

论文

腺病毒介导eNOS转染高肺血流肺动脉高压大鼠模型的研究

冯晓丽 1, 朱晓波 1, 2, 陈欧 3, 苏宏 1, 马宇 1, 王一彪 1

山东大学 1. 第二医院儿科, 济南 250033; 2. 医学院, 济南 250012; 3. 护理学院护理基础研究室, 济南 250012

摘要:

目的 观察腺病毒介导的内皮型一氧化氮合酶基因(eNOS)转染对高肺血流肺动脉高压大鼠模型肺动脉高压形成的影响。方法 随机将40只大鼠分为假手术组、手术组、实验组和对照组,每组10只。手术组、实验组和对照组采用套管连接法建立左向右分流肺动脉高压模型,实验组采用气管吸入法转染重组腺病毒AdCMVeNOS,采用免疫组化法观察eNOS蛋白表达,采用比色法测定肺组织eNOS活性,测量各组大鼠平均肺动脉压(mPAP)、右心室平均压(mRVP)、平均颈动脉压(mCAP)、右心肥厚指数(RVHI),采用HE染色观察肺动脉形态学改变,计算管壁厚度与血管外径比值(WT%)。结果 实验组免疫组化染色可见全层血管壁内棕黄色颗粒,eNOS表达强度明显高于对照组(P<0.05),假手术组eNOS表达的阳性细胞介于实验组与对照组之间。手术组和对照组的eNOS活性比假手术组明显降低(P<0.05);实验组的eNOS活性显著高于对照组,且较假手术组亦明显升高(P<0.05)。手术组和对照组大鼠的mRVP、mPAP、RVHI和WT%均明显高于假手术组(P<0.05)。与对照组相比,实验组大鼠mRVP、mPAP、RVHI和WT%均显著降低(P<0.05);手术组与对照组各值之间差异不明显。结论 腺病毒介导的eNOS基因转染能够上调高肺血流肺动脉高压大鼠肺组织中eNOS表达及其活性,延缓肺动脉高压的发展和肺血管的重塑。

关键词: 一氧化氮合酶; 高血压, 肺性; 转染; 基因疗法; 大鼠, Wistar

Effect of adenovirus mediated human endothelial nitric oxide synthase gene transfection on pulmonary hypertension rat model induced by high pulmonary blood flow

FENG Xiao li 1, ZHU Xiao bo 1, 2, CHEN Ou 3, SU Hong 1, MA Yu 1, WANG Yi biao 1

1. Department of Pediatrics, Second Hospital of Shandong University, Jinan 250033, China; 2. School of Medicine, Shandong University, Jinan 250012, China; 3. Research Laboratory of Nursing Basics, School of Nursing, Shandong University, Jinan 250012, China

Abstract:

Objective To investigate the effect of adenovirus-mediated endothelial nitric oxide synthase (eNOS) gene transfection on the development of pulmonaryhypertension induced by high pulmonary blood flow. Methods Forty Wistar rats were randomly divided into four groups with ten rats in each group: the sham operation group, the operation group, the test group and the control group. Except forthe sham operation group, groups were developed into left-to-right shunt pulmonary hypertensiocuff technique. Recombinant adenovirus(AdCMVeNOS) was transfected into the test group using tracheal inhalation. We observed expression and activity of eNOS in the lung by immunohistochemistry and colorimetry, measured themPAP, mRVP, mCAP and RVHI, and calculated WT%. Results Brown spots in the full wall of pulmonary vessels were seen in the test group. The expression level of eNOS in the test group was significantly higher than that in the control group. The number of eNOS expression-positive cells in the sham operation group was lower than in the test group but higher than in the control group. The activity of eNOS obviously decreased in the operation and control groups compared with that in the sham operation group (P<0. 05), and increased in the operation groupcompared with those in the control and sham operation groups. The levels of mRVP, mPAP, RVHI and WT% were similar between the operation group and the control group,which were significantly higher than those in the sham operation group (P<0.05).The levels of the above four indicators were obviously lower in the test groupthan in the control group. Conclusion Adenovirus mediated eNOSgene transfection can increase expression and activity of eNOS in lung tissue of the pulmonary hypertension rat model induced by high pulmonary blood flow, and delays the development of pulmonary hypertension and pulmonary vascular remodeling.

Keywords: Nitric-oxide synthase; Hypertension, pulmonary; Transfection; Gene therapy; Rats, Wistar

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通讯作者: 王一彪 (1963- ), 男, 教授, 主要从事小儿心脏病研究

作者简介: 冯晓丽 (1983- ), 女, 硕士研究生, 主要从事小儿心脏病研究。 E-mail: xiaolifengki@yahoo.com

作者Email:

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