THE MECHANISM OF HYPERSUSCEPTIBILITY IN ISCHEMIC-REPERFUSION INJURY RATS WITH HYPERCHOLESTEROLEMIA

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Objective

The present study was undertaken to investigate the role of MPO in ischemic-reperfusion (I/R) injury rats with HC and to explore its related mechanism.

Methods

Sixty Sprague–Dawley (SD) rats were randomly divided into Sham, I/R+normal diet, I/R+Vehicle+HC diet, I/R+ABAH+HC diet groups. The cardiac function was evaluated by ultrasound cardiograph (UCG) and Powerlab system. The changes of Total Cholesterol (TC), Triglyceride (TG), Low Density Lipoprotein Cholesterol (LDL-c) and CK, LDH in serum were evaluated. Cardiomyocyte apoptosis was examined by TUNEL’s method. The activity of Ventricular MPO and NO were also measured. The mRNA and the protein expression of NOS were assessed by RT-PCR and Western blot.

Results

The lipid levels in vehicle+high cholesterol group was significantly higher than control group after feeding with high-cholesterol diet for 10 weeks. Compared with sham group, the CK and LDH content in I/R group increased significantly; Compared with normal diet I/R group, the CK and LDH content in HC I/R group increased significantly. And the apoptotic index in I/R group was significantly higher than that in sham group; the apoptotic index in HC I/R group was significantly higher than that in normal diet I/R group. The myocardial infarct size of HC I/R group was significantly enhanced as compared with normal diet I/R group. Compared with the normal diet I/R group, HC I/R group had lower LVSP and ±dp/dt max, higher MPO and NO activity, and the apoptosis index was also increased with a higher mRNA and protein express of iNOS; compared with I/R+Vehicle+HC diet group the expression of iNOS in I/R+ABAH+HC diet group decreased; and compared with control group, the mRNA and protein expression of eNOS in vehicle+high cholesterol group decreased significantly.

Conclusion

The MPO content and activity significantly increased in myocardial tissue of HC rats, which prompted the vulnerability of I/R rats with HC. The increased MPO content and activity accompanied by impaired NO signaling pathway.