Effect of CYP2D6 genetic polymorphisms on pharmacokinetics of tropisetron

Dal-Seok Oh, O.M.D.[1], Myo-Kyoung Kim, Pharm.D.[1], Joo-Youn Cho, Ph.D.[1], Hyeong-Seok Lim, M.D.[1], Kyoung-Seop Hong, M.D.[1], Jae-Yong Chung, M.D.[1], Kyun-Seop Bae, M.D., Ph.D.[2] So-Young Yi, M.S.[1], Sang-Goo Shin, M.D., Ph.D.[1], In-Jin Jang, M.D., Ph.D.[1]

[1]Clinical Pharmacology Unit, Department of Pharmacology, College of Medicine, Seoul National University, Seoul, Korea
[2]Clinical Research Support Center, Asan Medical Center, Seoul, Korea

Purpose: This study is aimed to evaluate the effect of CYP2D6 genotype on pharmacokinetics of tropisetron in Korean healthy subjects.

Methods: A single 5-mg capsule of tropisetron was administered orally to 13 healthy subjects. Plasma concentrations were determined by validated HPLC procedures and the data were analyzed by noncompartmental linear PK methods. Polymerase chain reaction (PCR)-based genotyping assays were used to identify four alleles; CYP2D6*1, CYP2D6*2x2, CYP2D6*5, and CYP2D6*10.

Results: Of the thirteen subjects, three subjects were wild type homozygotes (two carriers of *1/*1 and one of *1/*2 x2), four with heterozygotes (four of *1/*10), and six with mutant type homozygotes (four of *10/*10 and two of *5/*10). All tested pharmacokinetic parameters (AUC, Cmax, terminal half-life, and time above the effect concentration) showed significant differences in three genotypic groups. The AUC of heterozygotes and mutant type homozygotes were 2.2 and 8.4 folds higher than those of wild type homozygotes.

Conclusion: The presence of CYP2D6*5, CYP2D6*10, or CYP2D6*2X2 exerts important impact on the pharmacokinetics of tropisetron, which may influence the magnitude of clinical response of tropisetron therapy.

Key Words: tropisetron, CYP2D6 genotype, pharmacokinetics, Korean