Alteration of renal functional, oxidative stress and inflammatory indices following hepatic ischemia-reperfusion

Mehri Kadkhodaee¹, Saideh Mikaeili¹, Maryam Zahmatkesh², Freshteh Golab¹, Behjat Seifi¹, Hossein-Ali Arab³, Sedigheh Shams⁴ and Mitra Mahdavi-Mazdeh⁵

¹ Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
² Department of Neuroscience, School of Advanced Medical Technologies, Tehran University of Medical Sciences, Tehran, Iran
³ Department of Pharmacology, Faculty of Veterinary, Tehran University, Tehran, Iran
⁴ Children Medical Center, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
⁵ Department of Nephrology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Abstract. Liver ischemia/reperfusion (IR) injury is a complex phenomenon that may cause local as well as remote organ injuries. Reactive oxygen species (ROS) along with many pro- and anti-inflammatory cytokines are implicated in the development of organ injury. The renal functional, histological, oxidative stress and inflammatory indices were studied during a short and a longer period of liver IR. Rats were subjected to either sham operation or 90 min partial liver ischemia followed by 4 or 24 h of reperfusion. Serum ALT, AST, ALK and LDH levels, BUN and creatinine, renal MDA level, SOD and catalase activities were evaluated as well as serum IL-6 and IL-10 concentrations along with renal histological evaluation. Ninety minutes liver ischemia /4 h reperfusion caused an increase in BUN and renal MDA levels and a decrease in SOD and catalase activities. It also caused an increase in serum IL-6 and IL-10 levels. 24 h liver reperfusion resulted in a reduction in BUN levels and lower oxidative damages demonstrated by a decrease in renal MDA levels and an increase in renal SOD and catalase activities comparing to 4 h reperfusion group. Evaluations indicated improvement in histology such as less cytoplasmic vacuolation and lower tubular debris. Serum inflammatory indices (IL-6 and IL-10 levels) were also reduced. This study showed that liver IR damage causes renal injury including functional, inflammatory and oxidative status changes. The remote kidney damage was then improved by continuing reperfusion from 4 to 24 h.

Key words: Liver — Ischemia/reperfusion — Remote organ — Kidney — ROS — Oxidative stress

Abbreviations: ALK, alkaline phosphatase; ALT, alanine amino-transferase; AST, aspartate amino-transferase; BUN, blood urea nitrogen; Cr, creatinine; IL, interleukin; IR, ischemia/reperfusion; LDH, lactate dehydrogenase; MDA, malondialdehyde; ROS, reactive oxygen species; SOD, superoxide dismutase.

Introduction

Liver ischemia/reperfusion (IR) is a complication of liver surgery, especially during liver transplantation which results in inflammation and organ dysfunction (Fondevila et al. 2003). In addition, recent studies indicate that IR-induced acute liver failure (ALF) causes injuries of distant organs such as heart and lungs by systematic inflammatory responses (Weinbroum et al. 1997). However, the effects of acute liver injury on the induction of kidney injury have so far not been adequately addressed. In clinical settings, if acute kidney injury (AKI) concomitantly occurs in patients with ALF, mortality will significantly increase (Davis et al. 2002; Betrosian et al. 2007). In experimental studies, Behrends et al. in 2007 showed that