RESUMO

The glucocorticoids besides having a wide therapeutic action, when used in high doses or in a chronic manner can promote metabolic disorders, such as hyperglycemia, hyperlipidemia and insulin resistance (IR) and, therefore, the development of diabetes mellitus. Thus, IR has been considered a risk factor for development of cardiovascular diseases, such as atherosclerosis, myocardial infarction and hypertension. Despite a few studies have shown that glucocorticoids may lead to a peripheral vascular disease, the mechanisms by which glucocorticoid-induced insulin resistance impair vasodilation are incompletely understood. Thus, we aimed to investigate the mechanisms involved in reducing of vasodilation induced by insulin in mesenteric artery of rats with glucocorticoid-induced insulin resistance. Material and methods: Male Wistar rats were randomly divided into the control (CO, n=20), Dexamethasone (DEX n=20) groups. The group DEX received dexamethasone (DXA) for 7 days (2.0mg/kg/day). The animals were sacrificed and rings of mesenteric artery were mounted in an isometric system. After this, insulin sensitivity and vascular responses to insulin were assessed. Concentration-response curves to insulin were performed in control condition and in the presence of L-NAME (NOS inhibitor), L-NAME + BQ123 (endothelin (ET) antagonist) (ET-A). All data are expressed as mean ± S.E.M. Significant differences between groups were determined using Two-way ANOVA followed by Bonferroni’s post hoc test to compare the concentration-response curves obtained in mesenteric rings. Results: The rats treated with DEXA displayed insulin resistance (IR) and impaired insulin-mediated vasodilator responses. A reduction in endothelium-dependent vasodilation was observed in the DEX group (Rmax = 10.3 ± 0.7% vs. Rmax = 23.6 ± 2.5%; p < 0.001). NOS inhibition reduced vasorelaxation from both groups and caused vasoconstriction in DEX (CO group: Rmax = 23.6 ± 2.5% to 3.7 ± 1.1%, p < 0.001) and (DEX group: Rmax = 10.3 ± 0.7% to -4.9 ± 0.7%, p < 0.001). That insulin-induced vasoconstriction on L-NAME inhibition was abolished by the ET-A antagonist (CO group: Rmax = 3.7 ± 1.1% to 2.2 ± 1.1% and DEX group: Rmax = -4.9 ± 0.7% to 0.1 ± 1.3%, p < 0.05. In summary, these results suggest that insulin resistance induced by dexamethasone changes insulin-induced vasodilatation, by reducing the NO bioavailability and increased ET availability, inducing endothelial dysfunction in metabolic diseases.