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论著

钙调神经磷酸酶的抑制参与大鼠心脏缺血后处理的保护作用

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摘要 目的：研究缺血后处理（I-postC）对缺血/再灌注(I/R)大鼠心肌钙网蛋白（CRT）及其下游钙调神经磷酸酶（CaN）信号转导途径的影响，探讨I-postC保护I/R心脏的机制。方法：采用Wistar大鼠在体心脏I/R模型，检测血流动力学及血浆乳酸脱氢酶（LDH）和肌酸激酶（CK-MB）含量，以TTC法和TUNEL法分别检测心肌梗死面积和细胞凋亡，发色底物法测定心肌CaN活性，免疫印迹法检测心肌组织CaN和CRT蛋白表达。结果：CaN抑制剂环孢霉素A显著缩小I/R所致的心肌梗死面积(P<0.05)，抑制细胞凋亡(P<0.01)，但对心功能无明显改善(P>0.05)；与I/R组比较，I-postC组心功能改善（P<0.01），心肌梗死范围缩小（P<0.01），LDH和CK-MB漏出减少（P<0.01），细胞凋亡率降低（P<0.01），并显著抑制I/R诱导的心肌组织CaN活性升高（P<0.05）及CaN和CRT表达上调（P<0.05），与缺血预处理组比较差异无显著，但对I/R心肌的保护作用强于单纯环孢霉素A组。结论： I-postC至少部分通过抑制CRT-CaN信号途径，减轻大鼠心肌I/R损伤。

关键词 缺血后处理 再灌注 钙调神经磷酸酶 钙网蛋白

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Inhibition of calcineurin is involved in cardioprotection induced by ischemic postconditioning in rats

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Abstract

<FONT face=Verdana>AIM: To demonstrate the mechanisms underlying cardioprotection induced by ischemic postconditioning (I-postC) via studying the alteration of calreticulin (CRT)/calcineurin (CaN) signaling pathway in rat heart subjected to ischemia/reperfusion (I/R).
METHODS: The model of myocardial I/R injury in vivo was made by occluding the left anterior descending artery for 45 min followed by 24 h of reperfusion in Wistar rats.Hemodynamics and activity of lactate dehydrogenase (LDH) and creatine kinase-MB (CK-MB) in plasma were measured.Myocardial infarct size was measured by 2,3,5- triphenyltetrazolium chloride (TTC) staining and cardiomyocyte apoptosis was detected using in situ TDT-mediated dUTP nick end labeling (TUNEL).The activity of CaN,the expressions of CaN and CRT in myocardium were detected by enzyme reaction phosphorus measurement and Western blotting analysis,respectively.
RESULTS: Cyclosporin A,the inhibitor of CaN,limited significantly myocardial infarct size and cardiomyocyte apoptosis induced by I/R,but had no significant effect on cardiac function.I-postC ameliorated significantly the cardiac dysfunction induced by I/R.Compared with those in I/R group,the myocardial infarct size,the LDH and CK-MB activities in plasma and the cardiomyocyte apoptotic index were significantly reduced in I-postC group.In addition,I/R-induced upregulation of CaN activity,CaN and CRT expression were relieved by I-postC.No significant difference was found between I-postC and ischemic preconditioning groups.I-postC had stronger protective effect on the reperfused heart compared with cyclosporin A.
CONCLUSION: The findings indicate that I-postC protects myocardium against I/R injury,at least in part,via inhibiting the CRT/CaN signaling pathway.</FONT>

Key words Ischemic postconditioning Reperfusion Calcineurin Calreticulin

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