

Benefits of using angiotensin receptor blockers for pulmonary fibrosis treatment

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ABSTRACT

Pulmonary fibrosis is one of the common and chronic respiratory system disease with unknown etiology. There is no definitive pharmacological treatment for pulmonary fibrosis. The role of inflammation and angiotensin in initiation and progress of pulmonary fibrosis was demonstrated. Angiotensin receptor blockers administrated in different cardiovascular diseases. Some studies indicated the beneficial effect of angiotensin receptor blockers in treatment of pulmonary fibrosis in animal models. Therefore, this study indicates the angiotensin receptor blockers as promising and novel treatment of lung fibrosis.

Keywords: angiotensin receptors blockers, bleomycin, pulmonary fibrosis.

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Pulmonary fibrosis is a lethal and progressive interstitial respiratory disease and is characterized by increased deposition of the extracellular matrix (ECM) in the lungs, proliferation of myofibroblasts, and inflammation, which ultimately results in respiratory failure (1).

To date, there is no approved treatment for pulmonary fibrosis. Corticosteroids have been administrated; however, their use was limited to severe cases, and they were associated with a wide range of side effects (2).

Renin is an aspartyl protease that cleaves angiotensinogen to angiotensin (Ang) I, which is then converted to Ang II by the angiotensin-converting enzyme (ACE). Ang II exerts biological effects by binding to its receptors, angiotensin receptor 1 (AT1) and angiotensin receptor 2 (AT2). The renin-angiotensin system (RAS) exerts

regulatory effects on blood pressure and electrolytic and volume homeostasis (3).

At the same time, RAS is one of the pathogenic factors that play an essential role in the pathogenesis of pulmonary fibrosis (4).

Angiotensin receptor blockers (ARBs) are used for the treatment of hypertension, congestive heart failure, and other cardiovascular complications [5]. Some studies have investigated the effect of ARB in the treatment of pulmonary fibrosis.

Studies conducted by Otsuka et al. (2004) have shown that candesartan plays an important role in neutrophilic infiltration in the lung, and ameliorated pulmonary fibrosis caused by decrease in the concentration of neutrophils in bronchoalveolar lavage (BAL) fluid in the bleomycin exposure group (6).

Research conducted by Marut et al. on the use

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of irbesartan as an AT1 blocker showed inhibitory effects on nitric oxide production and inflammation events (7).

Losartan alleviated pulmonary fibrosis by reducing the transforming growth factor β (TGF- β) expression in lung tissue (8).

The results of our previous study demonstrated the protective effect exerted by valsartan as an antagonist of angiotensin receptor in bleomycin-induced pulmonary fibrosis by decreasing the collagen content in lung tissue (9).

Liu et al. (10) showed that valsartan could inhibit the expression of TGF- β and stimulate the expression of hepatocyte growth factor (HGF) in lung tissue, thereby ameliorating pulmonary fibrosis (10).

Ang II exerts proliferative and pro-fibrotic effects on fibroblasts by acting on AT1 receptors[11], and stimulates the expression of TGF- β and connective tissue growth factor (CTGF), two key pro-fibrotic mediators in the progression of pulmonary fibrosis (12, 13).

Ang II also up-regulates collagen gene expression in human lung fibroblasts[14] and induces the proliferation of fibroblasts and collagen deposition[6, 13]. Ang II also stimulates apoptosis of alveolar epithelial cells (APCs), which is a key stage in the development of lung fibrosis (15).

The close association between RAS and the initiation and progression of pulmonary fibrosis and the beneficial effect of ARBs in the treatment of pulmonary fibrosis, as shown by different studies, indicate that ARBs that have fewer side effects and are well-tolerated by patients, especially elderly patients, can be used as a promising and novel treatment for pulmonary fibrosis.

Conflict of Interests

Authors have no conflict of interests.

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