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论著

δ阿片受体激活对过氧化氢损伤的心肌细胞的保护作用

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摘要 目的 研究δ阿片受体激活剂*D*-丙（2）-*D*-亮-（5）-脑啡肽（DADLE）对过氧化氢（H_2O_2）损伤的心肌细胞的保护作用及其机制。方法 分离乳大鼠心肌细胞，培养48 h后分为正常对照、H_2O_2（200 μmol·L^{-1}）、H_2O_2+DADLE（1 μmol·L^{-1}）、H_2O_2+DADLE+纳曲吲哚（10 μmol·L^{-1}）和H_2O_2+DADLE+U0126（10 nmol·L^{-1}）组，继续培养48 h。用［^{3}H］TdR掺入法检测心肌细胞增殖反应，流式细胞仪检测心肌细胞凋亡百分率，乳酸脱氢酶（LDH）活性测定试剂盒测定培养上清LDH活性，硫代巴比妥酸显色法测定细胞内丙二醛（MDA）含量，黄嘌呤氧化酶法测定细胞内超氧化物歧化酶（SOD）活性，Western蛋白印迹法检测细胞外信号调节激酶磷酸化(p-ERK)水平。结果 ①与正常对照组比较，H_2O_2组心肌细胞［^{3}H］TdR掺入值明显降低，细胞凋亡率升高；培养上清LDH活性和MDA含量明显增加，SOD活性和Ap-ERK/AERK的比值降低。②与H_2O_2组比较，DADLE可使心肌细胞［^{3}H］TdR掺入值升高，细胞凋亡率下降；培养上清LDH活性和MDA含量降低，SOD活性和Ap-ERK/AERK的比值升高。③分别加入δ阿片受体拮抗剂纳曲吲哚和ERK拮抗剂U0126，DADLE对上述指标的逆转作用被抑制。结论 δ阿片受体激活对H2O2损伤的心肌细胞具有保护作用，其机制可能与其增强心肌细胞的抗氧化功能及促进ERK磷酸化有关。

关键词 受体, 阿片样, δ 肌细胞, 心脏 过氧化氢 细胞外信号调节MAP激酶类 超氧化物歧化酶

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Protection of δ-opioid receptor stimulation against injured myocardial cells by hydrogen peroxide

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Abstract

AIM To study protective effect of ［*D*-Ala^2, *D*-Leu^5］-enkephalin (DADLE) against hydrogen peroxide (H_2O_2) induced myocardial cell injury and its possible mechanisms. **METHODS** Myocardial cells were isolated from neonatal rats and cultured for 48 h. Then the cells were randomly assigned into normal control, H_2O_2（200 μmol·L^{-1}）, H_2O_2+DADLE(1 μmol·L^{-1}), H_2O_2+DADLE+naltrindole(10 μmol·L^{-1}) and H_2O_2+DADLE+U0126(10 nmol·L^{-1}) groups and cultured for another 48 h. ［^{3}H］TdR incorporation assay and flow cytometry were used to measure the cell proliferation and apoptosis rate. The lactate dehydrogenase (LDH) activities in culture supernatant measured by using LDH activity kit. The superoxide dismutase (SOD) activity and malondialdehyde (MDA) content in cells were measured with xanthine oxidase method and color reaction of thiobarbituric acid, respectively. The expressions of extracellular signal-regulated kinase (ERK) and phosphorylated-ERK (p-ERK) were observed with Western blot. **RESULTS** ① Compared with normal control group, the incorporation of ［^{3}H］TdR in myocardial cells of H_2O_2 group was significantly lower, apoptosis rate was higher, LDH activity and MDA content in cells were higher, while SOD activity in cells was lower. In addition, the ratio of Ap-ERK/AERK was decreased. ② Compared with H_2O_2 group, the incorporation of ［^{3}H］TdR in H_2O_2+DADLE group was significantly higher, apoptosis rate was lower, LDH activity and MDA content in cells decreased, while SOD activity increased significantly. The ratio of Ap-ERK/AERK was increased. ③ δ-Opioid receptor antagonist naltrindole and ERK antagonist U0126 inhibited this effect of DADLE on the above index changes induced by H_2O_2. **CONCLUSION** The δ-opioid receptor has protective effect against H_2O_2-induced myocardial cell injury, and its possible mechanism may be related to its promotion of antioxide capacity and ERK phosphorylation.

Key words receptors opioid δ myocytes cardiac hydrogen peroxides extracellular signal regulated MAP kinases superoxide dismutase

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