

Concomitant Substances Increase Risk of Major Medical Outcomes Among Single-Ingredient Acetaminophen Self-Harm Exposures Reported to the National Poison Data System (NPDS) (January 2013-December 2023)

Alicia M. Dalton^a, Hannah Burkett^a, Andrew A. Monte^{a,b}

^aRocky Mountain Poison and Drug Safety – Denver Health, Denver, CO

^bUniversity of Colorado School of Medicine, Department of Emergency Medicine

Background: Incidence of self-harm has been increasing in the United States (US) across all modalities, including pharmaceuticals. The death rate following a pharmaceutical exposure is low compared to other self-harm methods, but pharmaceutical ingestion remains the most common method, which results in a large overall number of deaths every year. Over-the-counter medications (OTCs) are widely available making this medication group of particular importance. Further, self-harm is increasing for many OTC products including acetaminophen, ibuprofen, and diphenhydramine, likely due to wide availability. Due to the ubiquitous use as an OTC, this work focuses on single-ingredient acetaminophen exposures. We hypothesize that polysubstance exposures lead to worse medical outcomes due to the clinical effects of the concomitant substance.

Methods: Self-harm exposures involving at least one single-ingredient acetaminophen product were obtained from NPDS from 01 January 2013 through 31 December 2022. Self-harm was defined as an exposure reason of “*Intentional-Suspected Suicidal*”. Major medical outcome (MMO) was defined as an outcome of either “*death*” or “*major effect*”. Exposures were excluded if they were not followed to a known medical outcome, were under the age of 6 years old, or had incomplete data. Data were stratified by exposures to single-ingredient acetaminophen only and polysubstance single-ingredient acetaminophen exposures (single-ingredient acetaminophen in addition to a concomitant substance). We assessed the five most frequently reported concomitant substances taken with single-ingredient acetaminophen, and calculated odds ratios of a MMO for each compared to single-ingredient acetaminophen exposure alone utilizing logistic regression.

Results: From January 2013 through December 2022 there were 442,867 single-ingredient acetaminophen exposures among patients age 6 years or older. Of these, 58.1% (n=257,123) were self-harm. After removal of exposures not followed to a known medical outcome, the final data set consisted of 235,026 self-harm exposures involving single-ingredient acetaminophen. Half of the exposures (50.2%, n=118,078) were polysubstance and 6.3% (n=14,818) resulted in a MMO. The odds of a polysubstance exposure resulting in a MMO was 1.13 (95%CI: 1.08, 1.18) compared to single-ingredient acetaminophen alone. Death occurred in 0.3% (n=372) of single-ingredient acetaminophen only exposures and 0.6% (n=738) of polysubstance exposures. Major effect occurred in 4.2% (n=4,961) of single-ingredient acetaminophen alone and 7.4% (n=8,747) of polysubstance exposures. Concomitant substance frequencies were highest for: ibuprofen (n=32,676), ethanol (n=22,734), benzodiazepines (n=11,194), aspirin (n=10,793) and OTC combination acetaminophen (a product with a combination of ingredients including acetaminophen; n=10,788). Compared to single-ingredient acetaminophen only, the odds of a MMO was 0.82 (95%CI: 0.76, 0.89) for exposures with ibuprofen, 0.90 (95%CI: 0.81, 1.00)

with OTC combination acetaminophen, 1.10 (95%CI: 1.00, 1.20) with aspirin, 1.10 (95%CI: 1.02, 1.18) with ethanol, and 1.43 (95%CI: 1.32, 1.55) with benzodiazepines. Odds ratios were significantly higher for concomitant substances that can cause sedation.

Conclusions: Ethanol, aspirin and benzodiazepines, taken in combination with single-ingredient acetaminophen, increased odds of MMO while other common concomitant substances did not. These results indicate that outcomes among self-harm single-ingredient acetaminophen exposures are impacted by the concomitant substance involved.