

## **Epidemiology and Treatment of Z-Drug Toxicity as Reported by Medical Toxicologists: a ToxIC Database Study**

Richard J Chen<sup>1</sup>, Muhammed Ershad<sup>1</sup>, Sharan Campleman<sup>2</sup>, David Vearrier<sup>3</sup>, On Behalf of the ToxIC Investigators Consortium (ToxIC)

<sup>1</sup>Einstein Healthcare Network, Philadelphia, PA, USA.

<sup>2</sup>American College of Medical Toxicology, Phoenix, AZ, USA.

<sup>3</sup>University of Mississippi Medical Center, Jackson, MS, USA

**Background:** Z-drugs (eszopiclone, zolpidem, zopiclone, and zaleplon) are a class of GABAergic medications that are commonly prescribed as alternatives to benzodiazepines for the treatment of insomnia. Post marketing experience with these medications has demonstrated that they have adverse effect profile and addictive potential similar to benzodiazepines.

**Research Question:** What is the epidemiology, signs/symptoms, and treatment of Z-drug toxicity as reported by the ToxIC Registry?

**Methods:** We performed a retrospective analysis of all cases of Z-drug toxicity reported to the ToxIC Registry from 2010 through 2018, inclusively.

**Results:** A total of 886 cases involving Z-drugs were reported to the ToxIC Registry from 2010 through 2018. Zolpidem was the most common exposure, involving 809 (91%) of all cases. There was no trend in the relative frequency of individual Z-drug mentions over the study period ( $p = \text{NS}$ ). Patients aged 19–65 years constituted 82% of cases with the second most common age range being 13–18 years (8%). Females comprised the majority of cases overall ( $n = 561$ , 63%) and for each adult age group. Most cases (92%) of toxicity were due to intentional ingestion, either due to misuse/abuse or attempted self-harm. The most common adverse effect was CNS depression (71%) followed by respiratory depression (17%) and delirium (12%). The most common treatment modalities were IV fluid resuscitation (27%) followed by endotracheal intubation (15%). Most cases (78%) involved coingestants, most commonly non-z-drug sedative hypnotics (56%) followed by antidepressants (38%). No deaths were reported following isolated exposure to Z-drugs. However, there were three deaths reported among patients with multiple ingestions.

**Conclusion:** Z-drug toxicity most commonly occurs due to intentional overdose with clinical effects similar to benzodiazepine toxicity. Treatment is primarily supportive in nature. This data suggests that Zdrug overdoses have low mortality with significant clinical effects resulting only in combination with other xenobiotics.