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论著

博来霉素致大鼠肺纤维化模型肺组织的动态病理变化及其发生机制

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摘要 目的： 了解博来霉素（BLM）致大鼠肺纤维化模型肺组织的动态病理变化，探讨BLM致肺纤维化的作用机制。方法：60只雄性SD大鼠采用随机数字表法分为正常对照组（N组）和肺纤维化模型组（B3、B7、B14、B28、B56组），每组10只。除N组外，其余各组采用气管内注入BLM致大鼠肺纤维化模型， 分别于3、7、14、28、56 d处死各组大鼠，右肺行苏木精-依红（HE）、Masson胶原及天狼猩红染色，测定左肺羟脯氨酸（HYP）的含量。 RT-PCR法半定量测定转化生长因子-1（TGF-β1）、基质金属蛋白酶-9（MMP-9）和基质金属蛋白酶组织抑制物-1（TIMP-1）mRNA在肺内的表达。免疫组化法观察TGF-β1、MMP-9及TIMP-1蛋白在大鼠肺组织的表达。结果：(1) 模型组大鼠肺组织HYP含量显著高于N组（P<0.05），模型组大鼠肺组织肺泡炎症的程度也明显重于N组，B14、B28和B56组大鼠肺纤维化的程度明显重于N组，大鼠在灌注BLM后不同时点其肺组织有着不同的病理变化。 (2) TGF-β1、MMP-9及TIMP-1在正常组大鼠肺脏中即有表达，但表达较弱，灌注BLM后它们的表达均增强，不同时点它们在肺组织内的分布有不同的特点。结论：给予后不同时点大鼠肺组织有着不同的病理变化特点，TGF-β1、MMP-9和TIMP-1在BLM诱导的肺纤维化形成过程中起着重要的调节作用。

关键词 博来霉素； 肺纤维化； 转化生长因子β； 基质金属蛋白酶-9； 金属蛋白酶1组织抑制剂

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Kinetics of pathologic changes in bleomycin-induced murine pulmonary fibrosis model

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Abstract

<FONT face=Verdana>AIM: To Investigate the kinetics of pathologic changes in bleomycin-induced pulmonary fibrosis in rats. METHODS: Sixty male SD rats were randomized as a negative control group and pulmonary fibrosis model groups (B3, B7, B14, B28, B56 sub-groups). Except for control group, rats in the other groups were intratracheally administered with bleomycin. Animals in pulmonary fibrosis model groups were sacrificed on day 3, 7, 14, 28 and 56. The sections of the right lung were stained by HE, Masson and sirius red. The left lung was weighed and its hydroxyproline content was assayed. The mRNAs of TGF-β1, MMP-9 and TIMP-1 in the lung homogenate were measured by semi-quantitative RT-PCR. The expressions of TGF-β1, MMP-9 and TIMP-1 in lungs were observed by immunohistochemistry. RESULTS: (1) The content of lung hydroxyproline in pulmonary fibrosis model groups was significantly increased than that in control group (P<0.05). The pulmonary inflammation in pulmonary fibrosis model groups was significantly serious than that in control group, pulmonary fibrosis in B14, B28 and B56 groups was also significantly serious than that in control group. (2) A small quantity of TGF-β1, MMP-9 and TIMP-1mRNA were measured in normal lung, and the expression increased significantly after administration of bleomycin. Different expressions of TGF-β1, MMP-9 and TIMP-1 in different days after bleomycin administration were observed. CONCLUSION: The pathological changes in different days after bleomycin administration are different. TGF-β1, MMP-9 and TIMP-1 may play important roles in the pathogenesis of pulmonary fibrotic process.
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Key words Bleomycin Pulmonary fibrosis Transforming growth factor beta Metalloproteinase-9 Tissue-inhibitor of metalloproteinase-1

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