

Abstract

Ischemia-reperfusion (I/R) cannot be avoided in liver transplantation procedures, and apoptosis is a central mechanism of cell death after liver reperfusion. Protective effect of recombinant erythropoietin (rhEPO) on liver apoptosis has not been clearly investigated. This work investigated intraportal (IP) rhEPO-protective effect in a rat model of hepatic I/R-induced apoptosis and its appropriated time and dose of administration. Eight groups were included (n = 10/group): sham-operated, I/R (45 min ischemia and 2 h reperfusion), preconditioned rhEPO I/R (24 h or 30 min before ischemia), and postconditioned rhEPO I/R (before reperfusion) using two different rhEPO doses (1,000 and 5,000 IU/kg). When compared with the sham-operated group, the I/R group showed significant increase of serum levels of aspartate and alanine aminotransferases (AST, ALT), hepatic caspase-9 activity (894.99 ± 176.90 relative fluorescence units (RFU)/mg/min versus 458.48 ± 82.96 RFU/mg/min), and Fas ligand (FasL) expression, histopathological damages, and significant decrease in the antiapoptotic Bcl-xL/apoptotic Bax ratio (0.38 ± 0.21 versus 3.35 ± 0.77) rhEPO-improved ALT and AST but failed to reduce FasL expression in all groups compared with the I/R group. Thirty minutes and 24 h preconditioning with rhEPO (1,000 IU/kg) increased Bcl-xL/Bax ratio and reduced caspase-9 activity, and the same effect was observed when higher dose was given 24 h before ischemia. Preconditioning was more effective than postconditioning in improving caspase-9 activity, and no dose-dependent effect was observed. In conclusion, single IP rhEPO injection 30 min before ischemia has an advantage over rhEPO postconditioning in improving post-hepatic I/R-induced apoptosis with no additional time- and dose-dependent effects which may provide potentially useful guide in liver transplantation procedures.