[1]冉雪梅,赵燕,黄毅,等.阿奇霉素通过抑制Th17细胞功能活性改善小鼠哮喘炎症[J].第三军医大学学报,2013,35(05):421-425.

Ran Xuemei,Zhao Yan,Huang Yi,et al.Azithromycin improves inflammation by suppressing functions of Th17 cells in a mouse allergic asthma model[J].J Third Mil Med Univ,2013,35(05):421-425.

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阿奇霉素通过抑制Th17细胞功能活性改善小鼠哮喘

《第三军医大学学报》[ISSN:1000-5404/CN:51-1095/R] 卷: 35 期数: 2013年第05期 页码: 421-425 栏目: 论著 出版日期: 2013-03-15

Title: Azithromycin improves inflammation by suppressing functions of Th17 cells in a mouse allergic asthma model

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关键词: 阿奇霉素; Th17细胞; 中性粒细胞; 哮喘

Keywords: azithromycin; Th17 cells; neutrophil; asthma

分类号: R562.25; R967; R978.15

DOI: -

文献标识码: A

摘要: 目的 研究阿奇霉素对Th17应答增强致气道以中性粒细胞浸润为主的小鼠哮喘炎症的作用。 方法 采用卵蛋白(OVA)+ 内毒素(LPS)联合致敏, OVA激发的方法建立Th17应答增强致气道中性粒细胞浸润为主的哮喘小鼠模型, 48只BALB/c 雌性小鼠随机分为对照组、哮喘组、阿奇霉素组、地塞米松组(n=12)。采用HE染色观察肺组织病理改变; 小鼠肺功能仪检测气道高反应性(airway hyperreactivity, AHR); 肺泡灌洗液(bronchoalveolar lavage fluid, BALF)行细胞分类计数; ELISA检测外周血OVA特异性IgE及BALF中IL-17、TNF-α、IL-8、IL-5和IFN-γ浓度; Q-PCR检测肺组织Th1、Th2和 Th17细胞分化。 结果 用OVA联合LPS的方法可以复制既有Th2活化和肺内嗜酸性细胞增多, 又有Th17表达增强和明显中性粒细胞炎症的哮喘小鼠模型。与哮喘组比较, 阿奇霉素组气道炎症细胞浸润明显改善, 特别是中性粒细胞比例显著降低(P<0.05)。同时还有BALF中IL-17、TNF-α、IL-8、IL-5水平显著降低(P<0.05); 肺组织Th17细胞分化减少(P<0.05)以及 AHR改善(P<0.05)。而地塞米松组与哮喘组比较, 虽然 BALF嗜酸性细胞比例显著降低, 但BALF中细胞总数、IL-17、TNF-α、IL-8水平及肺组织Th17细胞分化均无明显差别(P>0.05)。 结论 阿奇霉素可抑制Th17细胞分化、减少炎症介质分泌从而抑制炎症细胞浸润,由此减弱Th17应答增强致气道中性粒细胞增高的小鼠哮喘炎症。

Abstract: Objective To determine the effect of azithromycin on the inflammation in

Th17-mediated mouse allergic asthma model with increased neutrophils around airways. Methods Th17-mediated mouse allergic asthma model with increased neutrophils around airways was established by sensitization with ovalbumin (OVA) and LPS, and challenge with OVA. Forty-eight healthy female BALB/c mice were randomly divided into 4 groups, control, asthma group, azithromycin group and dexamethasone group. Pathologic changes of lung tissue were observed by microscopy. Non-invasive measurements of airway resistance were used to measure allergen-induced airway hyperreactivity (AHR).Total cells and cell proportions in bronchoalveolar lavage fluid (BALF) were observed. The concentrations of OVA-specific IgE in the serum and of IL-17, TNF-α, IL-8, IL-5, and TNF-γ in the BALF were measured by ELISA. The polarizing levels of the Th1, Th2 and Th17 cells were detected by Q-PCR. Results Combining OVA and LPS could establish a mouse model of allergic asthma with Th2 activation and eosinophils increase in the lung, and simultaneously, enhanced Th17 expression and apparent neutrophilic inflammation. Compared with the asthma group, azithromycin attenuated inflammatory cells infiltration in airway, and decreased N% significantly (P<0.05). Moreover, the levels of IL-17, TNF-α, IL-8, and IL-5 in the BALF were reduced in azithromycin treated group (P<0.05). In addition, azithromycin effectively attenuated Th17 cells differentiation in lung tissue (P<0.05) and reduced AHR (P<0.05). However, in the dexamethasone group, even though E% in the BALF was reduced significantly compared to asthma group, there was no significant difference between the dexamethasone group and asthma group in total cell number, levels of IL-17, TNF-α, and IL-8 in the BALF and differentiation of Th17 cells in lung tissue (P>0.05). Conclusion Azithromycin can attenuate inflammation in Th17-mediated mouse allergic asthma model with increased neutrophils around airways. The underlying mechanism may be the inhibition of inflammatory cells infiltration by reducing Th17 differentiation and decreasing secretion of inflammatory mediators.

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备注/Memo: -