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INSULIN TREATMENT INCREASES BOTH PLASMA AND CARDIAC ADIPONECTIN LEVELS AND THUS REDUCES MYOCARDIAL ISCHEMIA/REPERFUSION INJURY IN TYPE 1 DIABETIC MICE

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Objective Adiponectin is a protein secreted predominantly by differentiated adipocytes, which plays a protective role in the development of insulin resistance and exerts beneficial actions on the hearts subjected to ischemia/reperfusion (I/R) insult. Insulin has been proved to reduce myocardial I/R injury in both normal and diabetic ones. These suggest the relationship between the insulin and adiponectin effects in diabetes. The present study aimed to investigate the effect of insulin treatment on the systemic and local cardiac adiponectin levels and on the myocardial I/R injury in type 1 diabetic mice.

Methods type 1 diabetic mice were rendered through 5 days of daily intraperitoneal injection with 40 mg/kg STZ, and confirmed by markedly elevated fasting-blood glucose levels (>11.1 μmol/l). Insulin (5 IU/kg·d) was administrated for a 14, 7 or 1 day duration, respectively, since diabetic models were established. MI/R was performed by Langendorff perfusion ex vivo in hearts from the 14 day duration mice, in which the hearts were subjected to 40 min of ischemia and 60 min of reperfusion.

Results The plasma adiponectin level in type 1 diabetic mice increased on the day 7 but decreased on the day 14 ($p<0.01$ vs control). At the same time, cardiac adiponectin mRNA level in type 1 diabetic mice gradually decreased ($p<0.01$ vs control). The diabetic hearts showed an increased infarct size and cardiomyocytes apoptosis ($p<0.01$). Insulin treatment increased both the plasma and cardiac adiponectin level in diabetic mice ($p<0.05$), and decreased the infarct size and cardiomyocytes apoptosis in type 1 diabetic mice ($p<0.01$ vs diabetic). Compound C pretreatment (an inhibitor of AMPK) partly inhibited the effect of insulin treatment ($p<0.01$).

Conclusions Insulin treatment increases both plasma and cardiac adiponectin levels, which is at least partly responsible for the cardioprotective effects of insulin treatment in diabetes.