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Self-Harm as a Contributor to the "Fourth Wave": Suicidality in Stimulant Overdoses

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Background & Introduction: Recent data have shown that there is an evolving "Fourth Wave" of drug overdoses involving stimulants with, or without, co-exposure to opioids,[1] and at least one survey-based study found a correlation between suicidal ideation with stimulant misuse and stimulant use disorder.[2] Similarly, recent studies of opioid overdoses presenting to emergency departments have found that a significant minority of these cases had a component of passive or active suicidality.[3,4] This was predominantly found to involve use of pharmaceutical opioids rather than illicit opioids.[4] However, despite the warranted focus on the role of intentional self-harm as a contributor to opioid overdoses, limited literature exists regarding the role of intentional self-harm attempts using stimulants. The American Society of Addiction Medicine has recently called for further research into the relationship between stimulant overdose and mental health conditions including suicidality. This study assessed the reasons for deliberate stimulant exposures resulting in serious toxicity utilizing the Toxicology Investigators Consortium (ToxIC) Core Registry.[5] Our a priori hypothesis was that a pattern similar to that observed with opioid overdoses would be seen with stimulant overdoses: namely, that a clinically significant proportion of overdoses involving pharmaceutical stimulants would be characterized by some degree of suicidal intent.

Methods: The ToxIC Core Registry collects pre-specified data on consecutive patients cared for by participating medical toxicologists.[5] Cases of intentional pharmaceutical or nonpharmaceutical stimulant exposures in patients ≥11 years between 2014–2023 were included. Pharmaceutical stimulants were defined as Food and Drug Administration-approved medications that were used as labelled. All other stimulants, including misuse of prescription stimulants, were defined as nonpharmaceuticals. Comparator drug groups were pharmaceutical opioid analgesics, non-opioid analgesics including gabapentinoids, sedative-hypnotics, and antidepressants. Because all cases in the Core Registry required medical toxicology consultations, they were deemed to be serious. The ToxIC Core Registry was approved by a central Institutional Review Board (IRB) and by the IRBs of participating institutions.[5] Patient characteristics were summarized by frequency count and percentages for categorical variables and medians and interquartile ranges for continuous variables. Bivariate statistical tests used were Fisher's Exact Test and Chi-Square Test for categorical variables and Kruskal–Wallis Test for continuous variables. Linear regression analyses were performed to evaluate the time trend in the proportion of patients with stimulant suicide attempts and misuse compared to the overall total of Core Registry cases per year. Ninety-five percent confidence intervals were calculated for slope regression coefficients. All analyses were conducted in R 4.3.3.

Results: Over the ten-year course of the study, 75,724 cases were entered into the ToxIC Core Registry, of which 5428 (7.2%) involved any stimulant use. The most commonly reported pharmaceutical stimulant was methylphenidate (22% of stimulant cases). Cocaine and methamphetamine were the most commonly reported nonpharmaceutical stimulants (17% and 15% of stimulant cases, respectively).

Of all 5428 stimulant cases entered in the ToxIC Core Registry, 4847 were patients aged ≥11 years. After the exclusion of 1377 cases of withdrawal, stimulant use disorder treatment, and other toxicologic evaluations, there were 3470 cases of intentional stimulant use. Among these included cases, 1980 (57.1%) were due to stimulant misuse, of which 1556 (78.6%) patients were taking the stimulant to elicit a pleasurable sensation. Some degree of intentional self-harm was expressed by 988 (28.5%) of included cases as a motivation for their stimulant use, and 803 (81.3%) of these self-harm cases expressed actual suicidal intent, defined as having at least some intent to die. Patients with suicidal intent thus constituted 23.1% of all cases of intentional stimulant use. Pharmaceutical stimulants alone were involved in 836 (84.6%) of self-harm attempts, compared to 346 (17.5%) of misuse cases involving pharmaceutical stimulants alone ($P < 0.001$). Of these self-harm attempts involving only pharmaceutical stimulants, 692 (82.8%) expressed some degree of suicidality. In contrast, there were 89 (9.0%) cases of self-harm using nonpharmaceutical stimulants, of which 58 (65.2%) expressed suicidal intent. In addition, there were 63 (6.4%) cases of combined pharmaceutical and nonpharmaceutical self-harm exposures, with 53 (84.1%) of these expressing suicidal intent ($P = 0.002$). The median age of all stimulant exposure cases was 33.0 years (IQR 23.0–44.0). However, for cases of self-harm, the median age was 19.0 years (IQR 15.0–34.0; $P < 0.001$). Among the suicidal patients, the median age for pharmaceutical-only stimulant overdoses was 17.0 (IQR 13.5–29.3), versus 35.0 (IQR 26.3–40.8) for nonpharmaceutical-only suicide attempts, and 37.0 (IQR 24.0–45.0) for suicidal patients who took both pharmaceutical and nonpharmaceutical stimulants ($P < 0.001$). Among all stimulant cases, 3042 (62.8%) were females. However, a greater proportion of females had some intent of self-harm (55.4% versus 43.3%; $P < 0.001$). Among patients expressing suicidal intent, 278 (40.2%) of pharmaceutical-only cases were males, compared to 38 (65.5%) of nonpharmaceutical-only cases and 28 (52.8%) of patients using both types ($P = 0.001$). No significant time trends were seen for all intentional stimulant exposures, exposures due to stimulant misuse, or for suicidal intent during the study time period.

Conclusion & Discussion: In this study, 28.5% of all intentional stimulant exposures had a self-harm component, and 23.1% of these had at least some suicidal intent. This result is very similar to our previous findings for opioid overdoses after intentional opioid exposure, for which 27.7% of cases were found to be due to self-harm attempts, and 23.6% had some actual suicidal intent.[4] In addition, we found that 89.1% of suicidal cases involving stimulants used pharmaceutical stimulants (745/803 cases involved a pharmaceutical stimulant either alone or in combination) rather than illicit stimulants. This is also similar to our findings with intentional opioid overdoses, where 86.4% used pharmaceutical opioids in their suicide attempt.[4] Although a majority of stimulant overdoses involved nonpharmaceutical stimulant misuse, over a quarter of serious stimulant overdoses in our cohort were due to self-harm (most with suicidal attempt). Thus, an assessment of potential suicidality should be considered in all patients with stimulant overdoses, particularly in cases of pharmaceutical stimulant overdoses. Limitations of this study include that the ToxIC Core Registry may not be representative of all patients presenting with stimulant overdoses and likely overrepresents serious cases, and no definitive laboratory verification of stimulant identity was done in many cases.