Aerobic Exercise Attenuates Myocardial Injury Through Activation of SIRT1 Signaling in T2DM Rats

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Objective Myocardial injury caused by elevated blood glucose is a major risk factor for type 2 diabetes mellitus (T2DM) cardiomyopathy. Aerobic exercise can significantly improve the energy metabolism and is widely used in clinic to prevent and cure T2DM and other metabolic diseases. Myocardial injury can be attenuated after aerobic exercise. Some researches showed SIRT1 is a histone deacetylation enzyme activated by NAD+/NADH, and mainly distributes in the heart, liver, etc. SIRT1 plays an important role in controlling the insulin secretion, which can regulate glucose and lipid metabolism and some other important biological functions. It is not known whether the myocardial injury was reduced by regulating the level of SIRT1 after aerobic exercise. The purpose of the research was to illustrate the regulatory mechanism of decreased myocardial injury after aerobic exercise, and provided theoretical basis for early prevention and treatment of T2DM myocardial injury.

Methods There were two stages in the experiment. At the first stage, 30 male SD rats, 12-month old, were randomly divided into two groups, the control group (CC, fed with standard diet and kept sedentary, 8 rats), the high-sugar-lipid fodder for T2DM model Group (DC, kept sedentary, 22 rats). High sugar and high fat diet formula for 10% lard, 20% sucrose, egg yolk powder 8%, 0.1% sodium deoxycholate, 61.9% basic feed, AIN-93g, provided by animal experimental center of Hebei Province. After 5-week high-sugar-lipid fodder, the DC rats were injected streptozocin (STZ, 35mg/kg), the FBG of the tail vein were measured after 12h, and FBG≥7.0mmol/L was defined as T2DM model. Six rats were excluded because of low FBG (<7.0mmol/L). At the second stage, all of the rats were fed with standard diet. The T2DM rats were randomly assigned to the T2DM group (DC, kept sedentary, 8 rats) and T2DM combined with aerobic exercise, (DE, run on treadmill at 15m/min ~ 19m/min, 45min/d, slope 5%, 6d/w, 5W, 8 rats). The myocardial tissue sections were stained with hematoxylin and eosin (HE) to observe the histological changes. The level of serum insulin was examined by ELISA kits. The content of serum glucose, the activity of SOD and the content of MDA in heart were examined by reagent kits after 5 weeks. The expression of SIRT1 protein in heart were measured using Western blot. ELISA kits were used for the determination of the NAD+/NADH ratio.

Results (1) The myocardial sections of CC can be observed clear cell contour, bright color, arranged closely and neatly, and nuclear distribution in cells border and nuclei of uniform size. In DC myocardial sections, myocardial cell contour was fuzzy, nuclei were relatively large, reduced the number of nuclei and inward migration. The broken cells and part of the cells and nuclei overflow can also be seen. The shape of nucleus was irregular and shifted to the internal. In myocardial cell sections of DE rats, the cell profile was relatively clear, and arranged more orderly, a larger number of nuclei, generated less shift. (2) The plasma insulin of DE were obviously lower than that of DC (P<0.01). The content of serum glucose of DE was significantly decreased compared with that of DC (P<0.01). (3) The ratio of NAD+/NADH in DE heart was higher than that of DC (P<0.05). (4) The expression of SIRT1 in DE heart was higher than that of DC (P<0.05). (5) The activity of SOD in DE heart was increased while the content of MDA in DE was significantly decreased compared with those in DC (P<0.01).
Conclusions Aerobic exercise can effectively reduced the blood glucose level of T2DM rats. The NAD+/NADH ratio in the myocardium of T2DM rats were increased after the aerobic exercise. As a result, the content of SIRT1 protein in myocardial cells of T2DM rats were increased after the aerobic exercise, which resulted in the increased SOD activity and antioxidant capacity in the cardiac muscle cells, which lead to the attenuated myocardial injury in T2DM rats.