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论著

L-精氨酸通过抑制凋亡途径对脂多糖导致的急性肺损伤的作用

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摘要 目的 探讨一氧化氮供体*L*-精氨酸（*L*-Arg）对大鼠不同病程阶段的急性肺损伤（ALI）的影响及机制。方法 采用注射内毒素脂多糖（LPS）的方法制备大鼠肺损伤模型。健康雄性SD大鼠，随机分为：① 对照组；② LPS组；③ *L*-Arg治疗组。各组按治疗时间又分为给LPS 1 h后治疗3 h（1 h+3 h）组和给LPS 6 h后治疗3 h（6 h+3 h）组，并在给予LPS 1和6 h后再分别ip给予生理盐水(对照组及LPS组)和*L*-Arg 500 mg·kg^{-1}(*L*-Arg治疗组）治疗3 h。采用流式细胞术检测肺细胞凋亡率；Western蛋白印迹法检测胱天蛋白酶3(caspase 3)蛋白的表达；免疫组化法测定Bcl-2和Bax蛋白的表达；电镜观察肺组织病理变化。结果 与对照组比较，LPS 1 h+3 h及LPS 6 h+3 h组细胞凋亡率和caspase 3蛋白表达明显升高，Bcl-2蛋白表达下降，Bax表达增加，Bcl-2/Bax比值降低，肺组织出现明显的病理变化。与LPS 1 h+3 h组相比，*L*-Arg 1 h+3 h组细胞凋亡率〔(23.8±2.8)% *vs* (15.4±2.3)%〕，caspase 3(0.80±0.06 *vs* 0.67±0.10)和Bax蛋白表达(0.115±0.012 *vs* 0.091±0.014)显著降低，Bcl-2蛋白表达(0.067±0.011 *vs* 0.075±0.009)和Bcl-2/Bax比值 (0.586±0.114 *vs* 0.833±0.142)显著升高；肺组织病理改变明显减轻。*L*-Arg 6 h+3 h组细胞凋亡率和caspase 3蛋白表达低于LPS 6 h+3 h组，肺组织病理改变稍有减轻。结论 较早给予*L*-Arg可减轻ALI，其机制可能与降低caspase 3和Bax蛋白表达、增强Bcl-2蛋白表达有关。

关键词 精氨酸 细胞凋亡 呼吸障碍

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Effects of *L*-arginine on lipopolysaccharides-induced acute lung injury by inhibiting apoptotic pathway

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Abstract

AIM To investigate the effect and mechanism of *L*-arginine(*L*-Arg) on lipopolysaccharides(LPS)-induced acute lung injury (ALI). **METHODS** Models of ALI were established by injection (iv) with LPS 5 mg·kg^{-1} in male SD rats. The rats were randomly divided into 3 groups: ① saline group; ② LPS group; ③ *L*-Arg group. The rats in each group were further divided into 2 subgroups according to *L*-Arg-supplemented time: 1 h+3 h group and 6 h+3 h group. *L*-Arg 500 mg·kg^{-1} or saline (saline and LPS groups) was administrated at 1 or 6 h after LPS injection, respectively. The treatment lasted for 3 h, and the rats were sacrificed at 4 or 9 h after LPS injection. Apoptotic rate, caspase 3, and Bcl-2 and Bax were evaluated by flow cytometry, Western blot analysis and immunohistochemistry, respectively; meanwhile, the pathological changes of lung tissue were observed by electron microscope. **RESULTS** Compared with saline group, apoptosis of pulmonary cells and caspase 3 expression were significantly increased, Bcl-2 was decreased, while Bax was elevated in alveolar and airway epithelial cells in LPS group. Compared with LPS 1 h+3 h group, *L*-Arg 1 h+3 h decreased apoptotic pulmonary cells 〔(23.8±2.8)% *vs* (15.4±2.3)%〕; moreover, expressions of caspase 3 (0.80±0.06 *vs* 0.67±0.10) and Bax (0.115±0.012 *vs* 0.091±0.014) were significantly decreased, while expression of Bcl-2 (0.067±0.011 *vs* 0.075±0.009) and Bcl-2/Bax ratio (0.586±0.114 *vs* 0.833±0.142) in alveolar and airway epithelial cells were markedly increased, and lung damage was alleviated. *L*-Arg 6 h+3 h also reduced apoptotic pulmonary cells and caspase 3 expression compared with LPS group, but the lung injury relieved slightly. **CONCLUSION** Relatively early administration of *L*-Arg can protect lungs from LPS-induced injury through inhibiting cell apoptosis, as well as increasing the expression of anti-apoptotic protein Bcl-2 and decreasing the expression of proapoptotic protein Bax and caspase 3.

Key words arginine apoptosis respiration disorders

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