QTc Prolongation in a Young Healthy Patient Receiving Citalopram 40 mg

To the Editor: Citalopram is a selective serotonin reuptake inhibitor (SSRI) recommended for treatment of major depressive disorder (MDD) and other psychiatric conditions such as anxiety disorders.[1,2] Like other SSRI agents, in premarketing research citalopram has been shown to have a safe cardiac profile within normal serum range compared to tricyclic antidepressants.[2,3] However, studies[4–10] have reported that citalopram may cause torsades de points arrhythmia and QTc prolongation in some patients.

Accordingly, in 2011, the US Food and Drug Administration (FDA)[11] published a warning concerning QTc prolongation with citalopram doses greater than 40 mg/d. In 2012, the FDA limited the maximum daily dose to 20 mg for high-risk individuals.[12]

Case report. In 2015, a 29-year-old man with MDD was admitted to a psychiatric ward in Tehran, Iran. He had attempted suicide twice in the past few weeks by hanging himself. He was immediately rescued and transported to a general hospital and discharged after a thorough evaluation. He had no personal or family history of medical conditions including cardiac problems.

During this hospitalization, he received 10 sessions of electroconvulsive therapy (ECT), and citalopram was prescribed in an initial dose of 10 mg/d, gradually reaching 40 mg/d. The ECT sessions were completed before the daily 40-mg dose was reached. In addition to citalopram, quetiapine 25 mg was also started and then gradually titrated to 100 mg twice daily. The pretreatment electrocardiogram (ECG) showed a QTc interval of 400 ms. After 33 days of taking citalopram (4 days of 40 mg/d), another ECG was ordered. Mean QTc was calculated in the leads 2, V5, and V6 using the Bazett formula (QTc = QT/RR0.5).[13] Measurement on these leads are known to exhibit the greatest positive and negative predictive values in detection of abnormal QTc.[14] The longest QTc measured was 477 ms in lead 2. His vital signs were stable (blood pressure: 90/60 mm Hg, heart rate: 75 bpm, and respiratory rate: 15 breaths/min). The heart examination was unremarkable. Biochemical tests (blood urea nitrogen, creatinine, sodium, potassium, calcium, phosphorous, magnesium) were completed, and the findings were within normal limits.

The patient was offered further cardiac and genetic tests, which he refused. A daily ECG was also requested. After the citalopram dose was decreased to 20 mg/d, his QTc interval returned to borderline level (442 ms). Citalopram was tapered and discontinued within 8 days. The patient was discharged with a QTc of 418 ms, which is within normal limits.

Citalopram is mainly metabolized in the liver via multiple isoforms of cytochrome P450 (CYP). CYP2C19, one of those isoenzymes with high genetic polymorphism, is mainly involved in citalopram *N*-demethylation.[15–17] Although this drug may prevent torsades de points within the clinical serum range,[18] desmethylcitalopram may cause QTc prolongation in large doses.[19] In previous studies,[8,9] in contrast to our case, QTc prolongation was mainly seen in patients with overdoses, cardiac problems, and electrolyte disturbances or in combination with CYP2C19 inhibitors. Therefore, one possible explanation for our findings might be that the patient is a poor metabolizer of CYP2C19.

Quetiapine could have contributed to QTc prolongation in our patient; however, this is not probable for a couple of reasons. First, QTc measurements returned to a normal range despite continuation of quetiapine. Furthermore, there is paucity of research supporting QTc prolongation caused by quetiapine, and these studies are limited by small sample sizes,[20] patients with history of heart disease, and use of higher doses of both quetiapine and citalopram.[21]

Therefore, despite the need to replicate our findings, the probability of QTc prolongation with citalopram use should be kept in mind even in a young healthy patient with no known history of heart disease or electrolyte imbalance.

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