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论著

二硫代氨基甲酸吡咯烷对小鼠免疫性肝损伤的抑制作用

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摘要 目的 探讨二硫代氨基甲酸吡咯烷（PDTC）对免疫性肝损伤的抑制作用及其机制。方法 设正常对照、脂多糖（LPS）、卡介苗（BCG）、BCG+LPS、PDTC和BCG+PDTC+LPS组。除正常对照、LPS和PDTC组外，其余各组小鼠经尾静脉注射BCG（每只2.5 mg）。10 d后，LPS和BCG+LPS组分别给予LPS（0.2 mg·kg^{-1}，ip），PDTC和BCG+PDTC+LPS组在给予LPS前24和2 h分别给予PDTC（100 mg·kg^{-1}，ip），对照组给予等体积生理盐水。每组15只小鼠用于观察LPS处理后72 h的死亡率；每组6只小鼠于LPS处理后1.5 h处死，取肝脏，用RT-PCR检测肝脏组织肿瘤坏死因子α（TNF-α）和白细胞介素1β（IL-1β）mRNA表达水平，用凝胶电泳迁移率分析法测定肝脏核因子κB（NF-κB）结合活性；每组12只小鼠于LPS处理后6 h取血，处死，留取肝脏，测定血清谷丙转氨酶（GPT）活性、一氧化氮（NO）水平和肝组织还原型谷胱甘肽（GSH）含量，制备肝组织切片进行HE染色，观察组织病理变化。结果 与正常对照组比较，BCG和LPS组小鼠肝脏炎症细胞明显增加，血清GPT活性升高，肝脏GSH含量显著下降，肝脏TNF-α与IL-1β mRNA表达增强，各组均未见小鼠死亡；PDTC组除血清GPT活性升高外，上述其他指标均未发生明显改变。与BCG和LPS组比较，BCG+LPS组血清GPT活性进一步升高，并伴有大面积肝脏坏死和大量炎症细胞浸润，肝脏NF-κB结合活性显著升高，TNF-α和IL-1β表达进一步增强，GSH水平下降，血清NO水平增加，小鼠死亡率40%。与BCG+LPS组比较，PDTC预处理明显抑制BCG+LPS引起的肝脏NF-κB活性、TNF-α及IL-1β mRNA表达增强，升高肝脏GSH含量，降低血清GPT活性和NO水平，减轻BCG+LPS引起的肝脏炎症和坏死，未见小鼠死亡。结论 PDTC可抑制BCG+LPS引起的小鼠免疫性肝损伤，其机制可能与其抗炎和抗氧化作用有关。

关键词 二硫代氨基甲酸吡咯烷 脂多糖 卡介苗 免疫性肝损伤 炎症

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Inhibition of pyrrolidine dithiocarbamate on immunological liver injury in mice

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Abstract

AIM To investigate the inhibitory effect of pyrrolidine dithiocarbamate (PDTC) on immunological liver injury and its mechanism. **METHODS** All mice were randomly divided into normal control, lipopolysaccharides(LPS), BCG vaccine (BCG), BCG+LPS, PDTC, and BCG+PDTC+LPS groups, respectively. Except that in normal control, LPS and PDTC groups, the mice were injected intravenously (iv) with BCG (2.5 mg per mouse). Ten days later, the mice in LPS and BCG+LPS groups were injected with LPS (0.2 mg·kg^{-1}, ip), and the mice in PDTC and BCG+PDTC+LPS groups were injected with PDTC (100 mg·kg^{-1}, ip) at 24 and 2 h, respectively, before LPS. The mice in normal control group were ip normal saline. Fifteen mice in each group were observed for mortality rate 72 h after LPS treatment. Six mice in each group were sacrificed 1.5 h after LPS administration for determination of the expressions of tumor necrosis factor α (TNF-α) and interleukin 1β (IL-1β) mRNA with RT-PCR and nuclear factor κB (NF-κB) binding activity with electrophoretic mobility shift assay in hepatic tissue. Twelve mice in each group were sacrificed 6 h after LPS treatment for measurement of the serum glutamic-pyruvic transaminase (GPT) activity and nitric oxide (NO) level, and glutathione (GSH) content in liver tissue. Meanwhile, the liver histopathological changes were observed with HE staining. **RESULTS** In LPS and BCG groups, the serum GPT activity, TNF-α and IL-1β mRNA expressions and inflammatory cells in hepatic tissue increased, and liver GSH content decreased compared with the control group. No dead mouse was found in each group. In BCG+LPS group, the serum GPT activity, serum NO level, TNF-α and IL-1β mRNA expressions and NF-κB binding activity in hepatic tissue elevated, and hepatic GSH content declined more obviously compared with LPS and BCG groups. The hepatic necrosis and massive macrophage infiltration was observed, and the mouse death rate was 40%. PDTC pretreatment significantly decreased serum GPT activity and NO production. TNF-α and IL-1β mRNA expressions and NF-κB binding activity in hepatic tissue were attenuated by PDTC pretreatment. The liver GSH content also increased and hepatic inflammation and necrosis were improved. In addition, no dead mouse was found in BCG+PDTC+LPS group. **CONCLUSION** PDTC may inhibit the immunological liver injury, and the mechanism may be related with its anti-inflammation and antioxidant effects.

Key words pyrrolidine dithiocarbamate lipopolysaccharides BCG vaccine immunological liver injury inflammation

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