

尼群地平对兔心肌梗死的保护作用

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Protective effects of nitrendipine against myocardial infarction in rabbits

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ABSTRACT In rabbits the left circumflex coronary artery was ligated for 24 h. Nitrendipine (Nit) 10 mg · kg⁻¹ ig were given 1 h before ligation and 1, 4, and 7 h after ligation. Nit decreased myocardial infarctive size (MIS) from 25.2 ± 1.7% to 15.5 ± 1.6% ($P < 0.01$), lowered serum creatine kinase (CK) and lactate dehydrogenase isoenzyme 1 (LDH₁) from 381 ± 69 IU · L⁻¹ and 42 ± 6% to 281 ± 49 IU · L⁻¹ ($P < 0.01$) and 31 ± 8% ($P < 0.05$), diminished injury of myocyte ultrastructure, especially mitochondria and myofibrillae, in ischemic and infarctive zone. Nit exerted no significant effect on plasma level of norepinephrine (NE). The results indicate that Nit has protective effects against the acute myocardial infarction.

KEY WORDS nitrendipine; myocardial infarction; creatine kinase; lactate dehydrogenase isoenzymes; norepinephrine

摘要 观察尼群地平(Nit)对家兔冠状动脉左室支结扎24h致急性心肌梗死(AMI)的影响。结果显示: Nit缩小心肌梗死范围(MIS), 减少心肌释放肌酸激酶(CK)和乳酸脱氢酶同工酶1(LDH₁), 减轻缺血梗死区心肌细胞线粒体、肌原纤维等超微结构的破坏。但Nit对血浆去甲肾上腺素(NE)影响不明显。证明Nit对心肌梗死有保护作用。

关键词 尼群地平; 心肌梗死; 肌酸激酶类; 乳酸脱氢酶同工酶; 去甲肾上腺素

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尼群地平(nitrendipine, Nit)为新型的二氢吡啶类钙拮抗药, 可选择性舒张冠状血管⁽¹⁾, 增加冠脉血流量及氧含量, 同时能降低心肌耗氧量⁽²⁾, 对心肌供血有益。本文就Nit对家兔实验性急性心肌梗死(acute myocardial infarction, AMI)的作用进行探讨。

METHODS

家兔14只, 体重2.1 ± 0.3 kg, 雌雄不拘。实验分为两组: 给药组Nit(河北石家庄新华制药厂提供)溶于1% Tween-80配成10 mg · ml⁻¹ ig, 术前1 h及术后1, 4, 7 h各ig 10 mg · kg⁻¹; 对照组1% Tween-80 1 ml · kg⁻¹ ig, 给药次数和时间同给药组。戊巴比妥钠30 mg · kg⁻¹ iv麻醉, 不破胸膜开胸, 结扎冠状动脉左室支中点, 以心电图II导联ST段抬高作为冠脉结扎成功指标。

心肌梗死范围(myocardial infarctive size, MIS)的确定 术后24 h处死家兔取心脏, 剪除心底、心耳及右心室, 从心尖部开始向心底部将左室切成2-3 mm厚的肌片环, 浸于0.03%盐酸硝基四氮唑蓝溶液中, 置37℃水浴15 min组织化学染色。正常心肌染成紫蓝色, 梗死区心肌不着色。梗死区心肌重量占整个左室心肌的重量%为MIS。

血清肌酸激酶(creatine kinase, CK)和乳酸脱氢酶同工酶(lactate dehydrogenase isoenzyme, LDH-IE)的测定 术前和术后24 h耳动脉取血, 1000 × g离心5 min分离血清, 按肌酸显色法测定CK, 按聚丙烯酰胺凝胶电泳法测定LDH-IE。

心肌细胞超微结构的观察 取对照组和给药组梗死区心肌各7例, 经戊二醛及锇酸先后固定, 邻苯二甲酸二丙酯包埋, 轴-铅复染, H-600型透射电镜观察。

血浆去甲肾上腺素(norepinephrine, NE)的测定 术前和术后24 h从耳动脉取血, 注入含肝素的预冷试管中, 1000 × g离心5 min, 分离血浆, LC-6A系列高效液相色谱电化学测定法⁽³⁾测定NE浓度。

RESULTS

对 MIS 的影响 对照组和给药组家兔左室重无显著性差异; 但给药组左室心肌梗死重 0.58 ± 0.13 g 及 MIS $15.5 \pm 1.6\%$ 均低于对照组左室心肌梗死重 0.81 ± 0.12 g ($P < 0.01$) 及 MIS $25.2 \pm 1.7\%$ ($P < 0.01$).

对血清 CK 和 LDH-IE 浓度的影响 对照组冠脉阻塞 24 h 较阻塞前血清 CK 和 LDH₁, LDH₂ 升高均有显著性; 给药组与对照组相比, 冠脉阻塞 24 h 血清 CK 和 LDH₁ 降低有显著性 (Tab 1).

Tab 1. Effects of nitrendipine on serum creatine kinase (CK) and lactate dehydrogenase isoenzymes (LDH-IE) of rabbits in coronary artery ligation for 24 h. $n=7, \bar{x} \pm s. *P > 0.05, **P < 0.05, *P < 0.01$ vs control; $^+P > 0.05, ^{++}P < 0.05, ^{+++}P < 0.01$ vs preoperation.**

	CK/ IU · L ⁻¹	LDH-IE/%	
		LDH ₁	LDH ₂
Preoperation	168 ± 43	25 ± 6	26 ± 4
Control	381 ± 69 ⁺⁺⁺	42 ± 6 ⁺⁺⁺	33 ± 6 ⁺⁺
Nitrendipine	281 ± 49 ^{***}	31 ± 8 ^{**}	29 ± 3 [*]

对心肌细胞超微结构的影响 对照组梗死区壁层肌细胞的线粒体均出现重度的嵴断裂、崩解以至消失, 并见明显的絮状致密体, 肌原纤维结构破坏等典型不可逆性坏死性病变. 给药组梗死区壁层肌细胞线粒体仍保持膜双层和嵴的结构, 嵴的排列也较规则, 絮状致密体少见, 多数肌原纤维结构仍保持完整 (Fig 1, plate 1).

对血浆 NE 浓度的影响 对照组和给药组冠脉阻塞 24 h 较阻塞前 NE 浓度升高均有显著

性 ($P < 0.05$); 给药组与对照组相比, 阻塞前及阻塞 24 h 时 NE 均无显著差别.

DISCUSSION

Nit 选择性舒张冠脉⁽¹⁾, 增加冠脉血流量及氧含量, 同时可降低心肌耗氧量⁽²⁾. 本文结果表明, Nit 能缩小 MIS, 减少心肌细胞释放 CK 和 LDH₁, 减轻缺血梗死区心肌细胞线粒体, 肌原纤维等超微结构的破坏, 证明 Nit 对 AMI 有保护作用. Nit 抗 AMI 作用的主要机制是改善缺血心肌细胞氧供需矛盾, 也与其减少缺血心肌细胞中 CK 等酶释放入血液, 在高能磷酸代谢中起着保持高能磷酸的含量⁽⁴⁾; 保护线粒体, 肌原纤维结构, 减少心肌坏死有一定关系. MIS 缩小对心功能的恢复带来有益作用.

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