HO-1 mediates the effects of HBO pretreatment against sepsis

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摘要

Abstract

Background. We have recently shown that attenuation of sepsis-induced lung injury by hyperbaric oxygen (HBO) pretreatment involves expression regulation of inducible nitric oxide synthase (iNOS) and heme oxygenase (HO)-1. This study was performed to determine the effects of HBO pretreatment on acute kidney and liver injuries in septic rats and the roles of iNOS and HO-1. Materials and methods. One group of adult male rats (n = 48) were pretreated with HBO. The other group of rats (n = 48) breathed air at normal atmospheric pressure instead. Rats in each group were randomly allocated to receive injection of lipopolysaccharide (LPS), normal saline (N/S), LPS plus hemin (a HO-1 inducer), hemin, LPS plus SnPP (a HO-1 inhibitor), SnPP, LPS plus hemin plus SnPP, or hemin plus SnPP. Hemin and SnPP were injected at 1 h before HBO or air pretreatment. Rats were maintained for 6 h before sacrifice. Results. LPS caused prominent kidney and liver injuries as well as iNOS and HO-1 expression in stimulated rats. HBO pretreatment significantly attenuated LPS-induced kidney but not liver injury. However, in conjunction with hemin (a HO-1 inducer), HBO pre-treatment did attenuate LPS-induced liver injury. In addition, the inhibition of iNOS expression by HBO pretreatment was associated with "super-induction" (i.e., further enhancement) of LPS-induced HO-1 expression. Furthermore, the therapeutic effect of HBO could be counteracted by SnPP (a HO-1 inhibitor). Conclusions. HBO pretreatment significantly attenuates LPS-induced acute organ injuries in septic rats. The beneficial effect of HBO pretreatment against sepsis is mediated, at least in part, by "super-induction" of HO-1.