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Original Article

The effect of AT1 receptor blockade on bax and bcl-2 expression in bleomycin-induced pulmonary fibrosis

Safaeian L., Jafarian A., Rabbani M., Mirmohammad Sadeghi H., Torabinia N., Alavi SA.

Corresponding Author:

Safaeian L

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Abstract:

ABSTRACT

Background and the purpose of the study: Recent studies have indicated the role of apoptosis and angiotensin in the pathogenesis of bleomycin induced-pulmonary fibrosis. Losartan, an angiotensin type 1 receptor (AT_1R) antagonist, has ameliorated apoptosis and fibrosis from bleomycin. In this study, alterations in the expression of apoptosis-regulatory genes (bcl-2 and bax) were investigated in different cells of lung tissue of mice treated with bleomycin in the presence of losartan.

Methods: Losartan (10 mg/kg, i.p.) was given to mice two days before administration of bleomycin (3 U/kg) and throughout the test period. After two weeks, lung tissues of mice were evaluated for fibrosis by biochemical measurement of collagen deposition and semiquantitative analysis of pathological changes of the lung. The expression of bcl-2 and bax was assessed by immunohistochemical assay using biotin-streptavidin staining method on paraffin-embedded lung tissues.

Results and major conclusion: Pre-treatment with losartan significantly ($P < 0.05$) reduced the increase in lung collagen content and also inhibited the histological changes induced by bleomycin. Immunohistochemical studies showed that losartan significantly ($P < 0.05$) reduced the bax/bcl-2 expression ratio in the alveolar epithelial cells, lymphocytes, macrophages and interstitial myofibroblasts. Losartan also inhibited the bcl-2 upregulation which was educed by bleomycin in neutrophils. By reduction of bax/bcl-2 ratio as a determinant of susceptibility of a cell to apoptosis, losartan exerted protective effects on the alveolar epithelial cells that may be important in the amelioration of pulmonary fibrosis. These results may help to better understanding of the role of angiotensin II and apoptosis in pulmonary fibrosis.

Keywords:

bcl-2, bax, bleomycin, pulmonary fibrosis, losartan

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