عنوان مقاله:

Beneficial effects of N-acetylcysteine on protease-antiprotease balance in attenuating bleomycin-induced pulmonary fibrosis in rats

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خلاصه مقاله:

Objective(s): The role of N-acetylcysteine (NAC) as an anti-oxidant in attenuating bleomycin-induced pulmonary fibrosis has been reported. However, its effect on parenchymal remodeling via regulating the protease-antiprotease balance is not fully defined. Therefore, the present study was designed to explore the possible role of matrix metalloproteinases (MMP), tissue inhibitors of metalloproteinases (TIMP) and transforming growth factor-β1 (TGF-β1) pathway and their modulation by NAC in attenuating bleomycin-induced pulmonary fibrosis in rats.Materials and Methods: Bleomycin sulphate (7 units/kg) was instilled inside the trachea to induce pulmonary fibrosis. The time course of TGF-β1, MMP-9, TIMP-1,3 mRNA and protein expression, TGF-β1 and hydroxyproline levels were evaluated on days 7, 14, and 28. NAC (0.3 mmol/kg and 3 mmol/kg) was administered in bleomycin-instilled animals.Results: NAC treatment significantly attenuated bleomycin-induced histopathological changes by decreasing interstitial inflammation and reducing the deposition of extracellular matrix proteins such as collagen. Moreover, it increased the mRNA and protein expression of MMP-9 and decreased the expression of TIMP-1,3 in alveolar epithelial cells (AECs), interstitial macrophages and inflammatory cells. Indeed, there was decrease in the MMP-9/TIMP ratio in bleomycin-instilled rats, which increased with NAC treatment. Moreover, NAC attenuated bleomycin-induced increased expression of TGF-β1 and total lung collagen levels.Conclusion: NAC attenuates bleomycin-induced pulmonary fibrosis by normalizing the protease-antiprotease balance and favoring the degradation of collegen to reduce fibrosis.

کلمات کلیدی:

Bleomycin, MMP-9, N-acetylcysteine, Pulmonary Fibrosis, TGF-β1, TIMPs