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Effect of Cytochrome P450 Oxidoreductase Ala503Val Genotype on the Pharmacokinetics of Amlodipine in Healthy Chinese Subjects

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***SUMMARY*. The aim of this study was to investigate the effects of cytochrome P450 oxidoreductase Ala503Val (POR*28 C>T) genotype on the pharmacokinetics of amlodipine in healthy Chinese subjects. Twenty-two male subjects were enrolled and genotyped for the POR*28 C>T gene. They were divided into three groups: subjects with POR*28 CC (n = 7), POR*28 CT (n = 8) and POR*28 TT (n = 7). After a single-dose administration of 5 mg amlodipine, plasma concentrations of amlodipine were measured and its pharmacokinetic characteristics were compared according to POR*28 C>T genotype. We found that the C_{max} values were highest in subjects with POR*28 TT (5.47 ± 0.91 ng/mL), lower in subjects with POR*28 CC (4.87 ± 0.99 ng/mL) and POR*28 CT (3.93 ± 1.08 ng/mL) in rank and showed a significant difference between those with TT and CT ($P = 0.008$). The $C_{max}/AUC_{0\text{-}inf}$ values, which were considered as a measure of the rate of drug absorption, were significantly higher in subjects with TT than in other two groups. However, there is no significant difference in $AUC_{0\text{-}t}$, $AUC_{0\text{-}inf}$, T_{max}, or $t_{1/2}$ values of amlodipine observed among the three POR*28 genotype groups. We demonstrated that POR*28 C>T polymorphism can affect the disposition of amlodipine in humans. But a clear relationship between POR*28 gene polymorphism and pharmacokinetics of amlodipine cannot be fully obtained in this study.**

KEY WORDS: Amlodipine, CYP3A, Gene polymorphism, P450 oxidoreductase, Pharmacokinetics.

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