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Quercetin protects against heat stroke-induced myocardial injury in male rats: Antioxidative and antiinflammatory mechanisms

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ABSTRACT

Heat stroke is characterized by hyperthermia, systemic inflammation, and multiple organ failure including arterial hypotension. This definition can be fulfilled by a rat model of heat stroke used in the present study. Anesthetized animals were exposed to heat exposure (43 °C for 70 min) and then returned to room temperature (26 °C) for recovery. One hour before heat exposure, an intraperitoneal dose of quercetin (30 mg/kg) or vehicle (normal saline 1 ml/kg) was administered to the experimental groups of rats. Additional injection was administered immediately after the onset of heat stroke. Immediately after the onset of heat stroke. Vehicle-treated rats displayed (i) hyperthermia; (ii) suppressed left ventricular function; (iii) decreased contents of cardiac total antioxiant capacity (e.g., superoxide dismutase, glutathione peroxidase, catalase); (iv) increased contents of cardiac oxidative capacity malondialdehyde and thiobarbituric acid reactive substances; (v) increased cardiac levels of pro-inflammatory cytokines tumor necrosis factor-α and interleukin-6; and (vi) decreased cardiac levels of an anti-inflammatory cytokine interleukin 10. Histopathologic and survival observation provided supportive evidence for biochemical analyses. These heat stroke reactions all can be significantly attenuated by quercetin therapy. Our data suggest that quercetin therapy might improve outcomes of heat stroke in rats by attenuating excessive hyperthermia as well as myocardial injury. The protective effects of quercetin could be attributed to anti-lipid peroxidative, anti-oxidant, and anti-inflammatory properties.

1. Introduction

Heat stroke is characterized by both arterial hypotension (due to subcutaneous vasodilation and splenic ischemia) and decreased cerebral perfusion (due to intracranial hypertension and arterial hypotension) [1,2]. Both arterial hypotension and myocardial infarction have been observed in heat stroke patients [3–5] and rodents [1,6]. Recent studies provide evidence that oxidative stress and inflammation plays a significant role in the pathogenesis of myocardial ischemia injury [7–9]. It is not known whether oxidative stress and inflammation is also involved in the genesis of hypotension and suppressed left ventricular function in heat stroke rats [6].

Quercetin, a natural flavonoid found in high quantities in fruits

Abbreviations: MAP, mean arterial pressure; HR, heart rate; NC, normothermic controls; V, vehicle; Q, quercetin; HS, heat stroke; PBS, phosphate buffered saline; CK, creatine kinase; PV, pressure-volume; CV, stroke volume; EDP, left ventricle (LV) end-diastolic pressure; ESP, LV end-systolic pressure; Pmin, minimum LV pressure; Pmax, maximum LV pressure; EDV, LV end-diastolic volume; ESV, LV end-systolic volume; Vmax, maximum dv/dt; Vmin, minimum dv/dt; SW, stroke work; Co, cardiac output; Ea, arterial elastance; Tau (γ), Glantz time constant of ventricular relaxation; EF, ejection fraction; TBARS, Thiobarbituric acid reactive substances; SOD, superoxide dis-mutase; GSH, reduced glutathione; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; IL-10, interleukin-10.

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and vegetables, is a potential antioxidant and free radical scavenger [10,11]. Quercetin protects against oxidative stress associated damages in a rat model of transient cerebral ischemia and reperfusion [12], spinal cord injury [13], and traumatic brain injury [11,12]. However, the role of this flavonoid on heat stroke-induced left ventricular dysfunction as well as myocardial oxidative injury and inflammation remains unclear. Therefore, in the present study, we investigated the cardioprotective effects of quercetin an acute myocardial injury rats by exposing them to heat stress. On the basis of this investigation, the possible mechanism of quercetin was elucidated.

