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Enhanced anti-ulcer effect of pioglitazone on gastric ulcers in cirrhotic rats: The role of nitric oxide and IL-1β

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Abstract:
Background: The frequency of gastrointestinal ulcerations is higher in cirrhotic patients than in the normal population. It has been shown that pioglitazone exhibits gastroprotective actions. This study was designed to investigate the effect of pioglitazone, on the gastric mucosal lesions in cirrhotic rats.
Methods: Different groups of bile duct-ligated and sham animals received solvent, or 5, 10 or 15 mg/kg pioglitazone, for 5 days in the last days of 28-day period of cirrhosis. On day 28, rats were killed 1 h after oral ethanol administration and the area of gastric lesions was measured. The serum of rats was also collected to evaluate serum concentrations of TNF-α and IL-1β. Histopathologic examination of liver specimens was also done with hematoxylin-eosin to show possible toxicity of pioglitazone in cirrhosis.
Results: Pretreatment with pioglitazone dose dependently attenuated gastric lesions induced by ethanol in both sham and cirrhotic rats, but this effect was more prominent in cirrhotic ones. L-NAME, a non-selective inhibitor of nitric oxide synthase, decreased pioglitazone-induced gastric healing effect in cirrhotic rats, while aminoguanidine, a selective inducible nitric oxide synthase inhibitor, increased pioglitazone-induced gastric healing effect in the same group. The protective effect of pioglitazone was accompanied by a fall in serum IL-1β level.
Conclusions: Chronic treatment with pioglitazone exerts a more prominent gastroprotective effect on the stomach ulcers of cirrhotic rats compared to control group probably due to constitutive nitric oxide synthase induction or inducible nitric oxide synthase inhibition. Suppression of IL-1β could be another mechanism in pioglitazone-induced healing effect of gastric ulcers in cirrhotic rats.

Key words:
pioglitazone, cirrhosis, gastric ulcers, nitric oxide, IL-1β, rat