Effect of pravastatin of left ventricular mass in the two-kindeny, one-clip hypertensive rats

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摘要

Abstract

We have demonstrated that myocardial ATP-sensitive potassium (KATP) channels are implicated in the development of cardiac hypertrophy in hyperlipidemic rabbits. We investigated the effect of pravastatin on 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. Twenty-four hours after the left renal artery was clipped, rats were treated with one of the following therapies for 8 wk: vehicle, nicorandil (an agonist of KATP channels), pravastatin, glibenclamide (an antagonist of KATP channels), hydralazine, nicorandil plus glibenclamide, or pravastatin plus glibenclamide. Systolic blood pressure, relative left ventricular (LV) weight, and cardiomyocyte sizes significantly increased in vehicle-treated 2K1C rats compared with those in sham-operated rats. Treatment with either nicorandil or pravastatin significantly attenuated LV hypertrophy/ body weight compared with the vehicle, which was further confirmed by downregulation of LV 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. 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