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论著

单硝酸异山梨醇酯对比格犬心肌缺血再灌注损伤的保护作用

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摘要 目的 观察单硝酸异山梨醇酯（ISMN）对比格犬心肌缺血再灌注损伤（MIRI）的保护作用，探讨其可能的作用机制。方法 30只比格犬随机分为6组：假手术组，缺血再灌注（I/R）组，维拉帕米（VP）0.15 mg·kg^{-1}组，ISMN 3 ,6 和12 mg·kg^{-1}组。采用结扎冠状动脉左前降支90 min，再灌90 min的方法建立比格犬I/R模型，各组动物分别于缺血前10 min股静脉注射生理盐水及相应剂量药物。手术前后不同时间点记录心电图；TTC染色法测定心肌梗死面积；比色法检测血清肌酸激酶（CK）、乳酸脱氢酶（LDH）、超氧化物歧化酶（SOD）活性及丙二醛（MDA）含量；ELISA法测定不同时间点血清中C反应蛋白（CRP）表达。结果 与假手术组相比，I/R组缺血90 min心电图T波和S-T段明显抬高；再灌90 min，出现大面积心肌梗死；血清中CK和LDH活性明显升高，SOD活性明显降低（P<0.01），MDA和CRP含量明显升高（P<0.01）。与I/R模型组比较，VP组和ISMN各剂量组在缺血90 min时心电图的T波和S-T段抬高幅度有所降低；再灌注90 min后，各给药组心肌梗死面积百分比明显减小（P<0.01）；血清中CK和LDH活性明显降低（P<0.05, P<0.01），SOD活性明显升高（P<0.05, P<0.01），MDA和CRP含量明显降低（P<0.05, P<0.01）。ISMN 3和6 mg·kg-1组对MIRI的治疗效果明显不如VP(P<0.05, P<0.01)，ISMN 12 mg·kg^{-1}的治疗效果与VP基本相当。结论 ISMN对MIRI具有保护作用；其作用机制可能与抗脂质过氧化物产生、提高SOD活力及抗炎有关。

关键词 单硝酸异山梨醇酯 心肌再灌注损伤

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Protective effect of isosorbide mononitrate on myocardial ischemia/reperfusion injury in beagles

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Abstract

OBJECTIVE To investigate the protective effect of isosorbide mononitrate (ISMN) on myocardial ischemia reperfusion injury(MIRI) in beagles and its possible mechanism ischemica/reperfusion (I/R). **METHODS** The MIRI model was induced by ligation of anterior descending of the left coronary artery for 90 min followed by reperfusion for 90 min. Then, 30 beagles were randomly divided into six groups: sham group, I/R group, verapamil(VP) 0.15 mg·kg^{-1} group, and ISMN 3, 6 and 12 mg·kg^{-1} groups. Ten minutes before ischemia, saline and corresponding doses of drugs were injected through the femoral vein respectively. Electrocardiography was monitored at different time points before and after operation, the infarction areas were evaluated by TTC staining method, the activities of creatine kinase (CK), lactate dehydrogenase (LDH), superoxide dismutase (SOD) and malondialdehyde (MDA) content were determined by colorimetric method, and the C- reactive protein (CRP) in serum was measured by ELISA kit. **RESULTS** Compared with sham-group, the T wave and S-T segment were obviously raised after 90 min ischemia, the myocardial infarct size emerged, the activities of CK, LDH and MDA content were increased (P<0.01), and the CRP level was decreased after 90 min reperfusion of I/R group. VP and ISMN pretrement could improve the changes caused by I/R after 90 min ischemia and 90 min reperfusion. The raised T wave and S-T segment were lowered, the infract size became smaller, the activites of CK and LDH, and the content of MDA and CRP decreased, and the SOD activity was increased (P<0.05, P<0.01). In terms of therapeutic effect, ISMN 3 and 6 mg·kg^{-1} dosage were lower than VP (P<0.05, P<0.01), but ISMN 12 mg·kg^{-1} could match VP. **CONCLUSION** ISMN has notable protective effect against myocardial damage in beagles. The mechanism may be related to anti-lipid peroxidation, enhancement of SOD activity and anti-inflammation.

Key words isosorbide mononitrate myocardial reperfusion injury

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