Title: Aprepitant exerts anti-fibrotic effect via inhibition of TGF-β/Smad3 pathway in bleomycin-induced pulmonary fibrosis in rats.

ABSTRACT

Bleomycin is a well-recognized antineoplastic drug. However, pulmonary fibrosis (PF) is considered to be the principal drawback that greatly limits its use. Here, we sought to investigate ability of the neurokinin receptor 1 blocker, aprepitant, to prevent PF caused by bleomycin. Male adult Wistar rat groups were given a single intratracheal injection of bleomycin, either alone or in combination with aprepitant therapy for 3 or 14 days. Collagen deposition and a rise in transforming growth factor beta (TGF-β) immunoreactivity in lung tissue serve as evidence of bleomycin-induced PF. The serum levels of lactate dehydrogenase, alkaline phosphatase, and total antioxidant improved after aprepitant therapy. Additionally, it reduced the protein expressions of interferon alpha, tumor necrosis factor alpha, and lung lipid peroxidation. Moreover, aprepitant treatment led to an increase in the antioxidant indices glutathione, glutathione peroxidase, and catalase. Aprepitant is postulated to protect against bleomycin-induced PF by decreasing TGF-β, phosphorylating Smad3, and increasing interleukin 37, an anti-fibrotic cytokine, and G Protein-coupled Receptor Kinase 2. Aprepitant for 14 days considerably exceeded aprepitant for 3 days in terms of improving lung damage and having an anti-fibrotic impact. In conclusion, aprepitant treatment for 14 days may be used as an adjuvant to bleomycin therapy to prevent PF, mostly through inhibiting the TGF-/p-Smad3 fibrotic pathway.

Keywords: Aprepitant; Bleomycin; Pulmonary fibrosis; Smad3; TGF-β.

For more information: https://pubmed.ncbi.nlm.nih.gov/35931359/