

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

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## ABSTRACT

**Background:** Toxicity and side effects of long-term use of opioids are well studied, but little information exists regarding electrophysiological disturbances of opium consumption. While natural opium has been regarded safe to a great extent among traditional communities, concerns are emerging owing to the available evidence of QT prolongation that have been exposed during recent outcome surveillance of patients under opioid use. Potential QT prolonging interactions would raise a higher level of such concern in opium users during COVID pandemic and warrant attention.

**Materials and methods:** This study was designed to detect the prevalence of QTc prolongation among opium users and nonusers. Two groups were compared with regard to gender, age, and median QTc interval. Normal and prolonged QTc intervals of user group were compared with respect to age, sex, dose of opium consumption, and duration of opium consumption.

**Results:** 123 opium users and 39 controls were investigated. Median QTc interval in opium user and non-user group was 460 vs 386 milliseconds, respectively ( $p$  value < 0.001). In all, 59.3%, (95% CI: 50.51–67.62%) of cases and none of non-user had prolonged QTc interval ( $p$  value < 0.001). There was no significance between normal and prolonged QTc intervals with respect to dose and duration of opium use.

**Conclusion:** This study indicated that opium consumption is associated with QTc prolongation. This prolongation does not relate to dose and duration of opium use. Further study is propounded to assess the clinical significance of these results and to determine risk rating of opium compared to other opioids in this regard.

**Keywords:** Opioids, Opium, QT interval, QT prolongation.

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## INTRODUCTION

Cultivation of opium poppy (*Papaver somniferum*) and production of raw opium have been intertwined with many cultures around the world.<sup>1–7</sup> The opium market serves both for producing the medicinal preparations such as morphine and codeine and securing the illicit trade of heroin and opium. The traditional belief of beneficial properties along with the analgesic effect of opium has turned into the rising trend of a tremendous illegal and adulterated opium use leading to health and economic calamity.<sup>8,9</sup> Nevertheless, opium pharmaceutical product in the form of opium tincture has been recently introduced to control opioid withdrawal and reduce addiction harms.<sup>10–14</sup>

The effect of opioids on cardiac electrical activity has been the matter of concern for physicians and pharmacists, since considering the arrhythmogenicity of a drug can weigh up the pros and cons of treatment or to prioritize the drug administration.<sup>15</sup> In particular, the usage of the varying sedatives in perioperative settings and administration of specific therapeutics for COVID-19 patients with possible QT prolonging interactions would raise a higher level of such concern in opium users and warrant attention and further investigation. Many studies have elaborated the adverse and protective effects of opium use on cardiovascular risk factors.<sup>16–23</sup> Meanwhile, little evidence has documented the association of opium use with cardiotoxicity and heart electrophysiology.<sup>19</sup> Morphine is the main direct derivative of opium and accounts for 8–17% of the quantitative alkaloid content in opium.<sup>7</sup> Morphine has been considered low risk from the perspective of QT interval prolongation<sup>15</sup> and has been suggested for treating opioid

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addicts who have a prolonged QT interval.<sup>24</sup> However, opium is a mixture of several substances with different effects that may ensue the different clinical manifestations.<sup>9</sup> Yet, there is no evidence that opium consumption is associated with the higher prevalence of prolonged QT interval compared to non-user general population. Hence, we conducted this study to demonstrate whether there is association between opium use and prolongation of QT interval.