The effect of a newly synthesized ATP-sensitive potassium channel opener, MJ-355, on blood pressure and myocardial ischemia-reperfusion injury in rats.

許準榕
Lee YM;Peng YY;Sheu JR;Cheng CH;Yen MH.

Abstract

ATP-sensitive potassium (K(ATP)) channel openers, exerting a potent vasodilatory action, are useful in the treatment of cardiovascular disorders; e.g., hypertension and angina pectoris. This study was designed to evaluate the effect of MJ-355 (6-cyano-3,4-trans-3,4-dihydro-2,2-dimethyl-2H-3-hydroxy-4-[2-oxo-5S-(1-ethoxyethoxymethyl)-1-pyrrolidinyl]-1-benzopyran), a newly synthesized K(ATP) channel opener, on hemodynamics in spontaneously hypertensive rats and on myocardial ischemia-reperfusion injury in a rat model of 45 min left coronary artery occlusion followed by 1-h reperfusion. Intravascular injection of MJ-355 (0.005, 0.05 and 0.1 mg/kg) produced a dose-related reduction in mean arterial blood pressure. The depressor effect started 10-15 min after the administration and persisted for more than 3 h and was not accompanied by a reflex tachycardia. In myocardial ischemia, pretreatment of MJ-355 (0.02 mg/kg) significantly reduced the total number of ventricular premature contractions and ventricular tachycardia, total duration of ventricular fibrillation and the mortality. Additionally, a significant reduction in infarct size was noted in all of the MJ-355-treated groups. The hemodynamic and cardioprotective effects of MJ-355 were virtually abolished by pretreating the rats with glibenclamide (4 mg/kg, i.v. bolus), a selective K(ATP) channel blocker. In conclusion, MJ-355, through the activation of K(ATP) channels, exhibited antihypertensive and cardioprotective effects. It is suggested that MJ-355 should be useful in the treatment of hypertension and/or acute myocardial infarction.