Population pharmacokinetics of levosulpiride with genetic polymorphisms of *MDR1* gene in healthy subject

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**Aims**: The aim of this study was to evaluate the influence of multi-drug resistance (*MDR*) genetic polymorphisms on the population pharmacokinetics (PPK) of levosulpiride in healthy Korean subjects. **Methods**: A single oral dose of 25-mg levosulpiride was orally administered to 58 healthy male subjects. The serum concentrations of levosulpiride were measured up to 36 hr using HPLC method. We determined the polymorphic alleles of *MDR1* exon 12 C1236T, exon 21 G2677T, and exon 26 C3435T in each subjects using a polymerase chain reaction-restriction fragment length polymorphism. The PPK model was applied using a nonlinear mixed effects modeling method, and explored the possible influence of genetic polymorphisms in *MDR1* C1236T, G2677T, and C3435T on the PPK of levosulpiride. **Results**: A one-compartment model with first-order absorption and lag time well characterized the serum concentration data. Significant covariates for levosulpiride clearance (CL/F) were genetic polymorphisms of *MDR1* G2677T and C3435T. In the exon 21 2677TT and 26 3435TT genotype groups, the concentrations of levosulpiride were significantly higher than those of other groups (GG and CC) (*P*<0.05). However, statistically significant differences could only be observed among the genotype groups in exon 21 for the AUC₀⁻∞ and AUC₀⁻2h, area under the concentration-time curve up to 2 hr, which represents the absorption phase of levosulpiride (*P*=0.040 and *P*=0.033, Kruskal-Wallis Test). However, no significant differences were found among *MDR1* C1236T CC, CT and TT groups with regard to the PK parameters of levosulpiride. **Conclusions**: This study shows that genetic polymorphisms of *MDR1* exon 21 G2677T and exon 26 C3435T might explain the variability in PK of levosulpiride in the Korean population.