일반연제

Role of Genetic Polymorphism of CYP2C Families and Drug Interactions in Phenytoin Treatment

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Genetic polymorphism of *CYP2C* subfamily is responsible for the great interindividual variability in phenytoin pharmacokinetics. Also, inhibition of *CYP2C9* or *CYP2C19* enzymes by other drugs can alter the metabolic clearance of phenytoin. We examined the contribution of *CYP2C9* and *CYP2C19* genotypes and drug interactions to phenytoin treatment in 105 Korean epileptic patients. For genotyping, *CYP2C9*3*, *CYP2C19*2* and **3* allelic variants were identified by direct sequencing. On the basis of *CYP2C9* genotype, 94 patients (89.5%) were EMs (**1/*1*), 10 (9.5%) were IMs (**1/*3*), and 1 (0.9%) were PMs (**2/*3* or **3/*3*). For the *CYP2C19* genotype, 49 patients (46.6%) were EMs (**1/*1*), 49 (46.6%) were IMs (**1/*2* or **1/*3*), and 7 (6.7%) were PMs (**2/*2*, **2/*3*, or **3/*3*). The pharmacokinetic parameters for each patient were estimated from at least 2 serum phenytoin concentrations by Baysian analysis using Abbottbase Pharmacokinetic system. Five groups were categorized by *CYP2C9 and CYP2C19* genotypes. The results showed differences in their metabolic activity in terms of Vmax and Km between EM groups and IM groups of *CYP2C9*, while *CYP2C19* did not. Fifty-one patients (48.6%) were taking co-medications that could have interfered with phenytoin pharmacokinetics. In patients with phenytoin monotherapy, we found the genetic effect of *CYP2C19* on phenytoin pharmacokinetics was more statistically significant. In conclusion, *CYP2C9* polymorphism may be the major genetic factor responsible for the phenytoin metabolism in phenytoin monotherapy of Korean epileptic patients.