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论著

κ-阿片受体激动对异丙肾上腺素诱导的乳大鼠心肌细胞肥厚的抑制作用

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摘要 目的 通过观察选择性κ-阿片受体（κ-OR）激动剂U50488H抑制异丙肾上腺素（Iso）诱导的乳大鼠心肌细胞肥厚的作用及对细胞内游离钙离子浓度（[Ca^{2+}]$_i$）瞬变及钙调素依赖蛋白激酶Ⅱ（CaMKⅡ）表达的影响，研究κ-OR激动抑制Iso诱导的大鼠心肌细胞肥厚的信号传导机制。方法 以体外培养的乳大鼠心肌细胞为模型，应用β肾上腺素受体激动剂Iso 10 μmol·L^{-1}诱导心肌肥大，观察U50488H 1 μmol·L^{-1}的作用，并进一步探讨在CaMKⅡ特异性抑制剂KN93 0.2 μmol·L^{-1}，普萘洛尔2 μmol·L^{-1}及L-钙通道阻滞剂维拉帕米1 μmol·L^{-1}存在情况下，κ-OR的激活对心肌肥厚的作用。用Lowry法检测心肌细胞蛋白含量；消化分离法及计算机图像分析系统检测心肌细胞体积；[^{3}H]亮氨酸掺入法测定心肌细胞蛋白的合成；采用Till阳离子测定系统，以Fura-2/AM为荧光探针，观察心肌细胞[Ca^{2+}]$_i$瞬间变化；用Western蛋白印迹法测定CaMKⅡδB表达。结果 Iso 10 μmol·L^{-1}使心肌细胞总蛋白含量、体积和蛋白合成明显增加，U50488H 1 μmol·L^{-1}抑制Iso诱导的心肌肥大，且抑制程度与KN93 0.2 μmol·L^{-1}，普萘洛尔2 μmol·L^{-1}及维拉帕米1 μmol·L^{-1}相似，在KN93存在的情况下，U50488H抑制Iso诱导的心肌肥大作用增强；U50488H能降低Iso引起的心肌细胞[Ca^{2+}]$_i$瞬间变化升高；Iso能明显增强心肌细胞内CaMKⅡδB的表达，U50488H能降低其表达。结论 κ-OR激动剂U50488H可能通过降低心肌细胞[Ca^{2+}]$_i$瞬间变化和减少心肌细胞内CaMKⅡδB的表达，抑制Iso诱导的乳大鼠心肌细胞肥厚。

关键词 受体,阿片,κ 心肌肥大 U50488H Ca2+-钙调蛋白依赖性蛋白激酶

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Inhibitory effect of kappa- opioid receptor stimulation on isoprenaline induced myocardial hypertrophy of neonatal rats

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Abstract

AIM To observe the inhibitive effects and signal transduction by kappa- opioid receptor(κ-OR) stimulation on hypertrophic myocardial cells induced by isoprenaline (Iso) in neonatal rats. **METHODS** The total protein content was assayed by the method of Lowry. The cardiomyocytes volume was measured by computer photograph analysis system and the protein synthesis was assayed with [^{3}H] leucine incorporation method. [Ca^{2+}]$_i$ transient was measured by Till image system by cell-loading Fura-2/AM. The expression of Ca^{2+}-calmodulin dependent kinase Ⅱ (CaMKⅡ)δB was determined by Western blot. **RESULTS** Iso enhanced the total protein content, the cardiomyocyte volume and the protein synthesis in myocardial cells. U50488H showed the function on reducing the previous mentioned indices induced by Iso, which were similar to KN93, propranolol and verapamil. U50488H also attenuated the hypertrophy and the expression of CaMKⅡδB induced by Iso through decreasing the [Ca^{2+}]$_i$. **CONCLUSION** Kappa-opioid receptor stimulation can abolish the hypertrophic response induced by Iso, which is partially via attenuating the augment of [Ca^{2+}]$_i$ and the high expression of CaMKⅡδB induced by Iso.

Key words receptors opioid kappa myocardial hypertrophy U50488H Ca2+-calmodulin dependent kinases

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