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38. Toxin-induced QTc prolongation: exposure and patient characteristics associated with ventricular dysrhythmias

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Background: Toxin-induced QTc prolongation (QTP) is relatively common, but ventricular dysrhythmias such as torsade de pointes are rare. This study aimed to identify which patients with toxin- induced QTP are at particularly high-risk for ventricular dysrhythmias.

Methods: This was a retrospective analysis of data from the Toxicology Investigators Constortium (ToxIC) Core Registry between January 2016 and March 2023. Patients aged !13 years or older with severe QTP (defined in ToxIC as the presence of a QTc >500 milliseconds during the encounter) after a single sub- stance exposure resulting in a medical toxicology encounter were included. Patients with encounters in the outpatient setting or primarily for withdrawal were excluded, as were those with missing outcome data and those for whom the treating medical toxicologist documented the signs and symptoms as unrelated or unknown if related to the exposure. The primary outcome was ventricular dysrhythmias as documented in ToxIC. Secondary out- comes included death during hospitalization, cardiac arrest, and use of electrical or pharmacological pacing. Independent varia- bles included demographics, exposure circumstances, exposure substance category, QTc value on initial electrocardiogram, and clinical features (electrolyte abnormalities, hypothermia, tachycar- dia, bradycardia, and metabolic acidosis [pH <7.2 per ToxIC]). Free text sections of the registry were searched to identify add- itional information not recorded elsewhere. Cohort characteristics were reported with descriptive statistics. Univariate analysis was utilized to identify factors associated with outcomes. These fac- tors were entered as independent variables in a multivariable logistic regression model with ventricular dysrhythmias as the dependent variable; age, sex, race, and QRS widening (>120 milliseconds per ToxIC) were included as confounders. Subgroup analyses were planned for any substance categories found to be independently associated with ventricular dysrhythmias.

Results: Of 38,049 patients screened, 1,022 were ultimately included. The median age was 34 (IQR 19–51) years, and 630 (61.6%) were female. Fifty-eight (5.68%) developed ventricular dysrhythmias, of which four (0.4%) were specifically denoted as torsade de pointes in free text sections. Thirty-seven (3.62%) developed cardiac arrest, and 38 (3.72%) died. Twelve (1.17%) underwent electrical pacing, and 30 (2.94%) underwent pharmacological pacing with isoproterenol, epinephrine, or dopamine. One hundred ninety-one (17.1%) had documented potassium values. Opioid exposures (OR 3.06, 95% CI 1.28–7.05), hydrocarbon exposures (OR 152.3, 95% CI 13–3,507.4), acidosis (OR 2.93, 95% CI 1.34–6.16), and initial QTc value (OR 1.01, 95% CI 1.00–1.01) were independently associated with ventricular dysrhythmias. Bradycardia did not independently predict ventricular dysrhythmias but did confer

increased odds (OR 2.39, 95% CI 0.77–6.96) and was associated with all secondary outcomes ($p < 0.01$). Model area under the curve was excellent (0.89). Among the opioid exposure subgroup, loperamide was associated with ventricular dysrhythmias (p1⁄40.002). Two (66.7%) hydrocarbon exposures developed ventricular dysrhythmias; both were difluoroethane.

Conclusion: *Torsade de pointes* is infrequent among patients with toxin-induced QTc prolongation, but those with opioid exposures or metabolic acidosis are at particularly high risk of ventricular dysrhythmias. Further studies should examine the role of electrolyte abnormalities, as this study contained limited information on electrolyte values.