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基础医学

不同剂量地塞米松对脓毒症小鼠肺组织糖皮质激素受体-α表达及肺损伤的影响

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摘要：

目的 观察不同剂量地塞米松(Dex)对脓毒症小鼠急性肺脏损伤的影响。方法 92只雄性昆明种小鼠随机分为假手术组(12只)、脓毒症组(20只)及Dex干预组(生理剂量组、应激剂量组和大剂量组，各20只)。采用盲肠结扎穿孔术复制脓毒症模型。术后24h时观察肺组织病理学改变，免疫组织化学法检测肺组织中糖皮质激素受体-α(GR-α)和核转录因子-κB(NF-κB)蛋白的表达，实时荧光定量PCR检测肺组织中GR-α 和NF-κB mRNA的表达，酶联免疫吸附法测定血浆中TNF-α、IL-1β水平。 结果①与脓毒症组相比，Dex干预组肺损伤均有所减轻，但仅其中的生理剂量组和应激剂量组明显减轻(P均＜0.05)。②生理剂量组和应激剂量组肺组织GR-α蛋白的表达均高于脓毒症组(P均＜0.05)。③生理剂量组和应激剂量组肺组织GR-α mRNA表达水平高于脓毒症组和大剂量组(P＜0.05)；Dex干预组肺组织NF-κB mRNA表达与脓毒症组相比，差异无统计学意义(P＞0.05)。④生理剂量组和应激剂量组血浆TNF-α、IL-1β含量低于脓毒症组和大剂量组(P＜0.05)。结论 在脓毒症小鼠模型中，生理剂量和应激剂量Dex均可上调肺组织GR-α的表达，减轻炎症反应与肺损伤程度，其作用均明显优于大剂量Dex。

关键词： 脓毒症；肺损伤；地塞米松；糖皮质激素受体-α；核转录因子-κB

Effects of dexamethasone with different doses on glucocorticoid receptor-α expression and lung injury in septic mice

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Abstract:

Objective To observe the effects of dexamethasone(Dex) with different doses on acute lung injury in mice with septic shock. Methods Ninety-two male Kunming mice were randomly divided into the following five groups: sham-operated group(n=12), sepsis group(n=20), Dex intervention groups (physiological-dose Dex group, stress-dose Dex group and high-dose Dex group， n=20 in every group). Sepsis models were replicated by cecal ligation and puncture method. 24 hours after the treatment, histopathological changes of the lung were determined by HE staining. The expressions of glucocorticoid receptor-α(GR-α) and nuclear transcription factor κB(NF-κB) proteins in lung tissues were investigated by immunohistochemical assays. The expressions of GR-α and NF-κB mRNA were detected by real-time PCR. The concentrations of TNF-α and IL-1β in the plasma were detected by ELISA. Results ① Compared with sepsis group, physiological-dose Dex group and stress-dose Dex group showed lower grades of pathologic changes which indicated acute lung injury(all P＜0.05). ② Compared with sepsis group, the expression of GR-α protein increased in physiological-dose Dex group and stress-dose Dex group(all P＜0.05). ③ The GR-α mRNA levels of physiological-dose and stress-dose group were higher than sepsis group and high-dose Dex group(P＜0.05); There was no difference in NF-κB mRNA levels among Dex intervention groups and sepsis group (P＞0.05). ④ The levels of plasma TNF-α and IL-1β in physiological-dose Dex group and stress-dose Dex group were lower than those in sepsis group and high-dose Dex group(P＜0.05). Conclusion In the sepsis mice model, both physiological and stress dose of Dex can up-regulate the expression of GR-α, thus reduce lung injury and alleviate inflammation in the lung tissue, which were much better than high dose of Dex.

Keywords: Sepsis; Acute lung injury; Dexamethasone; Glucocorticoid receptor-α; Nuclear factor kappa B

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