BIOSYNTHESIS OF COLLAGEN DURING DIMETHYLNITROSAMINE INDUCED HEPATIC FIBROSIS IN RATS

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The rate of biosynthesis of collagen and its turnover play a significant role in the progression of hepatic fibrosis. We have evaluated the rate of biosynthesis and metabolic turnover of liver collagen in dimethylnitrosamine (DMN) induced model of hepatic fibrosis in rats. The metabolism of liver collagen was studied after a single intraperitoneal injection of ^{3}H-proline in a dose of 1110 KBq/100 g body weight. The incorporation of ^{3}H-proline into collagen as ^{3}H-hydroxyproline was measured as an index of collagen biosynthesis. The total hydroxyproline and ^{3}H-hydroxyproline was measured after extraction and fractionation of liver collagen into neutral salt soluble, acid soluble and pepsin solubilized fractions. The total and ^{3}H-hydroxyproline levels in the urine were also measured in order to study the metabolic degradation of liver collagen. A significant increase was noticed in the rate of biosynthesis of liver collagen in all DMN treated animals with a maximum on the 21st day group. About 4 fold raise was recorded in the amount of liver total collagen. The urinary levels of total and labeled hydroxyproline were also increased significantly with a maximum excretion on the 7th day. There was no significant correlation between increase of liver hydroxyproline content and the enhanced urinary excretion of hydroxyproline. The results of the present study indicated a significant increase in the rate of biosynthesis and metabolic turnover of liver collagen during DMN induced hepatic fibrosis. It also demonstrated that the balance between synthesis and degradation is almost maintained in the early stages of fibrosis as a self defense mechanism, but it is totally impaired in the latter phase of the disease which results in deposition of collagen in the liver contributing to the progression of fibrosis.

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