PPAR-g LIGANDS ATTENUATE THE DEVELOPMENT OF INTESTINAL ISCHEMIA/REPERFUSION

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Activation of the peroxisome proliferator-activated receptor (PPAR)-γ receptor subtype regulates cellular proliferation and inflammation. The cyclopentanone prostaglandin 15-deoxy $\Delta^{12,14}PGJ_2$ functions as an endogenous ligand for PPAR-γ, rosiglitazone is a syntetic PPARg- specific agonist. Splanchnic artery occlusion shock (SAO) causes an enhanced formation of reactive oxygen species (ROS), which contribute to the pathophysiology of shock. Here we have investigated the effects of 15-d$^{12,14}PGJ_2$ and rosiglitazone in rats subjected to SAO shock. Treatment of rats with 15d-PGJ_2 and rosiglitazone (0.3 mg/kg in 10 % v v^{-1} dimethyl sulphoxide in saline, 30 min prior to ischemia), attenuated the mean arterial blood and the migration of polymorphonuclear cells (PMNs) caused by SAO-shock. 15d-PGJ_2 and rosiglitazone also attenuated the ileum injury (histology) as well as the increase in the tissue levels of myeloperoxidase (MPO) and malondialdehyde (MDA) caused by SAO shock in the ileum. Immunohistochemical analysis for nitrotyrosine revealed a positive staining in ileum from SAO-shocked rats. The degree of staining for nitrotyrosine was markedly reduced in tissue sections obtained from SAO-shocked rats which had received 15d-PGJ_2 or rosiglitazone. Reperfused ileum tissue sections from SAO-shocked rats showed positive staining for P-selectin and for anti-intercellular adhesion molecule (ICAM-1) in the vascular endothelial cells. 15d-PGJ_2 or rosiglitazone treatment markedly reduced the intensity and degree of P-selectin and ICAM-1 in tissue section from SAO-shocked rats. 15d-PGJ_2 or rosiglitazone treatment significantly improved survival. Taken together, our results clearly demonstrate that 15d-PGJ_2 or rosiglitazone treatment exerts a protective effect and part of this effect may be due to inhibition of the expression of adhesion molecules and peroxynitrite-related pathways with subsequent reduction of neutrophil-mediated cellular injury.