

论文

间尼索地平对野百合碱诱导的肺动脉高压防治作用及其抗5-羟色胺—细胞外信号调节激酶通路的机制探讨

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摘要:

研究间尼索地平对野百合碱诱导的肺动脉高压的防治作用及其作用机制。大鼠单剂量皮下注射野百合碱(60 mg·kg⁻¹)制备肺动脉高压模型。导管法测定肺血流动力学指标;光镜观察肺小动脉结构的改变;同时测定血清中MDA及SOD的含量(活性);免疫印迹法测定PCNA、ERK1和p-ERK的表达水平;免疫组化法观察5-HT和PCNA的表达。结果表明,与正常对照组相比,模型组大鼠的平均肺动脉压及右心指数明显增加;肺小动脉肌化程度加重;丙二醛含量显著升高,超氧化物歧化酶活性明显降低;PCNA和5-HT阳性细胞数目明显增加;PCNA蛋白表达及p-ERK/ERK1比率也显著增加,不同剂量间尼索地平在一定程度上逆转了上述变化。间尼索地平对野百合碱诱导的肺动脉高压表现出一定的保护作用。这一作用可能与其降低5-HT的表达,抑制ERK/MAPK信号通路有关。

关键词: 肺动脉高压 5-羟色胺 野百合碱 间尼索地平

m-Nisoldipine attenuates monocrotaline-induced pulmonary hypertension by suppressing 5-HT/ERK MAPK pathway

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Abstract:

Effect of new calcium antagonist *m*-nisoldipine (*m*-Nis) on MCT-induced PH in rats and its mechanisms were investigated. Rats were injected with a single dose (60 mg·kg⁻¹) of MCT subcutaneously to induce PH. Pulmonary haemodynamic measurement and lung tissue morphological investigations were undertaken. The MDA production and SOD activity in the serum were tested. PCNA, ERK1 and p-ERK expressions were analyzed by Western blotting. The expressions of 5-HT and PCNA were observed with immunohistochemistry. Results suggested that the PAP, right ventricular index and the degree of muscularization of small pulmonary artery were elevated markedly in MCT group, which was attenuated by *m*-Nis treatment. A significant reduction in MDA production and an increase in the SOD activity in the serum were also observed in all three *m*-Nis groups. The number of PCNA and 5-HT positive smooth muscle cells increased significantly in MCT group, and *m*-Nis treatment attenuated the expression obviously. Western blotting results suggested that the protein expression of PCNA and the ratio of p-ERK/ERK1 increased markedly in MCT group and decreased by *m*-Nis. In conclusion, *m*-Nis protected against MCT-induced PH by decreasing PAP, right ventricular index, PAMSCs proliferation and pulmonary artery remodelling, which may be related to the reduction of 5-HT and the suppression of the ERK/MAPK signal pathway.

Keywords: 5-hydroxytryptamine monocrotaline *m*-nisoldipine pulmonary hypertension

收稿日期 2008-05-04 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 张永健

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