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Glucose transporter type 4 mediates the cardioprotective effects of RAS antagonism in the Diabetic Heart

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Background and objectives: Diabetes mellitus (DM) is a risk factor for cardiovascular diseases specifically the ischemic heart diseases (IHD). Renin angiotensin system (RAS) affects the heart directly and indirectly. However, its role in the protection of the heart against ischemia and reperfusion (I/R) injury is not completely understood. The aim of the current study was to evaluate the efficacy of the angiotensin-converting enzyme (ACE) inhibitor and Angiotensin II receptor (AT1R) blocker or a combination thereof in protection of the heart against I/R injury.

Methods: Hearts isolated from adult male Wistar rats (n=8) with STZ-induced diabetes were used in this study. Hearts were subjected to I/R injury, treated with Captopril, ACE inhibitor, Losartan, AT1R antagonist or a combination thereof. Hemodynamic data was acquired online using software designed specifically for that purpose. Infarct size was evaluated using 2,3,5-Triphenyltetrazolium chloride (TTC) staining. Hearts lysates were used to evaluate the levels of apoptosis markers (caspase 3 and 8) and Glucose transporter type 1 and 4 (GLUT-1 and GLUT-4) using Western blotting. Pro-inflammatory cytokines were evaluated by enzyme linked immunosorbent assay (ELISA). Data were analyzed using two-way analysis of variance (ANOVA).

Results: Captopril and Losartan alone or in combination abolished the effect of I/R injury in the diabetic hearts. Captopril and Losartan alone or in combination resulted in a significant ($P<0.05$) recovery in the hemodynamics, reduced the infarct size and the apoptosis markers. Treatment with Captopril, Losartan and their combination significantly ($P<0.05$) reduced, pro-inflammatory cytokines and increased GLUT-4 protein levels. Conclusions: Blocking RAS system protected the diabetic heart from I/R injury. This protection followed a pathway that uses GLUT-4 axis to decrease the apoptosis markers and pro-inflammatory cytokines.

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Key words: Ischemia Reperfusion, RAS, Captopril, Losartan, Diabetes mellitus, Hyperglycemia.

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Biography

Dr. F. A. Babiker is a Professor at the department of physiology, faculty of medicine, Kuwait University, Kuwait. He is a molecular cardiologist with training and research experience at department of cardiology, faculty of medicine, Maastricht University, the Netherlands. Previously, he served as a research associate at the department of physiology, Cardiovascular Research Institute Maastricht (CARIM) and a lecturer at the premedical school, Maastricht University, Maastricht, the Netherlands. He worked on many projects on ischemia/reperfusion injury and heart failure.

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