

Rebamipide Retards CCL4 Induced Hepatic Fibrosis: A Role of PGE2

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Abstract : Rebamipide is an antiulcer drug with unique properties such as anti-inflammatory action. It induces endogenous prostaglandin e2 (PGE2). PGE2 is considered as a potent physiological suppressor of liver fibrosis. Aim of study: This study investigated the effect of rebamipide on hepatic fibrosis. Material and Method: Hepatic fibrosis was induced by intraperitoneal injections (IP) injection of CCL4 (0.45 mL/kg) in corn oil 1:5 twice a week for 4 weeks. Rats were divided into four groups as follow: Group 1 treated with CCL4 only, group 2 and 3 treated with CCL4 and rebamipide 60 mg/kg/day (group2) or 100 mg/kg/day (group3), and the fourth group was considered as control group and treated with vehicles. ALT, AST, and Bilirubin were assayed in serum. Antioxidant markers such as malondialdehyde (MDA) and superoxide dismutase (SOD) and fibrotic markers such as hyaluronic acid (HA) and procollagen-III (procol-III) were evaluated in liver tissues. IL-10 as well as PGE2 were also assayed in liver tissues. Pathologic changes in the liver were detected by hematoxylin and eosin staining. Collagen precipitation in liver tissues was visualized using masson trichrom stain. Results: Rebamipide inhibit CCL4 induced increase in ALT and AST significantly ($p < 0.05$). Rebamipide exerted an antioxidant effect as it inhibits CCL4 induced increased MDA level and decreased SOD activity. Fibrotic markers assay revealed that repamipide (60 or 100 mg/kg/day) decreased the level of procol-III and HA compared to CCL4 ($p < 0.05$). Oral administration of Rebamipide was associated with a significant increase ($p < 0.05$) of PGE2 and IL-10. Rebamipide especially at the dose of (100 mg/kg/day) restores liver histology structure and abolish collagen precipitation in liver tissues. Conclusion: Rebamipide retards hepatic fibrosis induced by CCL4 may be through the induction of PGE2 level.

Keywords : fibrotic markers, hepatic fibrosis, PGE2, rebamipide

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