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Attenuation of Endotoxin Induced Hepatotoxicity by Dexamethasone, Melatonin and Pentoxifylline in White Albino Mice: A Comparative Study

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Abstract : Sepsis is characterized by an overwhelming surge of cytokines and oxidative stress to one of many factors, gram-negative bacteria commonly implicated. Despite major expansion and elaboration of sepsis pathophysiology and therapeutic approach; death rate remains very high in septic patients due to multiple organ damages including hepatotoxicity.The present study was aimed to ascertain the adequacy of three different drugs delivered separately and collectively- low dose steroid-dexamethasone (3mg/kg i.p) ,antioxidant-melatonin(10 mg/kg i.p) ,and phosphodiesterases inhibitor - pentoxifylline (75 mg/kg i.p)in endotoxin-induced hepatotoxicity in mice. Endotoxin/lipopolysaccharides induced hepatotoxicity was reproduced in mice by giving lipopolysaccharide of serotype E.Coli intraperitoneally. The preventive role was questioned by giving the experimental agent half an hour prior to LPS injection whereas the therapeutic potential of the experimental agent was searched out via post-LPS delivering. The extent of liver damage was adjudged via serum alanine aminotransferases (ALT) and aspartate aminotransferase (AST) estimation along with a histopathological examination of liver tissue. Dexamethasone is given before (Group 3) and after LPS (group 4) significantly attenuated LPS generated liver injury.Pentoxifylline generated similar results and serum ALT; AST histological alteration abated considerably ($p \leq 0.05$) both in animals subjected to pentoxifylline pre (Group 5) and post-treatment(Group 6). Melatonin was also prosperous in aversion (Group 7) and curation (Group 8) of LPS invoked hepatotoxicity as evident by lessening of augmented ALT (≤ 0.01) and AST (≤ 0.01) along with restoration of pathological changes in liver sections ($p \leq 0.05$). Combination therapies with dexamethasone in conjunction with melatonin (Group 9), dexamethasone together with pentoxifylline (Group 10), and pentoxifylline along with melatonin (Group 11) after LPS administration tapered LPS evoked hepatic dysfunction statistically considerably. In conclusion, both melatonin and pentoxifylline set up promising results in endotoxin-induced hepatotoxicity and can be used therapeutic adjuncts to conventional treatment strategies in sepsis-induced liver failure.

Keywords : endotoxin/lipopolysacchride, dexamethasone, hepatotoxicity, melatonin, pentoxifylline
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