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The antifibrotic effect of sitagliptin against liver fibrosis induced by carbon tetrachloride in rats

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Statement of the Problem: Liver fibrosis is the common end stage for most chronic liver injuries which leads to irreversible cirrhosis with the risk of liver failure and hepatocellular carcinoma. Sitagliptin, a dipeptidyl peptidase 4 inhibitor (DPP4-I), has been developed as a new possible treatment for type-2 diabetes mellitus. It has been suggested that DPP4 is involved in the development of several liver diseases, such as chronic hepatitis C (CHC) and hepatocellular carcinoma (HCC). Other reports showed that DPP4 is expressed on the surface of reactive fibroblasts including activated HSCs. Therefore, this study was designed to assess the antifibrotic, antioxidant and anti-inflammatory effects of sitagliptin against liver fibrosis induced by CCl4 in rats and to foresee an unusual clinical application of sitagliptin.

Methodology & Results: The antifibrotic effect of sitagliptin was assessed using CCl4-induced experimental liver fibrosis model. Rats received CCl4 three times a week for 7 weeks, as well as daily oral treatments of sitagliptin (100 mg/kg) during the 7 weeks of intoxication. Hepatic fibrotic changes were estimated by measuring hepatic enzymes, markers of liver fibrosis, oxidative stress and inflammation as well as marker of HSCs activation. It was found that sitagliptin ameliorates liver fibrosis occurs mainly via inhibiting the fibrogenesis and proliferation of activated HSCs response via inhibiting the release of TGFβ1, attenuating the activation of hepatic stellate cells via reduction of α-SMA expression in liver, inhibition of hepatic oxidative stress and augmentation of anti-oxidant defenses and inhibition of proinflammatory cytokines as IL-6.

Conclusion & Significance: This study showed that sitagliptin attenuates the progression of liver fibrosis induced by carbon tetrachloride in rats. Looking forward on the clinical application, this study may introduce a new therapy for treating liver fibrosis in humans especially for diabetic patients suffering from liver diseases.

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