Aminoguanidine protects against intracranial hypertension and cerebral ischemic injury in experimental heatstroke

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摘要

Abstract

The aim of the present study was to ascertain whether aminoguanidine attenuated intracranial hypertension and cerebral ischemic injury in experimental heatstroke. Urethane-anesthetized rats were exposed to heat stress (ambient temperature of 43°C) to induce heatstroke. Control rats were exposed to 24°C. Mean arterial pressure, cerebral perfusion pressure, and cerebral blood flow after the onset of heatstroke were all significantly lower than in control rats. However, colonic temperature, intracranial pressure, heart rate, cerebral inducible nitric oxide synthase (iNOS)-dependent NO, and neuronal damage score were greater after the onset of heatstroke. Aminoguanidine (30 μmol/kg, i.v.; 30 min before the start of heat exposure) pretreatment significantly attenuated the heatstroke-induced hyperthermia, arterial hypotension, intracranial hypertension, cerebral ischemia and neuronal damage, and increased iNOS-dependent NO formation in the brain. The extracellular concentrations of ischemic (e.g., glutamate and lactate/pyruvate ratio) and damage (e.g., glycerol) markers in the hypothalamus were also increased after the onset of heatstroke. Aminoguanidine pretreatment significantly attenuated the increase in hypothalamic ischemia and damage markers associated with heatstroke. Delaying onset of aminoguanidine administration (i.e., 0 or 30 min after the start of heat exposure) reduced the preventive efficiency on heatstroke-induced hyperthermia, arterial hypotension, intracranial hypertension, cerebral ischemia, and increased iNOS-dependent NO formation in brain. These results suggest that aminoguanidine protects against heatstroke-induced intracranial hypertension and cerebral ischemic injury by inhibition of cerebral iNOS-dependent NO production.