Effect of Pravastatin on development of Left ventricular hypertrophy in Spontaneously Hypertensive Rats

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摘要

Abstract

Endothelin (ET)-1 has been implicated in the development of cardiac hypertrophy. We investigated the effect of pravastatin on development of ventricular hypertrophy in spontaneously hypertensive rats (SHR) and whether the attenuated hypertrophic effect was via reduced ET-1 expression . Normolipidemic SHR were treated with one of the following therapies for 8 wk: vehicle, the nonselective ET receptor antagonists bosentan, pravastatin, mevalonate, hydralazine, or combination of pravastatin + mevalonate from the age of 8 wk at the very early stage of cardiac hypertrophy. Treatment with bosentan and pravastatin significantly decreased left ventricular mass index for body weight and cardiomyocyte sizes isolated by enzymatic dissociation. The myocardial ET-1 levels and preproET-1 mRNA assessed using real-time quantitative RT-PCR were significantly higher (both $P < 0.001$) in the SHR compared with Wistar- Kyoto rats. The increased tissue ET-1 levels can be inhibited after pravastatin administration. Immunohistochemical analysis confirmed the changes of ET-1. Left ventricular mass index for body weight correlated positively with tissue ET-1 levels ($P = 0.0004$). A dissociation between the effects of blood pressure and cardiac structure was noted, because pravastatin and hydralazine reduced arterial pressure similarly. Pravastatin -induced effects were reversed by the addition of mevalonate . In conclusion, these results suggest a crucial role of cardiac endothelin system in the early development of ventricular hypertrophy in the SHR. Pravastatin is endowed with cardiac antihypertropic properties that are independent of its hemodynamic and hypolipidemic effects and appear to be related to their capacity to decrease cardiac ET-1 levels , which is linked to mevalonate metabolism