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Comparison of the Pharmacokinetic and Pharmacodynamic Properties of S-amlodipine and Amlodipine Racemate in Healthy Male Subjects

Min-Gul Kim

Seoul National University College of Medicine and Hospital

Background/Aims: SK310 is an S-form enantiomer of amlodipine, a third-generation dihydropyridine calcium antagonist that is prescribed in the management of angina and hypertension. The S-form of amlodipine is the therapeutically active component, while the "R" form is essentially inactive. This study was performed to compare the pharmacokinetic (PK) and pharmacodynamic (PD) properties of a newly developed S-amlodipine gentisate (SK310), with a racemate (amlodipine besylate, Norvasc??) in healthy male subjects.

Methods: A randomized, double-blind, double-dummy, two-period, two-way crossover study was conducted in 24 healthy male Korean subjects. All subjects received a single oral dose of 10 mg amlodipine besylate and a single oral dose of 5 mg S-amlodipine gentisate with a two-week washout period in between. Blood samples for determination of S- and R-form enantiomer concentrations of amlodipine were obtained during a 168-hour period after dosing, and plasma concentrations were determined by LC-MS/MS. Systemic vascular resistance, cardiac index, and stroke volume were measured by impedance cardiography. Safety assessments were also performed.

Results: The mean plasma concentration-time profiles of S-form enantiomer of amlodipine were virtually similar after oral administration of the S-amlodipine gentisate or amlodipine racemate. The ratios (90% confidence intervals) of geometric mean values were 1.08 (0.98～1.18) for Cmax and 0.96 (0.88～1.04) for AUC, respectively, indicating that the two drugs were pharmacokinetically equivalent in terms of S-form enantiomer. Significant changes from baseline values in systemic vascular resistance, cardiac index, and stroke volume were observed in two drugs, but the changes for S-amlodipine gentisate were comparable to those for amlodipine besylate. No clinically relevant changes were observed in safety profiles.

Conclusions: The 5 mg of S-amlodipine gentisate and 10 mg of amlodipine besylate were pharmacokinetically equivalent in terms of S-form enantiomer and showed similar PD characteristics in healthy male subjects.