Abstracts

EFFECT OF SIRT1 GENE ON CARDIAC FUNCTION AND LIFE

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Aims To observe effect of SIRT1 gene on cardiac function and life and study influence of SIRT1 gene on myocardial express of AMPK.

Methods Heart failure model of rats were set up by ligating left anterior descending artery, the sham group (n=10) and the heart failure group (n=11) were given normal dietary; the treatment group (n=11) was given resveratrol 2.5 mg/kg/d orally. Heart functions were tested by echocardiography in rats. Hearts of SIRT1(+/−) (n=4) and wild type (WT) (n=5) mice were perfused on Langendorff. Days of SIRT1(+/−) (n=3) and WT (n=3) mice life were recorded. H9c2 cells were cultivated with different concentrations of resveratrol (0, 10, 25, 50, 100 uM) for 24 hours, and SIRT1 overexpression H9c2 cell line cultivated in different concentrations of nicotinamide (0, 10, 20, 40 mM) for 24 h, SIRT1 and AMPK expressions by Western blotting.

Results Compared with the heart failure group, Resveratrol treatment group demonstrated a sharp decrease in mortality (p<0.01) and increase in left ventricular ejection fraction (LVEF) (46.84±6.06 vs 34.44±2.13 %, p<0.01). AMPK expression increased (p<0.05). Compared with wild type, LVPmax, +dP/dTmax, -dP/dTmax were significantly reduced in SIRT1 (+/−) mice (111.04±13.97 vs 141.90±6.63 mm Hg, 2944.33±461.02 vs 7122.73±1083.12 mm Hg/s, 2081.72±323.81 vs 4807.48±789.79 mm Hg/s, p<0.01 respectively), AMPK expression also decreased significantly in SIRT1 (+/−) mice hearts (p<0.01), Life of SIRT1 (+/−) mice is shorter than that of WT mice (p<0.01). Expression of SIRT1 and AMPK was significantly increased in H9c2 cells cultivated with resveratrol (50, 100 uM) as compared with control H9c2 cells (p<0.01), AMPK expression was significantly increased in H9c2 cells by SIRT1 overexpression (p<0.01), but reduced in groups of NAM (20, 40 mM) compared with control (p<0.01, respectively).

Conclusions These results indicate that SIRT1 may improve heart systolic and diastolic function via increasing AMPK expression.