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基础医学

瑞舒伐他汀逆转压力超负荷引起心肌肥厚的作用机制

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摘要：

目的 探讨瑞舒伐他汀(RSV)逆转腹主动脉缩窄术大鼠引起心肌肥厚的作用机制。方法 28只健康雄性Wistar大鼠随机分为假手术组、手术组、瑞舒伐他汀小剂量组［4mg/(kg·d)］和瑞舒伐他汀大剂量组［10mg/(kg·d)］，每组7只。腹主动脉缩窄术前5d及术后4周,各组均用相对应剂量的瑞舒伐他汀或生理盐水灌胃。术后4周结束实验，测量4组Wistar大鼠超声心动图参数、左室质量/体质量(LVW/BW)并观察左心室组织横截面细胞面积。采用RT-PCR法检测心肌组织中肥大相关因子ANF、β-MHC mRNA表达水平,Western blot法检测大鼠心肌细胞细胞核内GATA4、磷酸化的GATA4(p-GATA4)蛋白水平。结果 与假手术组相比，手术组舒张期室间隔厚度(IVSd)、左室后壁厚度(LVPWd)、左室质量/体质量(LVW/BW)和左室横截面心肌细胞面积(CSA)均明显增加(P＜0.01)。在瑞舒伐他汀小剂量组与瑞舒伐他汀大剂量组，IVSd、LVPWd、CSA较手术组明显减小(P＜0.01)，LVW/BW较手术组也有较明显的减小(P＜0.05)，且瑞舒伐他汀小剂量组与瑞舒伐他汀大剂量组结果无明显差异(P＞0.05)，即左心室肥厚明显减轻。手术组大鼠左室射血分数(LVEF)较假手术组明显减低，瑞舒伐他汀小剂量组与瑞舒伐他汀大剂量组有明显改善(P＜0.01)。 手术组ANF、β-MHC mRNA表达以及GATA4磷酸化水平较假手术组明显升高(P＜0.01), 瑞舒伐他汀小剂量组与瑞舒伐他汀大剂量组较手术组大鼠左心室组织中ANF、β-MHC mRNA表达以及GATA4磷酸化水平明显降低(P＜0.01)。结论 GATA4可能参与了压力超负荷性引起的心肌肥厚过程，瑞舒伐他汀可抑制压力超负荷性引起的心肌肥厚，其作用机制可能与降低GATA4活性有关。

关键词： 瑞舒伐他汀；压力超负荷；心肌肥厚；GATA4

The mechanism of Rosuvastatin on regression of pressure overload induced myocardial hypertrophy

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Abstract:

Objective To discuss the molecular mechanisms of Rosuvastatin (RSV) on regression of myocardial hypertrophy induced by abdominal aortic constriction. Methods Twenty-eight male Wistar rats were randomly divided into 4 groups: sham-vehicle (SH-V), abdominal aortic constriction-vehicle (AAC-V), abdominal aortic constriction-RSV［4mg/(kg·day)］(AAC-LO), and abdominal aortic constriction-RSV ［10mg/(kg·day)］(AAC-HI). There were 7 rats in each group. From 5 days pre-operation to 4 weeks post-operation, four groups were performed by gavage administration with equal volume of RSV and vehicle. The research was finished 4weeks after the surgery. Echocardiography data, the ratio of LV weight to body weight (LVW/BW) and left ventricle myocyte cross-sectional area were evaluated. Reverse transcription PCR (RT-PCR) was adopted to test ANF and β-MHC mRNA expression levels which were related to myocardial hypertrophy. Western Blots analysis was used to detect GATA4 and phospho-GATA4(Ser105)protein levels in rat myocardial tissue. Results Compared to SH-V group, thickness of interventricular septum in diastole (IVSd) , diastolic left ventricular posterior wall thickness (LVPWd), the ratio of left ventricular weight to body weight (LVW/BW) and myocyte cross-sectional area (CSA) were significantly increased (P<0.01) in AAC-V group. In AAC-LO and AAC-HI groups, IVSd, LVPWd and CSA were obviously decreased (P<0.01) and LVW/BW was also decreased (P<0.05) compared to AAC-V group, and there was no significant difference between AAC-LO and AAC-HI groups(P＞0.05). These results indicated that myocardial hypertrophy alleviated. Left ventricular ejection fraction (LVEF) in AAC rats was significantly decreased compared with SH V group (P<0.01). LVEF in AAC-LO and AAC-HI groups promoted distinctly (P<0.01) compared to AAC-V group (P<0.01). ANF and β-MHC mRNA expressions and phospho-GATA4 (Ser105) protein levels in AAC group were significantly increased compared to SH-V group (P<0.01), and in AAC-LO and AAC-HI groups these indexes were decreased obviously

compared to AAC group (P<0.01). Conclusion GATA4 may participate in the process of myocardial hypertrophy caused by pressure overload and RSV could reverse pressure overload-induced myocardial hypertrophy by decreasing GATA4 activity.

Keywords: Rosuvastatin; Pressure overload; Myocardial hypertrophy; GATA4

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