

论文

ADM和PAMP在高肺血流肺动脉高压形成中的变化及作用途径研究

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摘要:

目的 探讨来自同一前体的肾上腺髓质素(ADM)及肾上腺髓质素N末端20肽(PAMP)在高肺血流肺动脉高压形成中的变化及作用途径。方法 健康雄性Wistar大鼠21只,随机分为2组。将实验组(n=9)大鼠的左侧颈总动脉与颈外静脉用套管进行连接,对照组大鼠仅切颈动脉皮肤分别分离颈总动脉和颈外静脉后缝合皮肤,不进行血管连接术。术后12周,经右心导管测取大鼠肺动脉平均压(mPAP)、右心室/(室间隔+左心室)(RV/(LV+SP))重量比、中等肺动脉壁厚度所占管径百分比(MT%)。免疫组化法和Western blotting测定ADM、PAMP在大鼠肺组织中的分布及其相对含量变化。RT-PCR法检测大鼠肺组织中ADM、应力活化蛋白激酶(SAPK)、细胞外信号调节激酶(ERK1)基因表达量。结果 实验组大鼠术后mPAP与对照组比较明显升高(P<0.001);RV/(LV+SP)和MT%比例明显增加(P<0.001和P<0.01)。免疫组化结果显示ADM和PAMP棕色颗粒主要分布于血管平滑肌层;累积光密度(OD)及Western blotting结果显示实验组大鼠肺内ADM及PAMP蛋白表达量增加。RT-PCR结果显示实验组大鼠肺组织ADM、SAPK、ERK1 mRNA与对照组比较表达增强(P<0.01, P<0.001)。结论 高肺血流肺动脉高压形成中存在来自同一前体的ADM与PAMP之间的分子内调控现象;丝裂原活化蛋白激酶(MAPKs)信号通路可能参与了高肺血流肺动脉高压形成过程。

关键词: 肾上腺髓质素; 肾上腺髓质素N末端20肽; 高肺血流; 肺动脉高压; 丝裂原活化蛋白激酶

Roles and signal pathways of adrenomedullin and proadrenomedullin N-terminal 20 peptide in pulmonary hypertension due to high pulmonary blood flow in rat

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Abstract:

Objective To investigate the roles of adrenomedullin (ADM) and proadrenomedullin N-terminal 20 peptide(PAMP) in pulmonary hypertension due to high pulmonary blood flow in rat lungs. Methods 21 male Wistar rats were randomly divided into 2 groups. The left common carotid artery to external jugular vein shunt operations were performed on experimental rats to establish left to right shunt animal models. The common carotid artery and external carotid artery of the control group rats were isolated without connection. 12 weeks later, the mean pulmonary artery pressure (mPAP), the right ventricle to left ventricle plus septum ratio (weight, RV/(LV+SP)), and the percentage of media wall thickness (MT%) were calculated. The changes and relative protein contents of ADM and PAMP in the lungs were measured by immunohistochemical staining and Western blot analysis. The relative gene expression of ADM, p46-p54 stress-activated protein kinase (SAPK) and p44 extracellular signal-regulated protein kinase 1 (ERK1) were investigated by RT-PCR. Results The muscular and the tunica intima layer of the pulmonary artery were thicker in the experimental group than in the control group, and the mPAP increased significantly in the shunt group compared with the control group(P<0.001). The ratios of RV/(LV+SP) and MT% increased statistically in the experimental group in contrast to the control group(P<0.001 and P<0.01). Western blot and integrated optical density showed that the content of ADM and PAMP increased in the shunt group rats (P<0.01 and P<0.001). mRNA expression of ADM, SAPK and ERK1 was up-regulated in the experimental group compared to the control group (P<0.01 and P<0.001 respectively). Conclusions The phenomenon of intramolecular regulation of ADM and PAMP, which both derived from proadrenomedullin, existed in the development of pulmonary hypertension due to the left to right shunt. The mitogen-activated protein kinases (MAPKs) signal pathway has been activated in the formation of left to right shunt pulmonary hypertension.

Keywords: Adrenomedullin; Proadrenomedullin-N-terminal 20 peptide; High pulmonary blood flow; Pulmonary hypertension; Mitogen-activated protein kinase

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