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124. Antimuscarinic or Asleep: A Comparison of Antimuscarinic Effects Between Hydroxyzine and Diphenhydramine Poisoned Patients

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Background: First-generation H1 antihistamines, such as hydroxyzine and diphenhydramine, are generally categorized as having antimuscarinic findings. However, hydroxyzine has a much lower affinity for the human muscarinic receptor than many other medications in this class, such as diphenhydramine.

Hypothesis: The objective of this study was to compare the rates of antimuscarinic effects in hydroxyzine and diphenhydramine exposures.

Methods: This is a retrospective, cohort analysis that compared hydroxyzine and diphenhydramine exposures reported to the Toxicology Investigators Consortium (ToxIC). The study population included all patients with single-substance ingestions between January 1, 2000, and December 31, 2020. To determine the relative antimuscarinic effects and overall toxicity of each medication, we measured the percentage and relative risk (RR) of associated findings. We calculated 95% confidence intervals for the RR and compared percentages using Chi-squared testing.

Results: There were 134 hydroxyzine and 1,462 diphenhydramine ingestions reported to ToxIC during the study period. The median age was 17 years (IQR 14-29 years) and 62% were female. An anticholinergic toxidrome was reported less commonly (RR = 0.37, 95% CI: 0.27- 0.52) for hydroxyzine (21%) than diphenhydramine (57%). Other common anticholinergic effects were also less common with hydroxyzine including agitation (RR = 0.40, 95% CI: 0.26 to 0.61), delirium (RR = 0.48, 95% CI: 0.34-0.67), hallucinations (RR = 0.20, 95% CI: 0.09-0.44), and treatment with physostigmine (RR = 0.40, 95% CI: 0.22-0.74) and benzodiazepines (RR = 0.38, 95% CI: 0.26-0.55). CNS depression was more common with hydroxyzine (RR = 1.6, 95% CI: 1.2-2.2). Mechanical ventilation was less common for hydroxyzine (0% vs. 7.7%). There were eight deaths from diphenhydramine (0.55%) and one death from hydroxyzine (0.76%). However, it was unknown if that patient was exposed to hydroxyzine and signs and symptoms were deemed “unlikely” to be toxicologically related.

Conclusion: This study shows that patients who ingested hydroxyzine have significantly less antimuscarinic effects than patients who ingested diphenhydramine, a prototypical first-generation H1 antihistamine.