



IMPROVING POINT-OF-CARE DECISIONS

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March 25, 2008

Dear Healthcare Provider,

Important recent changes regarding the use of physostigmine have been made to our online drug database, which are not reflected in current editions of our print publications. We would like to alert you to the removal of physostigmine as a treatment option in tricyclic antidepressant (TCA), intrathecal baclofen, and some instances of anticholinergic drug overdose/acute toxicity.

Previous approaches to the management of TCA overdose events suggested that physostigmine may be effective in the reversal of CNS toxicities and/or vagolytic tachyarrhythmias originating from acute intoxication with agents likely to induce an anticholinergic syndrome. However, current clinical practice acknowledges the potential for significant toxicity resulting from this approach.

Clinically significant complications, including asystole and seizures, have been reported following the administration of physostigmine in TCA-poisoned patients. Patients with bradycardia and/or prolonged QRS duration may be at particular risk for physostigmine-associated toxicities. Therefore, physostigmine is not recommended in the setting of TCA intoxication. Treatment of these patients is complex and requires clinical decisions based upon patient-specific details. Consultation with a poison control center is highly recommended.

Physostigmine has also been proposed as possible adjunctive therapy for the treatment of baclofen intoxication following intrathecal administration. Pharmacologically, there is little justification for the use of physostigmine as baclofen exhibits cholinergic effects in overdose and physostigmine is an acetylcholinesterase inhibitor. However, the use of physostigmine received attention following reports of improvement in CNS and respiratory depression in baclofen-poisoned patients treated with physostigmine. Nonetheless, a number of published reports describe minimal benefit and increased risk of clinically significant adverse events (eg, cardiac arrest) with physostigmine use in baclofen intoxication. In addition, baclofen-poisoned patients typically respond well to supportive care. Therefore, current clinical practice does not advocate the use of physostigmine for baclofen-poisoned patients. Consultation with a poison control center is highly recommended.

Physostigmine continues to be recommended for the treatment of anticholinergic syndrome in the setting of pure anticholinergic intoxications (eg, Atropa belladonna [Deadly Nightshade], atropine, dimenhydrinate, diphenhydramine, and jimson weed [Datura spp] intoxications). Conversely, a number of other medications may possess dose-related anticholinergic properties, and thus physostigmine may have once been recommended in overdose treatment. However, the toxicity risks associated with physostigmine administration in the overdose setting are felt to outweigh the potential benefits and no longer justify the use of physostigmine. If a clinician feels that a patient may benefit from physostigmine administration, consultation with a clinical toxicologist or poison control center is highly recommended.

We appreciate your consideration of this important update and recommend that you keep this letter with our publication for future reference. Also, be sure to amend any other documents or protocols based on this information.

Sincerely,

Handwritten signature of Steven M. Kerscher in black ink.

Steven M. Kerscher
President and COO
Lexi-Comp, Inc

Sincerely,

Handwritten signature of Mark Bonfiglio in black ink.

Mark Bonfiglio, PharmD, RPh
Chief Content Officer
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