An Analysis of QTc Prolongation of Atypical Antipsychotic Medications and Selective Serotonin Reuptake Inhibitors Using a Large ECG Record Database
S-I. Park, K. Jang, S. Lee, I-J. Jang, K-S. Yu, J-Y. Chung
Seoul National University

Purpose
Several psychotropic drugs have been reported to be associated with corrected QT (QTc) interval prolongation. In the current study, we evaluated the effects on the QTc intervals of the atypical anti-psychotic drugs and SSRIs. The analysis of QTc intervals was performed using a large open-access QT database (ECG-ViEW) which consists of electrocardiogram (ECG) recordings from a Korean population. Additionally, we estimated the relationships between age, sex, and selected electrolyte levels on one hand, and the observed QTc interval on the other hand.

Methods
Frequency of the QTc prolongation intervals after each administration of 14 different atypical anti-psychotic drugs and selective SSRIs were compared to those after administration of the positive control drug, cilostazol and the negative control drug, diazepam. The 14 drugs were selected from the CredibleMeds® website, where drugs with known, conditional, and possible risk of torsade de pointes are listed. The patients were divided into two groups based on the QTc intervals, with the cutoff values of 460 ms for females and 450 ms for males. The number of patients were 63 for the QTc prolonged group, and 768 for the non-prolonged group. We compared the incidence of QTc prolongation after the drug administration using a chi-square test. Also, the effects of age, sex, and the levels of selected electrolytes (potassium, magnesium, and calcium) on the QTc intervals were estimated by linear regression analysis.

Results
The frequency of the QTc prolongation after administration of the 14 studied drugs were significantly lower than that of cilostazol (p < 0.001) with the odds ratio (OR) of 0.252 (95% confidence interval (CI), 0.163- 0.392). On the other hand, there were no statistically significant differences in the frequencies of the QTc prolongation of diazepam and the 14 studied drugs (p=0.142) with the OR of 0.702 (95% CI, 0.437-1.127). Whereas, typical antipsychotic drugs showed no significant difference with either cilostazol (p=0.120) with the OR of 0.608 (95% CI, 0.324-1.142) or diazepam (p=0.113) with the OR of 1.691 (95% CI, 0.878-3.257). Among the factors evaluated for possible association with QTc interval (age, sex, and the selected electrolyte levels), only age showed statistical significance (p=0.045).

Conclusion
These findings have shown that the atypical anti-psychotic drugs and selective SSRIs do not prolong the QTc interval significantly when compared with the positive control, cilostazol, and the frequency of the prolongation after dosing was similar to that of the negative control, diazepam. In addition, age showed a significant correlation with the QTc interval. This study results suggest that the atypical anti-psychotic drugs and SSRIs are less likely associated with the QTc prolongation than the typical antipsychotic drugs in the real clinical settings.