RESVERATROL ATTENUATES MYOCARDIAL ISCHEMIA/REPERFUSION INJURY VIA UPREGULATING ADIPONECTIN LEVEL AND MULTIMERISATION IN TYPE 2 DIABETIC MICE

Qiang Yang, Chao Gao, Haifeng Zhang, Yi Liu, Xiaoyan Lu, Shidong Feng, Jingyi Liu, Peilin Liu, Han Wang, Sun Lu, Yang Lu, Haichang Wang, Ling Tao

Department of Cardiology, Xijing Hospital, Center of Teaching Experiment, Fourth Military Medical University, Xijing, China

10.1136/heartjnl-2011-300867.85

**Objectives**

Type 2 diabetes (T2DM) exacerbated myocardial ischemia/reperfusion (MI/R) injury, accompanied by significantly lower adiponectin (APN) level and diminished APN multimerisation. Resveratrol, a natural polyphenol, promotes APN up-regulation and multimerisation both in adipocytes and mice by up-regulation of DsbA-L (a recently identified protein that facilitates APN multimerisation and stability). Therefore, the present study aimed to observe whether RSV attenuates MI/R injury in T2DM, and if so, to further investigate the underlying mechanisms.

**Methods**

T2DM was induced by high-fat diet (HD) feeding plus low-dose streptozotocin (STZ) injection. Mice received an HD since three weeks old for eight weeks. After three weeks of HD feeding, mice were intraperitoneally injected with 100 mg/kg STZ (Sigma). T2DM was confirmed by markedly elevated fasting-blood glucose level (>11.1 mmol/l) five weeks after injection. Mice were treated with 10 mg/kg RSV daily by intragastric administration for three weeks since five weeks of HD feeding. Compound C (an AMPK inhibitor) was administrated by intraperitoneal injection with 20 μg/g one h before MI/R. Mice were subjected to 30 min of ischemia and three h or 24 h of reperfusion.

**Results**

HD feeding plus low-dose STZ injection successfully induced T2DM. Compared to normal control, diabetic mice manifested higher fasting-blood glucose level, lower glucose tolerance in OGTT examination (n=12, p<0.05), but there
was no difference in plasma insulin levels. RSV alleviated MI/R injury in both normal and diabetic mice, as evidenced by decreased infarct size, cardiomyocytes apoptosis, caspase-3 activity, improved cardiac function (n=10, all p<0.05). Moreover, RSV treatment improved APN level, upregulated APN multimerisation both in plasma and adipose tissue, and increased DsbA-L expression in adipose tissue in diabetic mice (all p<0.01). Conversely, administration of AMPK inhibitor Compound C significantly attenuated the cardioprotective effects of RSV (all p<0.05).

**Conclusions** RSV upregulates adiponectin level and multimerisation in both plasma and adipose tissue in T2DM, and therefore attenuates MI/R injury.