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THIAZOLIDINEDIONE PRETREATMENT PROTECT AGAINST RENAL DAMAGE FOLLOWING EXPOSURE TO HEATSTROKE IN DIABETIC RATS

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BACKGROUND/AIMS Experiments were carried out to ascertain whether the expression of leptin and peroxisome proliferator-activated receptor-gamma nuclear receptor (PPAR- r) are involved in renal damage in heatstroke-induced circulatory shock.We validated the hypothesis that the PPAR-r-stimulating agent pioglitazone may confer renal protection in diabetes against heatstroke-induced injury in diabetic rats by stimulating the expression of leptin and PPAR-r.

METHODS We assessed the effects of heatstroke on mean arterial pressure (mSAP), heart rate (HR), renal blood flow (RBF), total peripheral vascular resistance (TPR), colonic temperature, blood gases, and serum levels of leptin and tumor necrosis factor-alpha (TNF-α) in rats with and without pioglitazone pretreatment for 2 weeks. In addition, heat shock protein (HSP) and expression of injury markers in the kidney was determined in different groups of normal and diabetic rats.

RESULTS/CONCLUSION mSAP, RBF, blood pH, onset time of heatstroke and survival time after heat stress were all lower in diabetic rats. However, blood lactate concentrations, TPR, levels of leptin and TNF-α were greater in diabetic rats exposed to heat stress. When exposed to the same level of heat stress, pioglitazone-pretreated diabetic rats had longer onset and survival times, greater RBF, higher leptin levels and lower TNF-α levels. Western blot assay revealed heat stress induced HSP and expression of injury markers in the kidney. After the onset of heatstroke, HSP and injury markers in the kidney were found to be significantly higher and lower in pioglitazone-pretreated diabetic rats and non-pretreated diabetic rats, respectively. Thus, it appears that the observed benefit of PPAR-γ stimulation is related to attenuation of tissue hypoperfusion and elevation of leptin and HSP expression during heatstroke in diabetic rats.

Keywords: Pioglitazone. Stress Protein. Diabetes Mellitus.