P31

Role of Kupffer Cells in Hepatic Drug Metabolizing Functions during Sepsis in Rats

S.H. Lee○, S.M. Lee
College of Pharmacy, Sungkyunkwan University

ABSTRACT

The present study was done to investigate the relationship between Kupffer cells and alteration of cytochrome P-450 (CYP)-dependent drug metabolizing enzyme activities during polymicrobial sepsis. Male rats were subjected to polymicrobial sepsis by cecal ligation and puncture (CLP) followed by fluid resuscitation. The gadolinium chloride ($GdCl_3$, 10 mg/kg), blocker of Kupffer cells, was pretreated intravenously at 48 h and 24 h prior to the induction of CLP. All assay parameters were determined at 24 h after CLP or sham operation. In CLP-treated rats, the mortality rate of animals increased to 50% and serum alanine (ALT) and aspartate aminotransferase (AST) levels also significantly elevated. However, this increase was not suppressed by $GdCl_3$ pretreatment. Microsomal lipid peroxidation markedly increased after CLP operation. This increase was significantly attenuated by pretreatment. Total cytochrome P-450 content and NADPH-cytochrome P-450 reductase activity were not changed after CLP operation, but $GdCl_3$ pretreatment reduced total cytochrome P-450 content. The hepatic microsomal CYP 1A1, 1A2, 2B1 and 2E1 activities in CLP-induced rats were also not significantly different from sham-operated rats. However, $GdCl_3$ pretreatment showed a moderate increase in CYP1A1 and 1A2 activities. Our findings suggest that Kupffer cells may be partly responsible for producing hepatocellular dysfunction during sepsis.