Predictors of Poisoning Severity in Diphenhydramine Overdose

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Background: Diphenhydramine (DPH) is a commonly used medication in OTC sleep aids and allergy formulations. DPH is frequently misused recreationally for its antihistaminergic and antimuscarinic effects and is involved in serious and fatal poisonings.

Objective: We describe the signs and symptoms (e.g., delirium/toxic psychosis, agitation, QRS/QT prolongation) associated with severe outcomes (e.g., ventricular dysrhythmias, intubation) in DPH overdoses using the ToxIC registry.

Methods: Retrospective review of the ToxIC registry database (2010– 2016). Descriptive analysis of all cases with diphenhydramine as the "primary agent" contributing to toxicity. Cases were excluded if there was any other primary agent.

Results: We identified 2465 cases with 864 cases remaining after exclusion criteria (female, 511/864; 59%). Clinical effects included delirium/toxic psychosis (n = 346, 42.1%), agitation (n = 286, 33.1%), tachycardia (n = 258, 29.8%), hallucinations (n = 179, 20.7%), coma/CNS depression (n = 151, 17.4%), seizures (n = 98, 11.3%), prolonged QTc (> 500 ms) (n = 60, 7%), and hyperreflexia/myoclonus/clonus/tremor (n = 40, 4%). There were three deaths (0.3%). Seizures were significantly associated with QRS widening (OR 4.83; 95% CI 1.85–12.58) and QTc prolongation (OR 1.99; 95% CI 1.04–3.81). Intubation was significantly associated with coma/CNS depression (OR 10.25, 95% CI 5.99–17.54), QRS widening (OR 15.65, 95% CI 6.11–40.09), and QTc prolongation (OR 3.05, 95% CI 1.5–6.21). Ventricular dysrhythmias were significantly associated with QRS widening (OR 37.28, 95% CI 9.52–145.9) and QTc prolongation (OR 9.5, 95% CI 2.6–34.6). Seizures, ventricular dysrhythmias, and intubation were not significantly associated with delirium/toxic psychosis and agitation.

Discussion: Severe DPH toxicity, manifesting as seizures, ventricular dysrhythmias, and need for intubation were all significantly associated with cardiac conduction disturbances (QRS/QTc prolongation) but not with delirium/toxic psychosis and agitation. Future studies should be aimed at prospective evaluation of chronology of symptom onset to better predict poisoning severity in DPH overdose and determine if early QRS/QTc prolongation can predict severe toxicity as it does with tricyclic antidepressants.