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## CARDIAC PROTECTIVE EFFECTS OF RESVERATROL AND SIRT1 IN OLD RAT WITH EMPHYSEMA INDUCED BY CIGARETTE SMOKE-EXPOSE AND LIPOPOLYSACCHARIDE INSTILLATION: ATTENUATION OF OXIDATIVE STRESS AND APOPTOSIS

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**Objective** To determine the Cardiac protective effects of resveratrol in old rat with emphysema.

**Material and Methods** Twenty-two months old SD rats were divided to control (CTL) group, smoking/lipopolysaccharide (SM/LPS) group and SM/LPS plus resveratrol (SM/LPS-Res) group. The SM/LPS group rats were exposed to Cigarette smoking (CS) (0.5 h/day) for eight weeks and instillation of LPS 200 μg/200 μl at the first day and the 25th day. SM/LPS-Res group rats were administered with resveratrol (25 mg/d/kg, 1 day before and throughout the experimental period) and exposed to the above-described cigarette smoking and LPS instillation protocol.

**Results** The cardiac hypertrophy ratio LVW/BW was increased in SM/LPS group as compared with CTL rats (3.20±0.30 vs 2.61±0.15, $p<0.05$), resveratrol can significantly decreased the LVW/BW as compared with the SM/LPS group (2.95±0.23 vs 3.20±0.30, $p<0.05$). Histological analyses and calculations of the cardiomyocyte cross-sectional area showed the average cardiomyocyte size in the LV of rats in SM/LPS group was higher than that in CTL group, the area of fibrosis in resveratrol treated emphysema rats was decreased from that of SM/LPS rats (28±9% vs 55±11%, $p<0.05$). Immunostaining of the sections for 8-OHdG showed that 8-OHdG expression was increased in cardiac tissue of SM/LPS rat which could be decreased by by treatment with resveratrol ($p<0.05$). Concentration of cardiac malondialdehyde (MDA) was higher in SM/LPS group than that in CTL group ($p<0.05$). Heart in rats of the SM/LPS group showed lower activity of SOD ($p<0.05$). Resveratrol significantly increased the activity of SOD in SM/LPS-Res group when compared with that in SM/LPS group ($p<0.05$). R-T Quantitative PCR detection for SIRT1 mRNA expression showed that SIRT1 mRNA was decreased in SM/LPS rats compared with CTL rats (2.7±1.7 vs 11.0±1.2, $p<0.05$) and increased by resveratrol (7.5±1.5 vs 2.7±1.7, $p<0.05$). Treatment of resveratrol increased the expression of SIRT1 protein in SM/LPS-Res rats. The immunofluorescence study showed that the SIRT1 protein was mainly localised in nuclei of cardiomycite, and increased in SM/LPS-Res rats compared with that in SM/LPS rats.

**Conclusion** Resveratrol attenuated cardiac oxidative damage and improved the ventricular remodeling, and enhance the decreased expression of SIRT1 in heart of old rats with emphysema. Thus there may be therapeutic modality for cardiac injury complicated in COPD.