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Frequency of Cytochrome P450 2C9 Mutant Alleles in a Korean Population and Pharmacokinetics of Glimepiride according to the CYP2C9 Genotype

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Background: The frequencies of CYP2C9 variants in the Korean population were evaluated again and the pharmacokinetics of glimepiride, a sulfonylurea hypoglycemic agent, was analysed according to the CYP2C9 genotypes.

Methods: Genotyping of CYP2C9*2 and CYP2C9*3 allelic variants was carried out in 100 Korean subjects and added to the previous data. 1 subject had CYP2C9 *1/*3 genotype and 1 had CYP-2C9*3/*3. Blood samples were collected at 0 (predose), 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 10, 12 hr after the oral administration of a dose of 2mg of glimepiride. The concentration of glimepride were measured with LC/MSMS. And the pharmacokinetic parameters were determined with WinNonllin.

Results: Values for pharmacokinetic parameter of control group (n=23) are 839.3 ?} 307.85 ??g/mL for AUC??(CV 36.68%), 2.55 ?} 0.993 L/h for CL(38.9%), 216.04 ?} 69.62 ??g/mL for Cmax (32.23%), 2.8 ?} 0.68 h for Tmax(24.2%), 2.9 ?} 0.64 h for t1/2(22%) and 0.246 ?} 0.0468h?1 for ke (19%). In the case of CYP2C9*3 homogygote, 1864.2 for AUC??, 0.463 for CL, 267.8 for Cmax, 4 for Tmax, 12.3 for t1/2, 0.0563 for ke.. The AUC?? of CYP2C9*3 homogygote was 222% of the respective value in control group and the t1/2 and mean residence time were more 420% of the control but the clearance was significantly reduced to 18% for the control. The distribution of AUC??, Tmax and t1/2 shows normal distribution (Shapiro-wilk, <0.05) and their probability for the PK values for CYP2C9*3 homogygote were less than 1%.

Conclusion: The frequency of CYP2C9 variants in Korean was evaluated again and subject of CYP-2C9*3 homozygote showed significantly different PK profiles of glimepiride.

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