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论著

内源性H_2S在CCK-8减轻脂多糖所致急性肺损伤中的作用

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摘要 目的：探讨内源性硫化氢(H_2S)在八肽胆囊收缩素(CCK-8)减轻脂多糖（LPS）所致急性肺损伤(ALI)中的作用。方法: 将84只SD大鼠随机分为正常对照组、LPS组（经气管内滴注LPS复制ALI）、NaHS(H_2S供体)+LPS组、炔丙基甘氨酸［胱硫醚-γ-裂解酶（CSE）抑制剂，PPG］+LPS组、CCK-8+LPS组、PPG+CCK-8+LPS组和CCK- 8组。给药后分别于4 h和8 h处死动物，测定肺湿/干比值；光镜观察肺组织形态学改变；化学法检测血浆H_2S含量，肺组织MDA含量、MPO活性和CSE活性；放免法检测肺组织P-selectin含量；RT-PCR检测肺组织CSE mRNA的表达；并行支气管肺泡灌洗，检测支气管肺泡灌洗液(BALF)中蛋白含量。结果: 气管内滴注LPS可引起肺组织明显的形态学改变；肺湿/干比值、BALF中蛋白含量及肺组织MDA、MPO活性和P-selectin水平增高；血浆H 2S含量、肺组织CSE活性及CSE mRNA表达下降。预先给予NaHS或CCK-8可显著减轻LPS所致的上述改变，且血浆H_2S含量、肺组织CSE活性及CSE mRNA表达高于相应的LPS组；预先给予PPG可加重LPS所致的肺损伤，而血浆H_2S含量、肺组织CSE活性及CSE mRNA表达分别低于相应的LPS组和CCK-8+LPS组。结论: CCK-8可通过内源性H_2S介导的抗氧化、抑制PMN黏附聚集等效应发挥减轻LPS所致肺损伤的作用。

关键词 急性肺损伤； 胆囊收缩素； 硫化氢； 脂多糖类

分类号 R363

Protective role of endogenous hydrogen sulfide in cholecystokinin octapeptid against acute lung injury induced by lipopolysaccharide

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Abstract

<FONT face=Verdana>AIM: To explore the role of endogenous hydrogen sulfide (H₂S) in the mechanism of cholecystokinin octapeptide (CCK-8) to alleviate acute lung injury (ALI) induced by lipopolysaccharide (LPS). METHODS: Eighty-four Sprague-Dawley rats were randomly divided into seven groups: control, LPS (instilled intratracheally to reproduce the model of ALI), NaHS (H₂S donor) +LPS, propargylglycine ［inhibitor of cysathionine-γ-lyase (CSE), PPG］+LPS, CCK-8+LPS, PPG+CCK-8+LPS and CCK-8 group. Animals were sacrificed at 4 h and 8 h after agent instillation. The wet and dry ratio (W/D) of the lung weight was measured and calculated. Morphological changes of lung tissues were observed. H₂S concentration in plasma, malondialdehyde (MDA) content, myeloperoxidase (MPO) and CSE activities in the lung were determined. Furthermore, the level of P-selectin of lung tissue was measured by radioimmunoassay, the CSE mRNA expression in the lung was detected by RT-PCR, and the protein content in bronchoalveolar lavage fluid (BALF) was detected.
RESULTS: Compared with control, severe injury of lung tissues and increase in W/D, protein content in BALF, MDA content, MPO activity and P-selectin level in the lung were observed in rats treated with LPS. LPS also lead to a drop in plasma H₂S concentration, lung CSE activity and CSE mRNA expression. Administration of NaHS before LPS could attenuate the changes induced by LPS, while H₂S concentration, CSE activity and CSE mRNA expression were higher than those in LPS group. However, pre-treatment with PPG

exacerbated the lung injury induced by LPS, H₂S concentration, CSE activity and CSE mRNA expression were lower than those in LPS and CCK-8 +LPS group, respectively.
CONCLUSION: CCK-8 attenuates LPS-induced acute lung injury by means of anti-oxidation and inhibition of PMN adhesion and aggregation, both of which are mediated by endogenous H₂S.</FONT>

Key words Acute lung injury Cholecystokinin Hydrogen sulfide Lipopolysaccharides

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