論 文 要 旨

Hepatocyte growth factor ameliorates methylglyoxal-induced peritoneal inflammation and fibrosis in mouse model

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【Background】

Peritoneal dialysis (PD) is essential for patients with end-stage renal disease. Peritoneal fibrosis (PF) is a complex inflammatory, fibrogenic process. No effective treatments are available to prevent these processes. Hepatocyte growth factor (HGF) possesses anti-inflammatory and anti-fibrotic properties. The aim of this study was to analyze whether HGF suppresses MGO-induced peritoneal inflammation and fibrosis in a mouse model.

【Methods】

PF was induced by intraperitoneal (IP) injections of MGO for 14 days. C57/BL/6 mice were divided into three groups: Sham group (only vehicle); Sham + MGO group (PF induced by MGO); and HGF + MGO group (PF mice treated with recombinant human-HGF). PF was assessed from tissue samples by Masson’s trichrome staining. Inflammation and fibrosis-associated factors were assessed by immunohistochemistry and quantitative real-time PCR.

【Results】

MGO-injected mice showed significant thickening of the submesothelial compact zone with PF. Treatment with HGF significantly reduced PM thickness and suppressed the expression of collagen I and III and α-SMA. Expression of profibrotic and proinflammatory cytokines (TGF-β, TNF-α, IL-1β) was reduced by HGF treatment. The number of macrophages, and M1 and M2 macrophage-related markers, such as CD86, CD206, and CD163, was reduced in HGF + MGO mice.

【Conclusion】

HGF attenuates MGO-induced PF in mice. Furthermore, HGF treatment reduces myofibroblast and macrophage infiltration, and attenuates the upregulated expression of proinflammatory and profibrotic genes in peritoneal tissues. HGF might be an effective approach to prevent the development of PF in patients undergoing PD.