EDITORIAL

Opium-associated QT Interval Prolongation: A Cross-sectional Comparative Study

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Consumption of opium and related products is illegal in many countries including ours. Considering the prevalent addiction with an estimated 0.27 million (2.5% of the source population) to be opioid-dependent, which got highlighted in a survey from Punjab,[1] this association of QT interval prolongation as reported by the authors in this study is of extreme clinical relevance to the perioperative physicians, anesthesiologists, and critical care specialists because of the severe interactions with many lifesaving drugs one may get caught unawares while dealing with these patients. The study assumes importance since no other published text has referred to such interactions in opium users before except for one study from Iran that described similar findings in patients with opium toxicity.[2] It assumes more relevance in the ongoing COVID pandemic where usage of drugs like hydroxychloroquine compound the risk of fatal arrhythmias because of QT prolongation.[3]

The QT interval denotes the time between the start of the Q wave and the end of the T wave which represents the ventricular depolarization and repolarization in electrocardiography (ECG). For eliminating the confounding effects of the heart rate on the QT measurement, a correction is introduced as represented by Bazette's formula (corrected QT; $QTc = QT/\sqrt{RR}$). The authors of this study have rightly used QTc for comparing the effects between the study and control group. A QT >450 ms and QTc >470 ms is considered as prolonged[4] and the risk of torsades de pointes (TdP) increases at QTc >500 ms.

Pharmacologically active compounds in raw opium are alkaloids. Morphine is the most abundant of around 40 such compounds (opiates) discovered which has found extensive usage in medicine and studied extensively. Conventionally, opium toxicity has been studied as its CNS depressant effects[5] but cardiac adverse effects have also been reported in the literature as (a) independent risk factor for coronary artery disease,[6] (b) strong risk factor for myocardial infarction.[7] On the contrary, the arrhythmogenic potential of the opioids like methadone (highest risk), tramadol, oxycodone (moderate risk), and to some extent buprenorphine (low risk) have been well documented for their potential to prolong the QT interval and precipitating dangerous arrhythmias like TdP.[8]

Drug-induced QT prolongation and TdP are chiefly because of the blockade of "rapid" outward current potassium channels.[9] Inhibitory effects on the human ether-a-go-go-related gene (hERG) have also been indicated in more recent studies especially with respect to methadone usage.[10]

The prolongation of repolarization results in subsequent inward depolarization current, known as an early after-depolarization—when accompanied by increased dispersion of repolarization, TdP is provoked.

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The list of drugs that can lead to QT prolongation is extensive and many of these are commonly used in perioperative and critical care settings; hence, it is imperative to have a ready reckoner of such drugs to avoid fatal adverse events.[11]

The risk of QT prolongation is increased in females, patients with organic heart disease (e.g., congenital long QT syndrome, myocardial infarction, congestive heart failure, dilated cardiomyopathy, hypertrophic cardiomyopathy, and bradycardia), hypokalemia, and hepatic impairment. The treatment of drug-induced TdP includes identifying and withdrawing the offending drug(s), replenishing the potassium concentration to 4.5–5 mmol/L, and infusing intravenous magnesium (1–2 g). In resistant cases, temporary cardiac pacing may be needed.

The importance of awareness about the drug interactions that can lead to prolongation of QT interval, cannot be overemphasized especially while dealing with opium users and this has been amply highlighted by the findings of this study which has shown in its results that raw opium use was associated with increased QTc intervals in comparison with non-user group and also male gender and older age were significant predictors of QTc prolongation in the user group. Authors have not been able to establish a correlation between the dosage and duration of opium usage with its arrhythmogenic potential. Although many studies have repeatedly established the dose-dependent effect of methadone and QT prolongation.[7,12]

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