

## **Rates of Serotonin Toxicity and Factors Associated with Seizures in SNRI Overdose: a Review of the Toxicology Investigators Consortium Database**

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**Background:** SNRI's are known to cause seizures and serotonin toxicity in overdose.

**Objective:** To investigate factors associated with seizures in SNRI overdose and compare rates of seizures and serotonin toxicity between these medications.

**Methods:** We queried the ToxIC database for SNRI overdoses. Cases involving co-ingestion of other epileptogenic agents (bupropion, tramadol, citalopram, TCA's) were excluded. We selected a number of a priori clinical features and calculated their association with seizure using odds ratios. We also compared rates of serotonin toxicity between medications.

**Results:** Rates of serotonin toxicity after overdose of venlafaxine, desvenlafaxine, and duloxetine were 15.6%, 16.3%, and 15.1%, respectively, with no statistically significant difference between them. Rate of seizures after overdose of venlafaxine (11.5%; 45/391) was higher than with duloxetine (3.8%; 8/204) ( $p = 0.02$ ), but not higher than with desvenlafaxine (7%; 3/43) ( $p = \text{NS}$ ). Factors associated with seizures after venlafaxine overdose were tachycardia  $> 140$  BPM (OR 2.59, CI 1.30– 5.12), QTc  $> 500$  ms (OR 3.48, CI 1.17–10.39), and hypotension (OR 5.61, CI 2.05–15.3). There were no factors that were statistically significantly associated with seizures after duloxetine and desvenlafaxine overdose, however low seizure rates limited our analysis. 86 J. Med. Toxicol. (2019) 15:53–107

**Discussion:** Tachycardia, QTc prolongation, and hypotension are associated with seizures in venlafaxine overdose. While rates of serotonin toxicity were consistent between groups, venlafaxine was associated with significantly higher rates of seizure than duloxetine. This finding suggests that duloxetine may be less epileptogenic than venlafaxine in overdose.

**Conclusion:** Venlafaxine appears to cause seizures in greater frequency than duloxetine in overdose. Additionally, there are multiple clinical features associated with seizures in venlafaxine overdose.