Serotonin Toxicity Case Characteristics and Associated Xenobiotics: a Review of the Toxicology Investigators Consortium (ToxIC) Database

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Background: Serotonin toxicity is a common cause of drug-induced altered mental status. However, there are no large case series evaluating the causes of serotonin toxicity, describing the symptomatology, or rate of treatment with antidotal therapy.

Research question: What are the patient characteristics and xenobiotics associated with the development of serotonin toxicity?

Methods: This study evaluated cases of serotonin toxicity in the ToxIC registry, a national database of prospectively collected cases seen at the bedside by medical toxicologists from > 50 geographically diverse sites that contains over 50,000 cases. The database was searched for Bserotonin syndrome^ between 1/1/2010–12/31/2016. Cases were excluded if multiple toxidromes were listed or if marked as Bunlikely tox related^ or Bunknown if tox related.^ Descriptive statistics were used to summarize demographics, signs/symptoms, outcomes, and associated xenobiotics. Results: Included were 1010 cases. Females made up 608 cases (60%). Ages: < 2 (3, 0.3%), 2–6 (8, 0.8%), 7–12 (9, 0.9%), 13–18 (278, 27.3%), 19–65 (682, 67%), and > 66 (35, 3.4%). Reasons for encounter: drug abuse (53, 5%), intentional 789, 78%), adverse drug event (95, 9%), and unintentional (66, 6%). Signs and symptoms: hyperreflexia/clonus/ myoclonus (601, 60%), agitation (337, 33%), tachycardia [HR > 140 bpm] (256, 25%), rigidity (140, 14%), seizures (139, 14%), hypertension [SBP > 200 mmHg; DBP >120 mmHg] (71, 7%), and hyperthermia [T > 105 F] (29, 3%). Complications: rhabdomyolysis (97, 10%), ventricular dysrhythmias (8, 0.8%), and death (1, 0.1%). Treatments: benzodiazepines 67% (677/1010) and cyproheptadine 15%(153/1010). One hundred ninety-two different xenobiotics were reported with 2046 total exposures. Antidepressants as a class were most commonly the 'primary agent' listed (915, 45%) with bupropion the most frequent over- all (147, 7.2%). Common non-antidepressants were dextromethorphan (95, 6.9%), lamotrigine (64, 3.1%), and tramadol (60, 2.9%).

Discussion: In this series, serotonin toxicity most often occurred in adult patients with intentional overdose. Antidepressants were most often listed as the primary agents of toxicity. Interestingly, bupropion, a norepinephrine/ dopamine reuptake inhibitor, was the most frequently mentioned xenobiotic. Benzodiazepines were commonly administered. Though often cited as a potential antidote, only 15% of patients received cyproheptadine. Severe toxicity was rare. Only a single death was reported.