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126. Seven-year trends in the reporting of multiple agent exposures involving opioids and sedativehypnotics/muscle relaxants to the ToxCIC Registry, 2010–2016

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Introduction: Opioids (OPI), sedative-hypnotics (SED) and muscle relaxants (MR) contribute a major proportion of all agents reported by medical toxicologists to the Toxicology Investigators Consortium (ToxCIC) case registry with these three drug classes responsible for over 20% of all agent fields. However, the relative contribution of each general class, as well as, individual agents has varied over time, often demonstrating a relatively flat or downward trend, particularly among opioids. The primary objective of this study was to determine trends in multi-drug use between these classes resulting in toxicological events.

Methods: The ToxCIC Registry is a prospectively collected cohort of patients evaluated by medical toxicologists. This descriptive analysis included all cases reported 1 January 2010– 31 December 2016 for patients with toxic exposure related to >1 agent (N = 16,633, 32.5% of all cases). Multi-drug events were categorized for specific OPI:SED/MR combinations, by both individual drug and specific SED/MR groupings [benzodiazepines (BZ), nonbenzodiazepines (NB), muscle relaxants, barbiturates (BA)]. Summary statistics included average annual percent change (AAPC) and significance testing of the proportions for trend (ptrend) using a 'case/total cases' metric (STATA/SE, Statacorp LP).

Results: An average of 258 cases involved exposure to at least one OPI:SED/MR combination annually over the 7-year period (range 189–322), representing 8.6–12.3% of multi-drug events in the registry (5-year average 10.9%). Linear tests for trend showed a consistent downward value (5.1% AAPC, 26.127 X2 26.127 p<.0001). Among the five most common opioids with any SED/MR, significant negative trends (p<.05) were observed for hydrocodone, methadone, and, oxycodone; and, a positive trend observed for heroin (X2 5.390, p = .02). Events reporting clonazepam with any opioid also demonstrated a significant downward trend (X2 4.352, p = .037), as did cyclobenzaprine, carisoprodol, and lorazepam. The OPI:alprazolam combination was negative but not significant. Utilizing BZ groupings in combination with individual OPI agents resulted in similar results – consistently negative trends with the exception of heroin:BZ (p18.8% AAPC, 5.487, p = .02). For NB, MR and BA groupings, relatively smaller numbers limited analysis by individual OPI; however, total OPI:MR combinations had a significant downward trend (4.3% AAPC, X2 9.411, p = .002).¹

Conclusions: Multiple drug events involving an OPI and SED/MR reported to the ToxCIC demonstrated downward trends in their relative contribution to the registry over this 7-year period. The major observed exception being heroin, which demonstrated positive trends in involvement when analyzed for all SED/MRs combined or for benzodiazepines alone. As the Registry continues to increase in size and accumulated years, the ability to identify stable estimates of trend will continue to improve.