Limb Ischemic Preconditioning Reduces Heart Injury after Severe Burn Injury in Rats

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Background

Post-burn cardiac shock causes myocardial damage and cardiac dysfunction at the early stage of severe burns. We showed that remote ischemic preconditioning (RIPC) protects heart against myocardial I/R injury. However, little is known regarding the effect of RIPC on heart after severe burn.

Initial aim of the study

We proposed the existence of RIPC-induced cardioprotection in severely burned rats and further investigate the underlying mechanisms.

Remote ischemic preconditioning

Methods

Male Sprague Dawley rats were assigned to sham-burn,control(CON), limb ischemic preconditioning group (RIPC), each group, n=8.

Rats were inflicted with 30% total body surface area full-thickness burn in a 97°C water bath for 18 s except for the sham rats. Immediately after burn injury, all rats were resuscitated with Ringer's lactate solution (4.0ml/kg/1%TBSA,i.p.). For RIPC intervention, rats received four cycles of 5 min of limb ischemia with 5 min reperfusion at 24 hours and 1 hour before burn injury. Hemodynamics were measured. 3 hours post-burn, hearts were taken for apoptosis measurements and westernblotting analysis. Myocardial mitochondria and cytosol were isolated to determine mitochondrial energy metabolism, cytochrome c release and mitochondrial membrane potential ($\Delta\Psi_m$). Blood samples were taken for serum levels of lactate dehydrogenase (LDH) and creatine kinase-MB (CK-MB) determination.

Results

RIPC restored cardiac function, increased Bcl-2 expression , decreasing Bax and Caspase-3 expression and enhancing Bcl-2/Bax ratios. RIPC preserved post-burn cardiac mitochondrial function by recovering ATP concentrations and decreasing AMP/ATP ratio ($P<0.05$ vs. CON). RIPC up-regulated $\Delta\Psi_m$ from 11.2 ± 2 in the CON to $17.2\pm 1.1\mu\text{g/mL}$ ($P<0.05$). RIPC caused a 40% lower of cytochrome c, than rats in CON ($P<0.01$). Serum levels of cardiac enzyme leakage were reduced in RIPC group.

RISK pathway (Akt, ERK1/2, and GSK3 β) phosphorylation was enhanced in RIPC-treated hearts compared to non-treated control groups ($P<0.05$), highlighting the crucial role of the RISK pathway in RIPC-induced heart protection after severe burn injury.

Summary

Limb ischemic conditioning effectively improves cardiac function, ameliorates myocardial damage and preserves mitochondrial function after severe burn injury. The underlying mechanism may involve RISK signaling pathways.