IInhibition of histone deacetylase on ventricular remodeling in infarcted rats

張念中

Lee Tsung-Ming;Lin Mei-Shu;Chang Nen-Chung

摘要

Abstract

Inhibition of histone deacetylase on ventricular remodeling in infarcted rats. Am J Physiol Heart Circ Physiol 293: H968 - H977, 2007. First published March 30, 2007; doi:10.1152/ ajpheart.00891.2006.- Histone deacetylase (HDAC) determines the acetylation status of histones and, thereby, controls the regulation of gene expression. HDAC inhibitors have been shown to inhibit cardiomyocyte growth in vitro and in vivo. We assessed whether HDAC inhibitors exert a beneficial effect on the remodeling heart in infarcted rats. At 24 h after ligation of the left anterior descending artery, male Wistar rats were randomized to vehicle, HDAC inhibitors [valproic acid (VPA) and tributyrin], an agonist of HDAC (theophylline), VPA + theophylline, or tributyrin + theophylline for 4 wk . Significant ventricular hypertrophy was detected as increased myocyte size at the border zone isolated by enzymatic dissociation after infarction. Cardiomyocyte hypertrophy and collagen formation at the remote region and border zone were significantly attenuated by VPA and tributyrin with a similar potency compared with that induced by the vehicle. Left ventricular shortening fraction was significantly higher in the VPA- and tributyrin -treated groups than in the vehicle-treated group. Increased synthesis of atrial natriuretic peptide mRNA after infarction was confirmed by RT-PCR, consistent with the results of immunohistochemistry and Western blot for acetyl histone H4. The beneficial effects of VPA and tributyrin were abolished by theophylline, implicating HDAC as the relevant target. Inhibition of HDAC by VPA or tributyrin can attenuate ventricular remodeling after infarction. This might provide a worthwhile therapeutic target.