56 Selective inhibition of inducible nitric oxide synthase attenuates renal ischemia and damage in experimental heatstroke

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摘要

Abstract

The aim of the present study was to determine whether the possible occurrence of renal ischemia and damage during heatstroke can be suppressed by prior administration of L-N6-(1-iminoethyl) lysine (L-NIL), a selective inducible nitric oxide synthase (iNOS) inhibitor. Urethane-anesthetized rats were exposed to heat stress (43˚C) to induce heatstroke. Control rats were exposed to 24˚C. Mean arterial pressure and renal blood flow after the onset of heatstroke both were significantly lower in vehicle-treated heatstroke rats than in normothermic controls. However, both the body temperature and renal damage scores were greater in vehicle-treated heatstroke rats compared with normothermic controls. Plasma nitric oxide (NO), creatinine, and blood urea nitrogen (BUN), as well as the renal immunoreactivity of iNOS and peroxynitrite all were significantly higher in vehicle-treated heatstroke rats compared with their normothermic controls. Pretreatment with L-NIL (3 mg/kg, administered intravenously and immediately at the onset of heat stress) significantly attenuated heatstroke-induced hyperthermia, arterial hypotension, renal ischemia and damage, increased renal levels of immunoreactivity of iNOS and peroxynitrite, and increased plasma levels of NO, creatinine, and BUN. Accordingly, pretreatment with L-NIL significantly improved survival during heatstroke. The results suggest that selective inhibition of iNOS-dependent NO and peroxynitrite formation protects against renal ischemia and damage during heatstroke by reducing hyperthermia and arterial hypotension.