일반연제 5

# Pharmacokinetics of Chlorpromazine with Respect to CYP2D6 Genetic Polymorphism in Korean Healthy Subjects

Yu Eun Sunwoo, Min-Jung Kim, Ji-Young Ryu, Wonku Kang, Kwang-Hyeon Liu, Hye Gyung Jang, Hyun-Ju Jung, Young-Ran Yoon, Jae-Gook Shin

Department of Pharmacology and Pharmacogenomics Research Center, College of Medicine, Inje University, Busan, Korea

Cytochrome P450 2D6 (CYP2D6) represents a variety of polymorphism. *CYP2D6*10B*, an allelic variant shown with a high frequency in Asian compared with Caucasian has been reported to decrease the enzyme activity. The effect of *CYP2D6*10B* allele was investigated on the pharmacokinetics of chlorpromazine (CPZ) in Korean healthy subjects. Three subjects with wild type, 7 with heterozygous mutation, and 4 with homozygous mutation were participated. Other mutation alleles which may affect this study were excluded. After a single oral administration of CPZ (50 mg), blood was serially taken up to 24 hour. Plasma concentrations of CPZ were measured by LC/MS/MS, and pharmacokinetic parameters were calculated by non-compartmental analyses. Mean peak plasma concentrations in heterozygous and homozygous mutants were 34 and 95% higher than that in wild group (8.7±8.5 ng/ml), respectively. Mean AUCs in both groups increased by 34 and 65% in comparison with that in wild group (60.6±65.8 ng*hr/ml), respectively. However, there was no statistical difference in both parameters due to the extreme interindividual variation. Other pharmacokinetic parameters including elimination rate constant did not show any significant differences among three groups either. *CYP2D6*10B* mutation seems to increase the plasma concentration of CPZ despite no statistical relevance. Further study in a sufficient number of subjects would be needed including analyses of metabolite profiles.