2. Materials and methods

2.1. Animals

Adult male Sprague-Dawley rats (236–314 g, Bio LASCO Taiwan Co., Ltd., Taipei, Taiwan) were used. According to guidelines of the

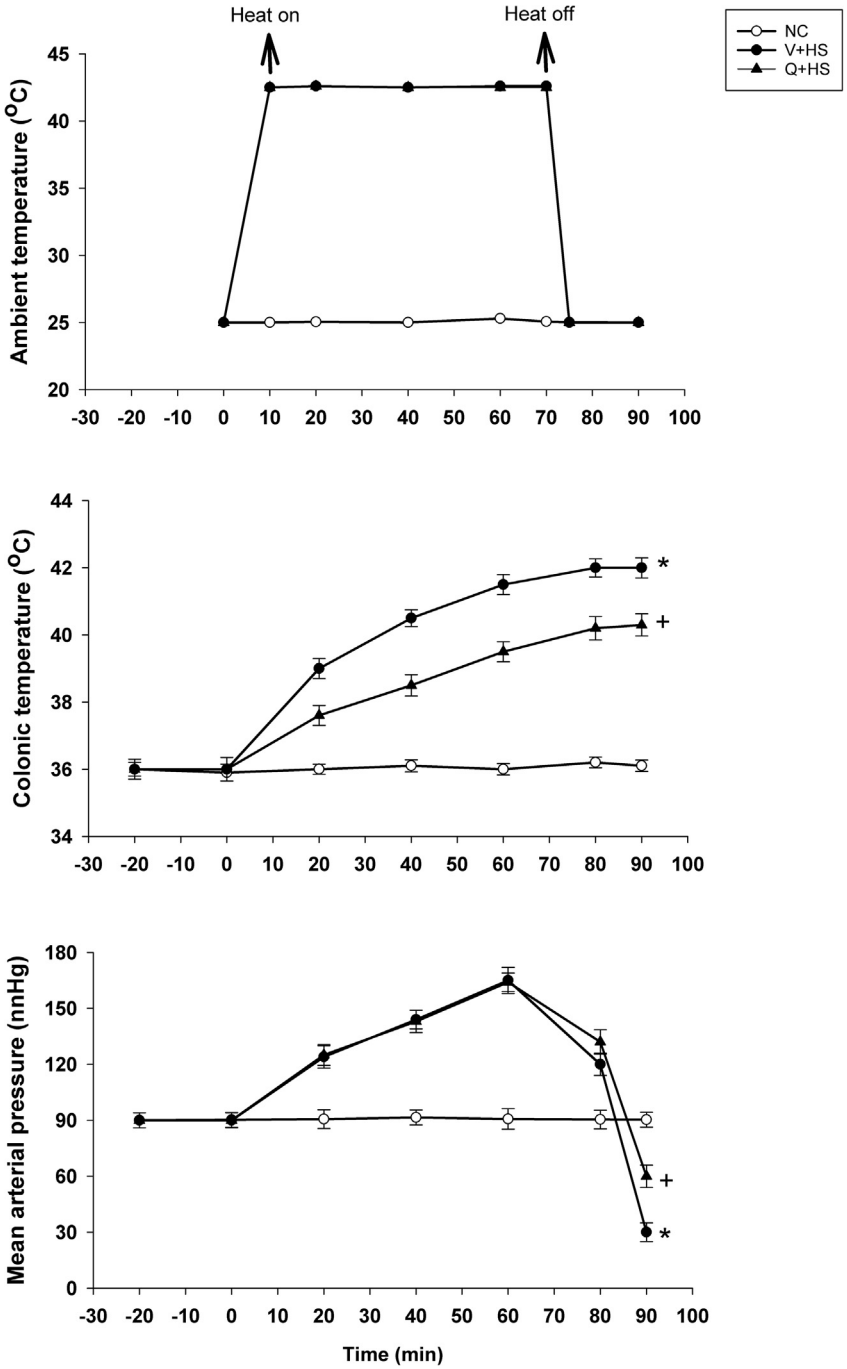

Fig. 1. Time course of change of ambient temperature, colonic temperature and mean arterial pressure in normothermic control rats (NC; room temperature exposure) (○), in rats pretreated with vehicle solution (V) received heat stress (HS) (43 °C for 70 min) (V + HS) (●), and in rats pretreated with quercetin (30 mg/kg) received heat stress (43 °C for 70 min) (▲). Data are means ± SD of 10 rats per group. $^{*}P < 0.05$, V + HS vs. NC; $^{+}P < 0.05$, Q + HS vs. V + HS. The ambient temperature was increased from 25 °C to 43 °C within 5 min by the heat (started from time "0" minute).