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药理学专栏

缺血预适应通过抑制TLR4/NF-κB信号通路保护大鼠心肌缺血再灌注损伤

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摘要:

目的: 研究缺血预适应对大鼠心肌缺血再灌注损伤的保护作用是否由toll样受体 4 (TLR4)/NF-κB 途径所介导,以及是否与促进降钙素基因相关肽(CGRP)释放有关。 方法: 结扎Sprague-Dawley 大鼠左冠状动脉前降支60 min, 复灌3 h 造成心肌缺血再灌注损伤。缺血预适应为结扎大鼠左冠状动脉前降支5 min, 复灌5 min, 共4个周期。RT-PCR分析心肌 *TLR4* mRNA表达。免疫组织化学法分析心肌TLR4 和NF-κB 蛋白表达。同时,测定心肌梗死面积、血浆CGRP浓度和血清肌酸激酶活性。结果: 缺血预适应显著减少心肌梗死面积,降低肌酸激酶活性,增高血浆CGRP水平。心肌缺血再灌注可显著上调TLR4 和NF-κB 表达,缺血预适应可抑制其作用。结论: 缺血预适应通过抑制TLR4/NF-κB 信号通路保护大鼠心肌缺血再灌注损伤,其作用与促进CGRP释放有关。

关键词: Toll样受体4 缺血再灌注损伤 缺血预适应 心脏 大鼠

Ischemic preconditioning protects against myocardial ischemia-reperfusion injury through inhibiting toll-like receptor 4/NF-κB signaling pathway in rats

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Abstract:

Objective To investigate whether the protection of ischemic preconditioning (IPC) against myocardial ischemia/reperfusion (I/R) injury is mediated by toll-like receptor 4 (TLR4)/NF-κB pathway, and whether these effects are related to the release of calcitonin gene-related peptide (CGRP). Methods Sprague-Dawley rats were subjected to 60 min of ligation of the left anterior descending coronary artery followed by 3 h of reperfusion to induce I/R injury. IPC was performed by 4 cycles of 3-min left coronary artery occlusion followed by 5-min reperfusion before the I/R. The expression of *TLR4* mRNA was determined by RT-PCR. TLR4 and NF-κB protein expression were analyzed by immunohistochemistry. Myocardial infarct size, CGRP concentration in plasma and activity of creatine kinase in serum were also measured. Results IPC significantly reduced the infarct size and creatine kinase activity concomitantly with the increase in plasma CGRP concentration. The expressions of TLR4 protein and mRNA and NF-κB protein were increased by myocardial I/R injury, and dramatically inhibited by IPC. Conclusion IPC protects against myocardial I/R injury by inhibition of TLR4/NF-κB pathway. These effects are related to the increased the release of CGRP.

Keywords: toll-like receptor 4 ischemia/reperfusion injury ischemic preconditioning heart rats

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