NF-κB INHIBITION BY PYRROLIDINE DITHIOCARBAMATE ATTENUATES GASTRIC ISCHEMIA - REPERFUSION INJURY IN RATS

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Purpose. Pyrrolidine dithiocarbamate (PDTC) is a potent antioxidant and an inhibitor of nuclear factor-kappa B (NF-κB). The present study examined the impact of PDTC preconditioning on gastric protection in response to ischemia-reperfusion injury (I/R) to the rat stomach. Methods. Male Wistar rats were recruited and divided into three groups. One group was subjected to gastric ischemia for 30 minutes and reperfusion for one hour. The second group of rats was preconditioned with PDTC (200 mg/kg intravenously), 15 minutes prior to ischemia and before reperfusion respectively. The third group of rats was sham- operated and served as the control group. Results. Gastric I/R injury increased serum lactate dehydrogenase level (LDH), vascular permeability of gastric mucosa (as indicated by Evans blue dye (EB) extravasation) and gastric content of inflammatory cytokine; tumor necrosis factor- α (TNF-α). Moreover, oxidative stress was increased as indicated by elevated lipid peroxides formation (measured as thiobarbituric acid reactive substances, TBARS) and depleted reduced glutathione (GSH) in gastric tissues. Nuclear factor kappa B (NF-κB) translocation was also detected by electrophoretic mobility shift assay. Microscopically, gastric tissues subjected to I/R injury showed ulceration, hemorrhages and neutrophil infiltration. Immunohistochemical studies of gastric sections revealed increased expression of p53 and Bcl-2 proteins. PDTC pretreatment reduced EB extravasation, serum LDH level and gastric TNF-α, and TBARS content and increased gastric GSH content. Moreover, PDTC pretreatment abolished p53 expression and inhibited NF-κB translocation. Finally, histopathological changes were nearly restored by PDTC pretreatment. Conclusions. These results clearly demonstrate that NF-κB activation and induction of pro-apoptotic protein p53 are involved in gastric I/R injury. PDTC protects against gastric I/R injury via, antioxidant, NF-κB inhibition, and reduction of pro-apoptotic protein p53 expression, which seems to be down stream to NF-κB, thus promoting cell survival.