Effect of pentoxifylline on hepatic injury caused in the rat by the administration of carbon tetrachloride or acetaminophen

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Abstract
The effect of pentoxifylline (PTX) on acute liver injury caused by CCl₄ or acetaminophen was studied in the rat. PTX was given twice daily (18, 36 or 72 mg/kg), intraperitoneally (ip) for 5 days prior to CCl₄ or acetaminophen. In addition, the effect of PTX administered simultaneously with CCl₄ or acetaminophen was evaluated. Rats were killed 72 h or 48 h after CCl₄ or acetaminophen administration, respectively. The administration of PTX at 72 mg/kg, conferred significant protection against the hepatotoxic actions of CCl₄, reducing serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) levels to 31%, 59.2% and 63%, respectively. Histological examination showed a decrease in centrilobular necrotic areas in rats pretreated with PTX. Histochemical investigation revealed a decrease in glycogen and protein contents caused by CCl₄ and these were prevented by PTX pre-treatment. When administered with CCl₄, PTX did not reduce CCl₄-induced hepatic injury. In contrast, hepatic injury induced by acetaminophen was prevented by prior or co-treatment with PTX. Accordingly, with 72 mg/kg of PTX, the elevation of AST, ALT and ALP levels was lower by 45%, 80.6%, 54.3% for the former and by 32.4%, 77.2%, 52.4% for the latter, respectively. Stained sections were subjected to morphometric evaluation using computerized image analyzer. Quantitative analysis of the acetaminophen area of damage showed a reduction by 34.8, 65.5 and 89.2% by 18, 36 or 72 mg/kg for PTX, respectively. Rats treated with PTX revealed more or less normal hepatocyte architecture as well as marked improvement in protein and glycogen content. The study demonstrates that prior but not co-toxicant administration of PTX in a model of CCl₄-induced liver injury results in less liver damage. In contrast, PTX is equally protective, when given either as a pretreatment or with acetaminophen exposure.

Key words: pentoxifylline, acetaminophen, carbon tetrachloride, liver injury rat