

MYOSTATIN EXPRESSION IN VENTRICULAR MYOCARDIUM IN A RAT MODEL OF VOLUME-OVERLOAD HEART FAILURE

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BACKGROUND : Mechanical stretch and in vivo acute hemodynamic overload increase myocardial myostatin expression. However, the expression of myostatin in chronic heart failure due to volume overload and after treatment with β -blockers is little known.

METHODS AND RESULTS : To test the hypothesis that myostatin plays a role in the failing myocardium because of volume overload, aorto-caval shunts were created for 4 weeks in adult Sprague-Dawley rats to induce volume-overload heart failure. Carvedilol at 50 mg/kg body weight, doxazosin at 3 mg/kg body weight, or N-acetylcysteine at 250 mg/kg body weight per day after surgery were given. The heart weight and body weight ratio increased from 2.7 ± 0.3 in the sham group to 3.8 ± 0.9 ($p<0.001$) in the shunt group. Left ventricular end-diastolic dimension increased from 7.1 ± 0.7 mm to 8.9 ± 1.4 mm ($p<0.001$). Treatment with carvedilol in the shunt group reversed the increase in heart weight and ventricular dimension to baseline values. Western blot showed that myocardial and skeletal myostatin proteins were upregulated in the shunt group. Real-time polymerase chain reaction showed that mRNA of myocardial myostatin increased in the shunt group. Treatment with carvedilol reversed both protein and mRNA of myocardial myostatin to baseline values. Treatment with N-acetylcysteine and doxazosin partially decreased myostatin mRNA and protein expression as compared with the shunt group. Increased immunohistochemical labeling of myostatin in the ventricular myocardium was observed in the shunt group and carvedilol again normalized the labeling.

CONCLUSION : Myocardial myostatin mRNA and protein expression were upregulated in the rat model of volume-overload heart failure. Treatment with carvedilol is associated with a reversal of abnormal regulation of myostatin in the failing ventricular myocardium.

Key words: myostatin, heart failure, volume overload