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Pharmacokinetic Evaluation of Orally Administered Pilsicainide in Healthy Koreans

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Background: Pilsicainide hydrochloride is an antiarrhythmic drug widely used in Japan. It shows antiarrhythmic properties by blocking sodium channels. We investigated the pharmacokinetics (PK) of a single oral dose of pilsicainide in healthy Korean male volunteers, and compared it to those of Japanese.

Methods: A parallel group, dose-escalation (50 mg and 100 mg), open-label study was conducted in 16 healthy male volunteers (8 per each dose group) at the Clinical Trial Center, Seoul National University Hospital. Plasma and urine samples were collected before dosing and at intervals up to 24 hours after single oral administration. In order to compare the PK parameters between Koreans and Japanese, we analyzed the Korean data together with PK parameters from an identical Japanese study, which was conducted separately but simultaneously with the Korean study.

Results: The mean AUCinf in Koreans were 2,865.7 and 5,460.8 ng*h/mL, Cmax were 501.6 and 868.8 ng/mL and terminal elimination half-lives (t1/2) were 4.7 and 5.4 hours in pilsicainide 50 mg and 100 mg groups, respectively. Maximum value of coefficients of variation among AUCinf, Cmax and t1/2 was 22.5%. The mean apparent volumes of distribution were 120.7 and 142.6 L, total apparent body clearances were 17.6 and 18.8 L/h and renal clearances were 13.9 and 15.7 L/h, in pilsicainide 50 mg and 100 mg group, respectively. PK parameters exhibited linear properties according to increasing doses. (P=0.451 and 0.208, dose-normalized AUCinf and Cmax, respectively). The geometric mean ratios (90% confidence intervals) for Koreans to Japanese were 1.04 (0.95~1.14; P=0.459) for AUCinf,, 1.01 (0.90~1.13; P=0.907) for Cmax and 1.10 (1.00~1.21; P=0.116) for t1/2.

Conclusion: The PK parameters of pilsicainide in Koreans showed relatively small interindividual variation, and were linear with respect to dose increments. Moreover, the results were not different with the PK parameters in Japanese.