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论著

1,8-桉油精对卵白蛋白致哮喘豚鼠的气道高反应性和炎症的抑制作用

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摘要 目的 探讨1,8-桉油精(1,8-cineol)对哮喘豚鼠肺功能的改善作用及其机制。方法 豚鼠第0天和第7天ip给予0.5 ml含卵白蛋白（OVA）20 μg的氢氧化铝凝胶致敏，28 d后OVA攻击制备哮喘模型。观察豚鼠OVA攻击后1 h，1,8-桉油精10，30和100 mg·kg^{-1}对豚鼠吸入OVA后1，2，3，4，10，20和30 min时气道阻力（R_{aw}）和肺顺应性（C_{dyn}）变化及支气管肺泡灌洗液（BALF）中白细胞数和细胞分类的影响，并测量豚鼠肺组织中嗜酸细胞阳离子蛋白（ECP）、白细胞介素4（IL-4）、IL-8和肿瘤坏死因子α（TNF-α）的含量。观察豚鼠OVA攻击后17 h再吸入乙酰甲胆碱(MCh)后，1,8-桉油精10，30和100 mg·kg^{-1}对R_{aw}和C_{dyn}及BALF中白细胞数和细胞分类的影响，并测量豚鼠肺组织中ECP，IL-4，IL-8和TNF-α的含量。结果 与正常对照组比较，豚鼠OVA攻击后1 h，在4 min时模型组Raw达到高峰；与模型组比较，1,8-桉油精30和100 mg·kg^{-1}明显抑制Raw增加(P<0.05)；在3 min时模型组C_{dyn}达到高峰，与模型组比较，1,8-桉油精10，30和100 mg·kg^{-1}均能明显抑制C_{dyn}降低(P<0.05)；模型组豚鼠肺组织ECP，IL-4和TNF-α含量明显高于正常对照组(P<0.05)；1,8-桉油精100 mg·kg^{-1}组ECP，IL-4和TNF-α含量均明显低于模型组(P<0.05)，模型组与正常对照组豚鼠肺组织IL-8含量无明显差异。与模型组比较，1,8-桉油精100 mg·kg^{-1}能明显减少BALF中白细胞数和嗜酸性粒细胞比例(P<0.05)。致敏豚鼠OVA攻击17 h后，模型组豚鼠R_{aw}与正常对照组比较显著升高(P<0.05)，模型组豚鼠C_{dyn}与正常对照组比较有显著性差异(P<0.01)，1,8-桉油精100 mg·kg^{-1}对MCh引起的R_{aw}的增加有明显的抑制作用，1,8-桉油精10，30和100 mg·kg^{-1}对MCh引起的C_{dyn}降低有明显的改善作用；与模型组相比，1,8-桉油精100 mg·kg^{-1}能明显减少BALF中白细胞数和中性粒细胞比例，降低肺组织ECP，IL-8和TNF-α含量(P<0.01)；模型组与正常对照组豚鼠肺组织IL-4含量无明显差异；1,8-桉油精30 mg·kg^{-1}也能降低哮喘豚鼠肺组织中ECP和TNF-α含量(P<0.01)。结论 在哮喘急性发作时，1,8-桉油精通过减少嗜酸性粒细胞，下调嗜酸性粒细胞的活性，从而抑制了哮喘的急性发作。在哮喘迟发相阶段，1,8-桉油精可通过下调IL-8水平，降低TNF-α活性，从而抑制或改善由IL-8水平升高导致的中性粒细胞聚集于支气管肺泡而直接引起的哮喘加重和持续状态。

关键词 1,8-桉油精 哮喘 气道高反应性 炎症 细胞因子

分类号 R285，R974

Inhibitory effects of 1,8-cineol on ovalbumin-induced lung inflammation and airway hyperresponsiveness in asthmatic guinea pigs

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Abstract

OBJECTIVE To investigate the effects of 1,8-cineol on lung functions and mechanism in asthmatic guinea pigs. **METHODS** The guinea pig model was performed by intraperitoneal injection of the 0.5 ml $Al(OH)_3$ gel containing OVA 20 μg. The guinea pigs were constructed by immunization of intraperitoneal injection on the 0 day and the 7th day, and the experiment was performed on the 28th day. The effect of 1,8-cineol 10, 30 and 100 ml·kg^{-1} on the airway resistance(R_{aw}) and dynamic lung compliance (C_{dyn}) of asthmatic guinea pigs 1 h after challenge of OVA. The changes in leukocyte and different kinds of leukocyte in bronchoalveolar lavage fluid (BALF) after the challenge of OVA have been studied. The levels of eosinophil cationic protein (ECP), interleukin(IL)-4, IL-8 and tumor necrosis factor (TNF)-α in lungs of guinea pigs were determined using enzyme-linked immunosorbent assay (ELISA). The changes in R_{aw} and C_{dyn} of asthmatic guinea pigs were investigated 17 h after challenge of OVA and inhalated methacholine (MCh). The changes in leukocyte and different kinds of leukocyte in BALF after the challenge of OVA have been studied. The levels of ECP, IL-4, IL-8 and TNF-α in lungs of guinea pigs were determined using ELISA. **RESULTS** 1,8-Cineol inhibited increase in R_{aw} and decrease in Cdyn from 1 to 30 min after challenge of OVA in model group. The levels of ECP, IL-4 and TNF-α in asthmatic model

group were higher than those in normal control group(P<0.05). The levels of ECP, IL-4 and TNF-α of 1,8-cineol 100 mg·kg^{-1} group were significantly lower than those in asthmatic model group (P<0.01). The level of IL-8 of asthmatic model group didn′t have any significant difference from that of control group. 1,8-Cineol 100 mg·kg^{-1} could significantly decrease the numbers of leukocyte and the percent of eosinophils in BALF. Seventeen hours after challenge of OVA, R_{aw} and C_{dyn} of asthmatic model group were higher than these of control group (P<0.05, P<0.01); 1,8-cineol 100 mg·kg^{-1} significantly inhibited the increase in R_{aw}, compared with model group (P<0.05); 1,8-cineol 10, 30 and 100 mg·kg^{-1} improved the decrease in C_{dyn} after MCh-induced in model group which were challenged by OVA after 17 h; 1,8-cineol 100 mg·kg^{-1} could significantly decrease the numbers of leukocyte and the percent of neutrophils, the levels of ECP, IL-8 and TNF-α compared with asthmatic group. The level of IL-4 in asthmatic model group didn′t have any significant difference from that in normal control group. **CONCLUSION** In the course of early stage of asthma, 1,8-cineol inhibites the asthma by decreasing the number of eosinophils and down-regulating the activity of EPO. In the course of later stage of asthma, 1,8-cineol inhibits or improves the aggravation and lasting states of asthma which is directly coursed by neutrophils accumulating in the BALF that related to the increase in IL-8.

Key words 1 8-cineol asthma hyperresponsiveness inflammation cytokines

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