

基础研究

促红细胞生成素对心肌缺血再灌注损伤大鼠心肌的保护作用

邱炯¹|赵玉伟¹|李法琦¹|周平¹|李万玉²

1.重庆医科大学附属第一医院老年病科心血管病组|重庆400016; 2.重庆医科大学药学院药剂学教研室|重庆400016

摘要:

目的:探讨促红细胞生成素(EPO)对心肌缺血再灌注(I/R)大鼠缺血及梗死面积的影响,阐明EPO对心肌I/R损伤的保护作用的机制。方法:采用在体大鼠心肌I/R模型,将24只健康雄性SD大鼠随机分为假手术组(n=8),以6-0号丝线在冠状

动脉左前降支下穿过,不予以结扎;I/R组(n=8),以6-0号丝线在冠状动脉左前降支下穿过,并结扎,在结扎线中埋置松解线,45 min后,松解结扎线,实现再灌注;EPO组(n=8),手术过程同I/R组,在再灌注开始即刻,给大鼠腹腔内注射重组人促红细胞生成素(rhEPO),5 000 U/kg-1。再灌注24 h后用多导生理仪记录大鼠血流动力学指标,包括收缩压(SP)、舒张压(DP)、左室收缩压(LVSP)、左室舒张压(LVDP)、左室舒张末期压(LVEDP)、心室收缩期室内

压上升最大速率(dp/dt max)和心室舒张期室内压下降最大速率(dp/dt min)的变化;用原位缺口末端标记法(TUNEL)检测心肌细胞凋亡;用Evan's blue和氯化三苯基四氮唑(TTC)进行心肌染色,测量心肌缺血及梗死范围。结果:45 min的缺血和24 h的再灌注血流动力学检测显示,3组大鼠SP、DP和LVSP无明显差异(均P>0.05);与假手术组比较,I/R组大鼠LVDP和LVEDP明显升高,但dp/dt max和dp/dt min明显下降(均P<0.05);与I/R组比较,EPO组LVDP、LVEDP、dp/d max和dp/dt min均有明显改善(均P<0.05)。TUNEL结果显示,与假手术组比较,I/R组和EPO组大鼠心肌细胞凋亡明显增加(均P<0.05);与I/R组比较,EPO组大鼠心肌细胞凋亡显著减少(P<0.05)。心肌染色显示,假手术组大鼠心肌无缺血区和梗死区;与假手术组比较,I/R组和EPO组大鼠心肌有明显缺血区和梗死区;与I/R组比较,EPO组大鼠缺血范围略为缩小,但差异无统计学意义(P>0.05),梗死范围明显减少(P<0.05)。结论:EPO能够显著缩小I/R大鼠的心肌缺血及梗死范围,减少心肌细胞凋亡,显著改善其血流动力学和心脏功能,进而对心肌I/R损伤起保护作用。

关键词: 促红细胞生成素; 心脏; 缺血再灌注损伤; 血流动力学状况; 细胞凋亡; 梗死面积

Protective effect of erythropoietin on myocardium of rats with ischemia-reperfusion injury

QIU Jiong¹, ZHAO Yu-wei¹, LI Fa-qi¹, ZHOU Ping¹, LI Wan-yu²

1.Group of Cardiovascular Diseases,Department of Geriatric Medicine, First Affiliated Hospital, Chongqing Medical University, Chongqing 400016, China; 2.Department of Pharmacy, School of Pharmacology, Chongqing Medical University, Chongqing 400016, China

Abstract:

Objective To probe the influence of erythropoietin (EPO) on ischemic size and infarction size of rats with myocardial ischemia-reperfusion (I/R) injury and to clarify the mechanism of the protective effect of EOP on myocardial I/R injury.Methods 24 healthy male SD rats were randomly divided into sham-operated group(n=8), I/R group(n=8) and EPO group(n=8).In sham-operated group, the 6-0 thread was passed through the left anterior descending(LAD) coronary artery of rats without further procedures; in I/R group, the LAD coronary artery were ligated and embedded slack line in the ligature line and reperfusion was performed 45 min later; in EPO group, the rats had the same surgical procedures as I/R group and were administered by intraperitoneal injection of recombinant human erythropoietin (rhEPO) 5 000 U/kg.The hemodynamic parameters including systolic pressure(SP), diastolic pressure (DP),left ventricular systolic pressure(LVSP),left ventricular diastolic pressure(LVDP),left ventricular end-diastolic pressure(LVEDP),maximal rate of increase of ventricular pressure(dp/dt max) amd maximal rate of decrease of ventricular pressure (dp/dt min)were determined by multiple channel electrophysiograph after 24 h reperfusion.The apoptotic index of cardiomyocytes was investigated by TdT-mediated dUTP nick end labeling(TUNEL) method.The ischemia and infarction size of hearts were measured by double staining with TTC-Evan's blue dye.Results After 45 min ischemia and 24 h reperfusion, there were no significant differences in SP, DP and LVSP between three groups(P>0.05). Compared with sham-operated group, LVDP and LVEDP were significantly increased while dp/dt max and dp/dt min were reduced remarkably in I/R group(P<0.05); compared with I/R group, LVDP and LVEDP were decreased significantly but dp/dt max and dp/dt min were increased remarkably in EPO

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group($P<0.05$).The results of the myocardial TUNEL staining revealed that the TUNEL positive cardiomyocytes were increased dramatically after I/R injury;but compared with I/R group, the apoptosis was reduced significantly in EPO group ($P<0.05$).The results of the myocardium staining showed that the myocardial infarction size was reduced in EPO group compared with I/R group ($P<0.05$).Conclusion EPO can significantly protect the heart from I/R injury through improving the hemodynamic status and heart function following the reduction of cardiomyocyte apoptotic and ischemic size as well as infarction size of the left ventricle of the rats with I/R injury.

Keywords: erythropoietin heart ischemia-reperfusion injury hemodynamics apoptosis infarction size

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通讯作者: 李法琦 (Tel: 023-89011635, E-mail: faqili_2006@yahoo.com.cn)

作者简介: 邱 炯 (1980-) |女|四川省成都市人|医学硕士|主要从事心血管疾病基础与临床研究。

作者Email: faqili_2006@yahoo.com.cn

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