

**THIAZOLIDINEDIONE AND STATIN PROTECT AGAINST MYOCARDIAL DAMAGE IN DIABETIC RATS SUFFERING FROM HEATSTROKE**

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**BACKGROUND/AIMS** Experiments were carried out to ascertain whether the expression of leptin and PPAR-r involved myocardial damage in heat stroke. We validated the hypothesis that pioglitazone and atorvastatin confer myocardial protection in diabetes against heat stroke-induced diabetic rats by stimulating the expression of leptin and PPAR-r.

**METHODS** We assessed the effects of heat stroke on mean arterial pressure (mSAP), heart rate (HR), cardiac output (CO) and stroke volume (SV), total peripheral vascular resistance (TPR), colonic temperature, blood gases, and serum levels of leptin and tumor necrosis factor-alpha (TNF- $\alpha$ ) in rats with and without pretreatment with pioglitazone and atorvastatin for 4 weeks. In addition, heat shock protein (HSP) and injury marker expression in the heart was determined in different groups of normal and diabetic rats. Heat stroke was induced by exposing the animals to high blanket temperature.

**RESULTS/CONCLUSION** mSAP, CO and SV, blood pH, onset time of heat stroke and survival time after heat stress were all lower in diabetic rats. However, blood lactate concentrations, TPR, levels of leptin and TNF- $\alpha$  were greater in diabetic rats exposed to heat stress. Diabetic rats with and without pioglitazone and atorvastatin pretreatment, when exposed to the same heat stress, had longer onset and survival times, greater CO and SV, longer latency times for onset of cardiac arrhythmia, higher leptin levels and lower TNF- $\alpha$  level in pioglitazone- and atorvastatin-pretreated diabetic rats. After the onset of heat stroke, HSP and injury markers in the heart were found to be significantly higher and lower, respectively, in pioglitazone- and atorvastatin-pretreated diabetic rats than diabetic rats without pretreatment. Thus, it appears that the observed benefit of PPAR-r receptor stimulator and statin is related to attenuation of cardiac arrhythmia and elevation of leptin and HSP expression during heat stroke in diabetic rats.

**Keywords:** Pioglitazone. Atorvastatin. Stress Protein.