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Granulocyte-Colony Stimulating Factor Administration Accelerates Hepatocellular Proliferation after Toxin Induced Liver Injury in Rats

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BACKGROUND-AIMS

It has been shown that Granulocyte-Colony Stimulating Factor (G-CSF) administration enhances and accelerates the proliferation of hepatocytes in rats subjected to partial hepatectomy (Eur J Gastroenterol Hepatol 1996; 8:805-809 & Clin Sci 1997; 92:315-320). The aim of the present study was to examine the effect of G-CSF administration on hepatocyte proliferation normally occurring after liver injury induced by either carbon tetrachloride (CCl_4), or thioacetamide (TAA), or D-galactosamine (D-GalN) injection.

METHODS

Intraperitoneal (ip) administration of either 1mL CCl_4, or 300mg TAA or 1g D-GalN/Kg of body weight in male Wistar rats caused severe liver injury followed by regeneration. G-CSF (Filgrastim; Granulokine, Hoffmann La Roche, Switzerland) was administered ip in rats at the time of maximum liver injury. The animals were sacrificed at different time points following toxin administration. Hepatic injury was estimated by AST and ALT activities in serum and liver histology. The rate of tritiated thymidine incorporation into hepatic DNA, the enzymatic activity of liver thymidine kinase, the assessment of mitotic index and Proliferating Cell Nuclear Antigen labeling index in hepatocytes, were used to estimate liver regeneration.

RESULTS

In the above mentioned different models of toxin-induced liver injury, G-CSF administration, enhanced and transposed at earlier time points the peak of hepatocyte proliferation, compared to that found in simply toxin-treated rats ($p<0.001$).

CONCLUSIONS

Our findings suggest that G-CSF treatment exerts mitogenic effect on the hepatocytes, accelerating the proliferating process which normally occurs after injury induced by either CCl_4 or TAA or D-GalN administration. The administration of factors able to accelerate hepatocyte proliferation represents an effective strategy for the treatment of liver failure, so G-CSF may be a potent hepatic mitogen for future clinical use.