CARDY-11

EFFECT OF PRAVASTATIN ON LEFT VENTRICULAR MASS IN THE TWO-KIDNEY, ONE CLIP HYPERTENSIVE RATS

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BACKGROUND/AIMS: We have demonstrated that myocardial ATP-sensitive potassium (KATP) channels are implicated in the development of cardiac hypertrophy. We investigated the effect of pravastatin on the development of ventricular hypertrophy in male normolipidemic Wistar rats with two-kidney one clip (2K1C) hypertension and whether the attenuated hypertrophic effect was via activation of KATP channels.

METHODS: Twenty-four hours after the left renal artery was clipped, rats were treated with one of the following therapies for 8 weeks: vehicle, nicorandil (an agonist of KATP channels), pravastatin, glibenclamide (an antagonist of KATP channels), hydralazine, nicorandil + glibenclamide, or pravastatin + glibenclamide. Systolic blood pressure, relative left ventricular weight, and cardiomyocyte sizes significantly increased in vehicle-treated 2K1C rats compared with those in sham-operated rats.

RESULTS: 2K1C rats in the nicorandil- and pravastatin-treated groups had significantly attenuated left ventricular hypertrophy/body weight as compared with the vehicle-treated group, which was further confirmed by downregulation of left ventricular atrial natriuretic peptide mRNA. Nicorandil-induced effects were abolished by administering glibenclamide. Similarly, pravastatin-induced beneficial effects were reversed by the addition of glibenclamide, implicating KATP channels as the relevant target. A dissociation between the effects of blood pressure and cardiac structure was noted because pravastatin and hydralazine reduced arterial pressure similarly.

CONCLUSIONS: These results suggest a crucial role of cardiac KATP channel system in the development of ventricular hypertrophy in the 2K1C hypertensive rats. Pravastatin is endowed with cardiac antihypertrophic properties probably through activation of KATP channels, independent of lipid and hemodynamic changes.

Keywords: Hypertension; Ion channels; Left ventricular mass; Statins; Rat.