events after receiving physostigmine.

Discussion
This retrospective review found few adverse events secondary to physostigmine administration.
Two reported seizures, one in the setting of a multi-drug ingestion, and in a patient with seizures reported prior to physostigmine administration.
One fatality in a patient who developed a wide complex tachycardia and experienced cardiac arrest 6 hours after physostigmine administration.

Conclusion
Physostigmine is a safe and effective antidote to treat anti-muscarinic delirium.

Limitations
- Retrospective study design.
- Information limited to patients and information reported to CPCS.
- Information ingestion history often based on patient report.
- Temporal relationships based upon report to CPCS.

References