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论述

小檗碱抗小鼠脂多糖性肺损伤的作用机制

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摘要 目的：探讨小檗碱(Ber)对抗脂多糖(LPS)性急性肺损伤(ALI)的作用机制。方法：雄性BALB/c小鼠随机分为对照组、ALI组和Ber防治组，分别予以双蒸水、Ber(50 mg/kg)灌胃，1次/d，连续3 d，于实验第3 d灌胃后1 h，腹腔注射生理盐水或LPS (20 mg/kg)。测定各组12 h肺湿/干重比值(W/D)，肺泡灌洗液(BALF)中微量总蛋白含量、白细胞(WBC)和中性粒细胞(PMN)总数；观察肺组织病理改变及磷酸化胞浆型磷脂酶A_2(cPLA$_2$)在肺组织中的表达。进一步用酶联免疫吸附法(ELISA)测定BALF中血栓素B_2(TXB$_2$)的含量，并测定肺组织丙二醛(MDA)的含量和超氧化物歧化酶(SOD)的活性。结果：ALI组，LPS 攻击后12 h肺W/D、BALF中蛋白含量、WBC 及PMN总数显著高于对照组(P<0.05)；病理检查发现肺间质充血、水肿，大量炎性细胞浸润。免疫组织化学观察显示肺组织中磷酸化cPLA$_2$的表达明显增加；同时，BALF中TXB$_2$含量、肺组织MDA的含量显著高于对照组(P<0.05)。Ber防治组，肺W/D、BALF中蛋白含量、WBC及PMN总数均明显低于ALI组；与ALI组比较，Ber防治组肺组织病理损伤明显减轻(P<0.05)；而且，肺组织中磷酸化cPLA$_2$的表达明显减少(P<0.05)； BALF中TXB$_2$含量和肺组织MDA的含量显著低于ALI组。结论：抑制肺组织cPLA$_2$的磷酸化并对抗脂质过氧化损伤可能是Ber防治小鼠脂多糖性肺损伤的重要机制。

关键词 小檗碱； 脂多糖； 急性肺损伤； 胞浆型磷脂酶A2； 小鼠； 丙二醛

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Mechanisms for protection of berberine against LPS-induced acute lung injury in mice

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Abstract

<FONT face=Verdana>AIM:To investigate the mechanisms by which berberine attenuates LPS-induced acute lung injury, and provide a new strategy for the treatment of the lung injury due to LPS.
METHODS:BALB/c mice were randomly assigned into three groups (control, LPS group, and berberine treatment group). Mice were administered intragastrically with distilled water (0.1 mL/10 g) or neutral sulfate berberine (50 mg/kg) once a day for 3 days, 1 h after intragastrical treatment on day 3, LPS (20 mg/kg) or normal saline was injected intraperitoneally (ip). All animals were sacrificed 12 h after LPS injection, the left lung tissue sections were prepared for histology analysis and the right lung were used to determine the ratio of wet to dry lung tissue weight (W/D). In another experiment, bronchoalveolar lavage fluid (BALF) was collected, and then the total protein content, and the amounts of white blood cells (WBC) and polymorphonuclear neutrophils (PMN) in BALF were determined. Furthermore, the phosphorylation of cytosolic phospholipase A₂ (cPLA₂) was detected with immunohistochemical analysis by using phospho-cPLA 2(Ser505) antibody, and the contents of thromboxane B₂ (TXB₂) in BALF, malondialdehyde (MDA) in the lungs, and activity of superoxide dismutase (SOD) in lung tissues were also determined.
RESULTS:LPS induced acute lung injury, activated cPLA₂, and increased TXB₂ content in the BALF and MDA level in the lung tissue. The pretreatment with berberine significantly attenuated lung injury, lung edema and protein leakage induced by intraperitoneal

injection of LPS. The expression of phospho-cPLA₂ in the lung tissues and TXB₂ content in the BALF in the berberine treatment group were lower than those in LPS group (P<0.05). In addition, the content of MDA in the lung tissue was lower in the berberine treatment group than LPS group (P<0.05), but there was no significant difference in activity of lung SOD between the berberine treatment and LPS group (P>0.05).
CONCLUSION:Pretreatment with berberine remarkably reduces the LPS-induced lung injury, which is, at least in part, through inhibiting phosphorylation of cPLA₂ and decreasing lipid peroxidation. These findings provide a new strategy for the prevention and treatment of LPS-induced acute lung injury.</FONT>

Key words Berberine Lipopolysaccharide Acute lung injuty Cytosolic phospholipase A2 Mice Malondialdehyde

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