探討保護性 HO-1 在給予 17-DMAG 治療熱中風鼠的角色

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摘要

熱中風 (Heat stroke; HS) 是一種具生命威脅性的疾病，其特點為中心體溫上升超過 40℃，且伴隨有譫妄、癲癇或昏迷等中樞系統異常之症狀。儘管積極的使其體溫下降並給予支持性治療，熱中風仍具有極高死亡率。因此，本實驗目的在以雄性 Sprague-Dawley (SD)大白鼠誘發熱中風模式時，未給予或預先給予熱休克 90 抑制劑 17-dimethylaminoe- thylamino-17-demethoxygeldanamycin (17-DMAG) 來評估熱休克發生期間 17-DMAG 是否能保護肝臟免於功能不良。將重 280-350 公克雄性 SD 大白鼠以 urethane (1.4 g/kg) 進行腹腔注射麻醉後，利用聚乙烯管在動物右側股動脈及股靜脈插管。動物分為兩組：(1) 溶劑(normal saline) + 熱中風(HS) 組：熱中風生成判斷以平均動脈壓迅速下降 25 mmHg 及大鼠肛溫大於 42℃ 視為熱中風生成; (2) 17-DMAG + HS 組：於熱中風前 20 小時腹腔注射 17-DMAG (5 mg/kg)。熱中風時實驗測量兩組動物的: (1) 平均動脈壓及心跳; (2) 血清肝功能生化參數; (3) 肝臟中第一型血基質氧化酶(Heme oxygenase-1, HO-1) 的表現量。實驗結果顯示：熱休克(HS)組之平均動脈壓及心跳比 17-DMAG + HS 組來得低，預先處理 17-DMAG 能有效改善平均動脈壓及心跳;預先給 17-DMAG (17-DMAG + HS) 組肝臟中之 HO-1 表現明顯比熱休克組(HS) 高。研究結果證明 17-DMAG 可以改善熱休克鼠血液動力學及肝功能，此可能與增加 HO-1 表現有關。

關鍵字：熱中風、熱休克蛋白 90 抑制劑、17-DMAG、第一型血基質氧化酶

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Heme Oxygenase-1 is involved in the protective effect of 17-DMAG in heat stroke rats Course

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Abstract

Heat stroke is a life-threatening illness characterized by an elevated core body temperature that rises above 40℃ and central nervous system dysfunction that results in delirium, convulsions, or coma. Despite adequate lowering of the body temperature and aggressive support treatment, the mortality of heat stroke is still high. Thus, the aim of the present study is to evaluate whether 17dimethylaminoethylamino-17- demethoxygeldanamycin (17-DMAG), a heat shock protein (HSP) 90 inhibitor, improves hemodynamic changes, and hepatic dysfunctions in heat stroke. Male Sprague-Dawley rats (280-350 g) exposed to heat as a model of heat stroke. The right femoral artery and vein of rats, under urethane (1.4 g/kg, ip) anesthesia, were cannulated with polyethylene tubing (PE 50). Two groups of animals were studied; (1) Vehicle-treated heat stroke group (HS group): heat stroke was induced by putting the rats into a chamber at 42℃. It is characterized when mean arterial blood pressure (MAP) dropped to a value of 25 mmHg from the peak level and Tco (core body temperature) elevated to about 42℃; (2) 17-DMAG + HS group: rats were pretreated with 17DMAG (5 mg/kg, ip) 20 h before heat stroke. The values of MAP and heart rate of rats in HS group were significantly lower than those of 17-DMAG + HS group. 17-DMAG significantly prevented hypotension, and elevated plasma level of GPT induced by heat stroke. The expression of HO-1 in liver of 17-DMAG + HS group was significantly higher than that of HS group. In conclusion, 17DMAG improves hemodynamics and hepatic function of heat stroke rats, which may be mediated by the increase of HO-1 induction.

Key Words: heat stroke; heat shock protein 90 inhibitor; 17-DMAG; HO-1