Clinical Trial of Barnidipine in Patients with Renal Parenchymal Hypertension -Dose-Response Analysis by Mixed Effect Modeling-

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Barnidipine is a potent and long acting dihydropyridine calcium channel blocker. The effectiveness and safety of barnidipine for the treatment of renal parenchymal hypertension were evaluate. The study consisted of two weeks of observation and six or eight weeks of treatment periods. During the observation period, a placebo capsule was administered once a day. During the treatment period, barnidipine 5mg was administered once a day for two weeks. If the hypotensive goal(decrease in systolic blood pressure > 20 mmHg or diastolic pressure > 10 mmHg) was not attained, the dose of barnidipine was escalated to 10 or 15mg at interval of two weeks. Dose-response data were analyzed by nonlinear mixed effect model(NONMEM) using linear and Emax pharmacodynamic model.

There were no significant changes in heart rate, renal function, daily urinary protein and sodium excretion, serum renin, aldosetrone, serum electrolytes, uric acid and liver function test before and after barnidipine treatment. Blood pressure was effectively reduced in 80.6% of the patients. Pharmacodynamic parameters for systolic blood pressure were maximal reduction(Imax) of 39.1 mmHg(coeffecient of variation; 38.7%) and dose of half maximal reduction(IC50) of 7.21mg(125.7%) and residual error of 37.9%. Pharmacodynamic parameters for diastolic blood pressure were Imax of 22.6 mmHg(0.06%), IC50 of 5.44mg(106.3%) and residual error of 50.8%.