The Use of Physostigmine by Toxicologists for Anticholinergic Toxicity

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Disclosures

No relevant financial disclosures
Anticholinergic Toxicity

In setting of overdose

Antihistamines

Tricyclic antidepressants

Antipsychotics

Botanicals
Physostigmine

Derived from Calabar Bean

Ordeal Beans to settle disputes

First Case Report for Atropine overdose in 1864
Physostigmine
The Good

Reversible cholinesterase inhibitor
Crosses blood brain barrier
Rapid onset
Duration 1-2 hours
Physostigmine

The Bad

Cholinergic Excess

Bradydysrhythmias

Concern for Seizures

 Likely repeated doses
Supporting Data

Rumack 1975: 707 cases treated with physostigmine

Micik 1976: A New Antidote

Hamilton 2000: Scopolamine in Heroin
Dissuading Data

1980: 2 Case reports

TCA with Physostigmine

Physostigmine vs Benzodiazepines

Burns et al, 2000

52 consecutive patients

Referred to Toxicologist

Anticholinergic agitation and delirium

Physostigmine vs Benzodiazepines

Physostigmine

Controlled agitation in 96%

Reversed Delirium in 87%

Physostigmine vs Benzodiazepines

Controlled agitation in 24%

Ineffective in reversing delirium

Physostigmine vs Benzodiazepines

Complications

- Rhabdomyolysis (5)
- Aspiration Pneumonia (2)
- Intubation (3)
- ETOH withdrawal (1)

- Rhabdomyolysis (4)
- Aspiration Pneumonia (4)
- Intubation (6)
- ETOH withdrawal (1)
- Delayed recovery (1)

Physostigmine vs Benzodiazepines

Summary

Better CNS stimulation reversal (94% v 24%)

Fewer complications (7% v 46%)

Clinical Questions

How often is physostigmine administered to patients with an anticholinergic toxidrome that are evaluated by a toxicologist?

Is there a correlation between adverse events and administration of physostigmine?
ToxIC Database

ACMT Toxicology Investigators Consortium

Network of Toxicologists from 44 institutions

Established in 2009 to promote research

Standardized form completed online by Toxicologists
ToxIC Data

January 1, 2012 - March 6, 2014

Anticholinergic Toxidrome

Treatment classified into 5 groups

Analyzed for Adverse Events
Toxic Data
815 Patients

- Physo only: 101
- Benzos only: 234
- Combination: 72
- Antipsychotics: 22
- None: 386

Physo Only: 29%
Benzos Only: 12%
Combination: 9%
Antipsychotics: 3%
None: 47%
Adverse Outcomes

Rhabdomyolysis Odds Ratios

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Physo Alone</td>
<td>2.19</td>
<td>0.1</td>
</tr>
<tr>
<td>Benzos Alone</td>
<td>2.84</td>
<td>0.01</td>
</tr>
<tr>
<td>Combination</td>
<td>7.02</td>
<td>0.03</td>
</tr>
<tr>
<td>Any Physo</td>
<td>0.39</td>
<td>0.01</td>
</tr>
<tr>
<td>Any Benzos</td>
<td>0.05</td>
<td>0.03</td>
</tr>
</tbody>
</table>

p-values for Rhabdomyolysis:
- Physo Alone: p=0.1
- Benzos Alone: p=0.03
- Combination: p=0.03
- Any Physo: p=0.01
- Any Benzos: p=0.03
Discussion

More likely to receive Benzodiazepines (28.7%) than Physostigmine (12.4%)
Discussion

Physostigmine

78% less likely to be intubated
Discussion

Benzodiazepines

1.8x more likely to require intubation

95% less likely to develop rhabdomyolysis
Limitations

Order of medications
Indication for medications
Did not analyze for central anticholinergic effects
Did not analyze for offending anticholinergic agent
ToxIC Case registry may not be representative of all centers
Information may be incomplete
Conclusions

Physostigmine may be underutilized

Physostigmine use was correlated with decrease in intubation
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Questions?
Sources


Suchard JR. Addressing Physostigmine’s Contraindication in Cyclic Antidepressant Ingestions. Journal of Emergency Medicine 2003; 25 (2) 185–191

