MDR-1 유전적 다형성에 따른 fexofenadine의 약동학 및 약력학 특성 분석

손지홍, 전형민, 김경아, 김을선, 윤영란, 차인준, 신재국

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The PK and PD of Fexofenadine in Relation to MDR1 Genetic Polymorphism in Korean Healthy Subjects

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To evaluate the effect of MDR1 genetic polymorphism on the PK and PD of fexofenadine, a known substrate of P-glycoprotein.

Sixteen male subjects whose MDR1 genotype was determined for C3435T in exon 26 using PCR-RFLP method were enrolled(8 subjects with C/C allele; 8 subjects with T/T). After single oral dose of 120mg fexofenadine, blood samples were serially drawn and urine was collected upto 24 hours. Histamine skin test was also conducted for 4 hours to measure pharmacodynamic effect of fexofenadine.

There was no significant difference of PK parameters(AUCinf, Cl/F, and Vd/F) except for Cmax of fexofenadine(Cmax: 550.3±226.8 and 760.4±168.6 ng/ml, $p<0.05$) between subjects with C/C and T/T allele. The mean AUC0-4, a parameter determined by absorption, of subjects with T/T allele was 36% greater than that of subjects with C/C(2049.5±527.8 vs 1510.0±658.9 ng/ml · hr, respectively), but this difference was not statistically significant. In histamine skin test, the mean AUEC0-4 (the area under the % changes for histamine induced flare and wheal area) of subjects with T/T allele tends to be greater than that of subjects with C/C allele(73.3±34.7 vs 47.0±41.0 % · hr, respectively). At 1 hour after dose, however, the % change of wheal area was significantly different between two groups (12.7±47.1% vs -35.3±122.9% for C/C and T/T allele)

In conclusion, these results suggest that MDR1 genetic polymorphism seem to be responsible at least in part for the variability of fexofenadine disposition.