中国药理学与毒理学杂志 2011 25 (1): 7-12 ISSN: 1000-3002 CN: 11-1115/R

论著

异丙酚对大鼠心肌缺血再灌注损伤的保护作用

解丽君，张建新，李兰芳，张勤增，郝 娜，李立萍，李国风

（河北省医学科学院药物所药理学研究室, 河北 石家庄 050021）

收稿日期 2010-3-9 **修回日期** **网络版发布日期** 2011-1-24 **接受日期** 2010-7-27

摘要 **目的** 探讨异丙酚的心肌保护作用及机制。**方法** 阻断大鼠左冠状动脉前降支30 min，再灌注2 h引起心肌缺血再灌注(I/R)损伤。缺血前10 min分别灌注异丙酚3，6及12 mg·kg^{-1}至再灌12 h后实验结束。记录心率和平均动脉压，并计算心率-血压指数；光镜电镜观察心肌组织的形态学变化；原位末端标记检测心肌细胞凋亡率；免疫组化染色和Western印迹检测心肌组织NF-κB和胱天蛋白酶3的表达。**结果** 与假手术组比较，I/R组平均动脉压、血压-心率指数分别下降了34%和32%（*P*<0.05）。光镜电镜观察显示，I/R组心肌纤维排列紊乱，心肌细胞间及核周高度水肿；NF-κB活化，明显从细胞浆移位于细胞核，表达量也显著增加（*P*<0.05）；胱天蛋白酶3表达增强（*P*<0.01），心肌细胞凋亡指数由5±2明显升高到35±5(*P*<0.05)。与I/R组相比，异丙酚6和12 mg·kg^{-1}组平均动脉压和血压-心率指数升高，而心肌形态学损伤有所改善；NF-κB从细胞浆向细胞核的移位被明显限制，NF-κB的表达量也明显低于I/R组（*P*<0.05）；心肌胱天蛋白酶3表达减弱，心肌细胞凋亡指数减少（*P*<0.05）。**结论** 异丙酚可能通过抑制NF-κB的活化，下调胱天蛋白酶3的表达，从而减轻心肌I/R损伤。

关键词 异丙酚 心肌再灌注损伤 核因子-κB 胱天蛋白酶3

分类号 R963

Protective effect of propofol on myocardium ischemia/reperfusion injury in rats

XIE Li-jun, ZHANG Jian-xin, LI Lan-fang, ZHANG Qin-zeng, HAO Na, LI Li- ping, LI Guo-feng

(Department of Pharmacology, Institute of Materia Medica，Hebei Academy of Medical Sciences, Shijiazhuang 050021, China)

Abstract

OBJECTIVE To explore molecular mechanisms of propofol in myocardial protection. **METHODS** Rat myocardium ischemia/reperfusion(I/R) injury was induced by occluding the left main coronary artery for 30 min and reperfusing for 2 h. Propofol 3, 6 and 12 mg·kg^{-1} was intravenously given 10 min before ischaemia till the end of experiment. Heart rate (HR) and mean arterial blood pressure (MAP) were recorded, and pressure- rate index (PRI) was calculated. The pathological changes of myocardium were examined by light and electron microscopy. Translocation of NF- κB in the cardiomyocytes was detected by immunohistochemistry. Expressions of NF- κB and caspase 3 were determined by Western blotting. The incidence of cardiomyocyte apoptosis was detected by TdT-mediated dUTP nick end labeling staining. **RESULTS** The cardiac function parameters (MAP, PRI) in I/R group were lower than those of sham group (*P*<0.05). Compared with I/R group, propofol 6 and 12 mg·kg^{-1} resulted in improvement in MAP and PRI, respectively (*P*<0.05). The pathological changes of myocardium induced by I/R injury, such as cardiomyocyte swelling and mitochondrial membrane swelling, the cristae disruption were significantly alleviated by propofol 6 and 12 mg·kg^{-1}. Compared with sham control group, expression of NF-κB in the nuclei markedly increased in I/R group (*P*<0.05). In addition, expression of capase 3 and apoptosic index were significantly increased (*P*<0.05). Compared with I/R group, propofol 6 and 12 mg·kg^{-1} significantly attenuated expression of NF-κB in the nuclei (*P*<0.05), decreased expression of caspase 3 in myocardium (*P*<0.05) and inhibited occurrence of cardiomyocytes apoptosis. **CONCLUSION** Propofol can inhibit NF-κB activation and down- regulate the expression of caspase 3 and as a result suppress cardiomyocytes apoptotic initation during the myocardium I/R injury, which may be one of the molecular mechanisms of its cardioprotection.

Key words propofol myocardial reperfusion injury nuclear factor-κB caspase 3

DOI: 10.3867/j.issn.1000-3002.2011.01.002

通讯作者 张建新 zhangjx100@163.com