

## Gender and Ethnicity on Quinidine-induced QT Prolongation and its Pharmacokinetics in Korean and Caucasian Healthy Subjects

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Drug-induced QT prolongation has known to be influenced by genetic factors and environmental factors, suggesting the possibility of interindividual and ethnic difference of QT prolongation. No controlled clinical trial has been addressed to drug-induced QT prolongation in Korean population. We evaluated quinidine-induced QT prolongation and its pharmacokinetics in Koreans and compared to those in 13 Caucasian subjects. Twenty-four Korean subjects (12 men and 12 women) received a single intravenous dose of quinidine (4mg/kg) over 20 minutes or placebo in a double-blind randomized crossover trial. The plasma quinidine concentrations were measured by HPLC, and QT intervals measured were corrected for heart rate using the Bazett's method. The population pharmacodynamic parameters were estimated by using NONMEM. Female subjects tend to have lower C<sub>max</sub> and higher clearance than those of male subjects, but their differences were not significant statistically. There were no significant differences of quinidine pharmacokinetics between Koreans and Caucasians. The population average QT<sub>c</sub> interval at baseline was consistently longer for women than for men without statistical significance in both ethnics. The ΔE<sub>max</sub> in Caucasian subjects was greater than that of Koreans (210 msec vs 137 msec), but estimated EC<sub>50</sub> values were also higher in Caucasians than in Koreans. In Caucasians, the average EC<sub>50</sub> and E<sub>max</sub> of female subjects were far greater than those of male subjects, suggesting higher QT prolongation in female subject compared to male subjects, especially at high quinidine concentration.

These results suggest that gender and ethnicity are expected to in part contribute to the individual susceptibility on quinidine-induced QT prolongation, but which is unlikely related to the pharmacokinetic differences. Further extended population study on drug induced QT prolongation would be helpful to clearly understand the effect of ethnicity and gender to this cardiac side effect.