Biochemical studies on collagen metabolism during dimethylnitrosamine induced hepatic fibrosis

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Impaired collagen metabolism and abnormal accumulation of collagens in the liver play a significant role in the pathogenesis of hepatic fibrosis. The current study was aimed to understand the up-regulation of various procollagens and impairment of collagen metabolism during the pathogenesis of experimentally induced hepatic fibrosis in rats. The liver injury was induced by intraperitoneal injections of dimethylnitrosamine (DMN) in doses of 1 mg /100 g body weight on 3 consecutive days of each week for 3 weeks. A group of control and treated animals were sacrificed on days 7, 14, and 21 after the start of DMN administration. The α-smooth muscle actin (α-SMA) was stained as a marker for the activation of hepatic stellate cells and onset of liver fibrosis. Procollagen type I peptide, procollagen type III peptide and procollagen type IV peptide (7S fragment) were determined in serum. Collagen metabolism was studied by measuring hydroxyproline levels in serum and liver and also urinary excretion of hydroxyproline on days 7, 14, and 21 from the beginning of exposure. Liver collagenase was also assayed. Measurement of pro-collagen peptides demonstrated a significant increase of all procollagens on days 7, 14, and 21 with a maximum increase on day 7. Studies on collagen metabolism demonstrated abnormal accumulation of collagen in the liver accompanied by modulating hydroxyproline levels in serum and increased urinary excretion of hydroxyproline. There was no correlation between collagen accumulation in the liver and increased urinary excretion of hydroxyproline. A significant increase was observed in liver collagenase levels on all days studied with a maximum on day 7. The results of the present study indicate increased synthesis and impaired metabolism of collagens during DMN induced hepatic fibrosis in rats. It is concluded that the regulation of collagen metabolism may be normal in the early stages of fibrosis but impaired in latter stages resulting in accumulation of collagens in the liver.

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