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论著

选择性内皮素A型受体拮抗剂GF063对内皮素-1诱导的心肌细胞肥大的影响

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摘要 **目的** 探讨选择性内皮素A型（ET_A）受体拮抗剂GF063对内皮素-1（ET-1）诱导的心肌细胞肥大的影响。**方法** 利用差速贴壁法分离得到原代SD乳鼠心肌细胞，心肌细胞用ET-1或ET- 1+GF063处理24 h，以BQ123为阳性对照，分别采用MTT比色法检测细胞存活、显微镜观察心肌细胞形态并计算细胞表面积、［^{3}H］亮氨酸掺入法测定心肌细胞蛋白质合成速率、RT-PCR法检测心肌细胞心钠素(ANP)mRNA表达。**结果** 与正常对照组比较，ET-1 10 nmol·L^{-1}作用24 h后，心肌细胞表面积明显增大80.6%，［^{3}H］亮氨酸掺入明显增多73%，ANP mRNA表达量明显增加80%(P<0.05)。单独给予GF063 1 nmol·L^{-1}~10 μmol·L^{-1}对心肌细胞存活率，细胞表面积，心肌细胞蛋白合成和ANP mRNA表达均无明显影响。但GF063 1 μmol·L^{-1}可以显著抑制ET-1诱导的心肌细胞表面积增大(P<0.05)，GF063 0.1和1 μmol·L^{-1}可显著降低心肌细胞蛋白合成(P<0.05)，GF063 10 μmol·L^{-1}抑制ANP mRNA表达升高(P<0.05)，作用强度与阳性对照药BQ123相当。**结论** GF063能够抑制ET-1诱导的心肌细胞肥大作用。

关键词 GF063 受体, 内皮素A 肌细胞, 心脏 心肌肥厚

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Effect of GF063, a new selective antagonist of endothelin A receptor, on cardiomyocytes hypertrophy induced by endothelin-1

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Abstract

OBJECTIVE To investigate effect of new endothelin A receptor (ET_A) antagonist di-*n*-butylaminocarbamyl-*L*-leucyl-*D*-tryptophany-*D*-40chloro- Phe (GF063) on cardiomyocytes hypertrophy induced by endothelin-1(ET-1). **METHODS** Primary culture of neonatal SD rat cardiomyocytes was prepared by differential adhesion. Cytotoxicity was determined by MTT assay, cell surface area was accounted by optical microscopy with image processing software, protein synthesis was measured by incorporation of ［ ^{3}H］leucine, gene expression was assessed by RT-PCR. **RESULTS** Compared with normal control group, after treated by ET-1 10 nmol·L^{-1} for 24 h，the surface area, incorporation of ［^{3}H］leucine and ANP mRNA expression in cardiomyocytes cells increased by 80.6%, 73% and 80% (P<0.05), respectively. Cardiomyocytes treated alone with GF063 1 nmol·L^{-1}-10 μmol·L^{-1} for 24 h, neither produce obvious cytotoxicity nor hypertrophy. GF063 1 μmol·L^{-1}+ET-1 10 nmol·L^{-1} in cardiomyocytes for 24 h can inhibited increases of cardiomyocytes surface area induced by ET-1, and the inhibition rate is 31.3% (P<0.05). GF063 1 and 10 μmol·L^{-1}+ET- 1 10 nmol·L^{-1} in cardiomyocytes for 24 h can inhibited increases of incorporation of ［^{3}H］leucine induced by ET-1, and the inhibition rate is nearly 100% (P<0.05). GF063 10 μmol·L^{-1}+ET- 1 10 nmol·L^{-1} in cardiomyocytes for 24 h can inhibited increases ANP mRNA expression induced by ET-1, and inhibition rate is 82.6% (P<0.05). The effects of GF063 mentioned above are similar to positive control drug BQ123 on cardiomyocytes hypertrophy induced by ET-1. **CONCLUSION** GF063, as a selective ETA receptor antagonist, can inhibit the hypertrophy of cardiomyocytes induced by ET-1.

Key words GF063 receptor endothelin A myocytes cardiac myocardia hypertrophy

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