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137. All antihistamines are not the same: a comparison of antimuscarinic effects between hydroxyzine and diphenhydramine poisoned patients

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Background: Antihistamines represent one of the most common poisonings reported to poison centers. In many medical textbooks, poisonings from first-generation H1 antihistamines, such as hydroxyzine and diphenhydramine, are considered as a group and are generally categorized as having antimuscarinic findings. While many medications in this class have a strong affinity for the human muscarinic receptor, such as diphenhydramine [K_i ¼ 20 ± 2 (nM)], hydroxyzine has a much lower affinity for these receptors [K_i ¼ 3,800 ± 100 (nM)]. The objective of this study was to compare the rates of antimuscarinic effects in hydroxyzine and diphenhydramine ingestions. The results of this study may inform providers of a more accurate clinical presentation of hydroxyzine poisoning.

Methods: This was a retrospective, cohort analysis that compared hydroxyzine and diphenhydramine exposures reported to the National Poison Data System (NPDS) from the American Association of Poison Control Centers. The study population included patients older than 13 years with acute, intentional, single-substance ingestions with known outcomes between January 1, 2000, and December 31, 2020. To determine the relative antimuscarinic effects of each medication, we measured the percentage and relative risk (RR) of the following findings: tachycardia, mydriasis, hallucinations/delusions, erythema/flushing, urinary retention, fever/hyperthermia, ileus, and physostigmine administration. To compare overall toxicity, we measured the rate of patients who experienced cardiac arrest, ventricular tachyarrhythmias, major CNS depression, intubation, death, and the NPDS outcome of major effects. We calculated 95% confidence intervals for the RR and compared percentages using Chi-squared testing.

Results: There were 25,629 hydroxyzine and 109,619 diphenhydramine ingestions that met the inclusion criteria. The median ages of hydroxyzine and diphenhydramine exposures were 25 and 24 years old, respectively. A higher percentage of hydroxyzine ingestions were women (72% versus 64%) and reported suicidality (89% versus 80%). Antimuscarinic effects were much more common in patients with diphenhydramine ingestions than hydroxyzine ingestions. Patients with diphenhydramine ingestions also had higher a percentage of severe toxicities including death (0.16% versus 0.02%), major effects (5.2% versus 1.3%), cardiac arrest (0.14% versus 0.01%), ventricular tachyarrhythmias (0.21% versus 0.04%), major CNS depression (1.98% versus 0.55%), and intubation (3.8% versus 0.8%) with p-values < 0.01.

Conclusions: This study shows that patients who ingested hydroxyzine have significantly less antimuscarinic effects and severe toxicities than patients who ingested diphenhydramine, a prototypical first-generation H1 antihistamine. These findings suggest that it is misleading to expect antimuscarinic findings in all first-generation H1 antihistamines, which is consistent with the pharmacology of hydroxyzine. Furthermore, despite the higher rate of patients with suicidal ingestions, patients with hydroxyzine exposures had lower rates of severe toxicity. This study is limited by the use of observational data collected for clinical care rather than research. However, there is no reason to expect that there were systematic differences in data collection between hydroxyzine and diphenhydramine cases.