Effect of pravastatin on left ventricular mass by activation of myocardial Katp channels in hypercholesterolemic rabbits

張念中

Lee Tsung-Ming;Lin Mei-Shu;Chou Tsai-Fwu;Tsai Chang-Her;Chang Nen-Chung

摘要

Abstract

Epidemiological studies showed that hypercholesterolemia was associated with a higher left ventricular mass. Myocardial ATP-sensitive potassium (KATp) channels have been implicated in the development of cardiac hypertrophy. We investigated the effect of pravastatin on hypercholesterolemia-induced ventricular hypertrophy and whether the attenuated hypertrophic effect was via activation of myocardial KATp channels. In this study, we evaluated the hemodynamic, biochemical, and morphological responses to pravastatin in cholesterol-fed (1%) rabbits. Male New Zealand White rabbits were randomized to either vehicle, nicorandil (an agonist of KATp channels), pravastatin, glibenclamide (an antagonist of KATp channels), or a combination of nicorandil and glibenclamide or pravastatin and glibenclamide for 8 weeks. The left ventricular weight and left ventricular myocyte sizes increased 8 weeks after cholesterol-feeding in comparison to that in normocholesterolemic rabbits. Pravastatin administration significantly decreased the left ventricular weight by 12% and cardiomyocyte cell areas by 30 %. Hyperlipidemic rabbits in the nicorandil- and pravastatin -treated groups significantly attenuated cardiomyocyte hypertrophy, as compared with the vehicle-treated group (3162 +/- 1277 mum(2), 3372 +/- 228 mum(2) versus 4388 +/- 163 mum(2) in the vehicle group, both $P < 0.0001$, respectively). 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. The results of the present study suggest a pathogenetic role of KATp channels in hypercholesterolemia- induced ventricular hypertrophy. The antihypertropic effects of pravastatin may be related to activation of KATp channels, and result in an amelioration of cardiomyocyte hypertrophy development by an atherogenic diet.