

Antifibrotics as a Novel Treatment for Benign Prostatic Hyperplasia

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Introduction and objective: Benign prostatic hyperplasia (BPH) is a histological disease that is characterized by prostate proliferation, smooth muscle dysfunction, and increased fibrosis. It affects 50% of men older than 50 years of age, often causing lower urinary tract symptoms (LUTS). The mechanism of BPH is poorly understood and the medications approved for treatment do not work in all cases, necessitating surgery. Fibrosis is associated with BPH and is characterized by increased deposition of collagen. However, it is not targeted by any medications approved for the management of the disease. We hypothesize that antifibrotics may be beneficial in decreasing collagen deposition in prostate and, thus, alleviation of LUTS. We are focusing on pirfenidone which is approved for the treatment of pulmonary fibrosis and halofuginone which is used to manage scleroderma.

Methods: 24-month-old mice with lower urinary tract dysfunction (LUTD) were given 5mg/kg/day halofuginone injected intraperitoneally for 6 weeks. Another group of 24-month-old mice was given 300mg/kg/day pirfenidone in peanut butter daily for 6 weeks. Appropriate controls were done for both treatment groups. The deposition of collagen of various thicknesses is evaluated in prostates and bladders of mice treated with antifibrotics. To isolate collagen in the tissues, we are using several staining methods. The relative percentages of extracellular matrix constituents are quantified in ImageJ and analyzed in Prism using a two-tailed Student's t-test.

Results: Antifibrotic treatments significantly decreased urinary frequency as measured by voiding spot assays (VSA). The halofuginone experiment showed a significant decrease in total collagen in ventral prostate lobes. The pirfenidone experiment showed a significant decrease in total collagen in the ventral prostate lobes, dorsolateral lobes, and bladder.

Conclusions: Antifibrotic treatments decrease LUTD potentially due to lower collagen deposition in mouse prostates. Further translational studies must be done to compare the effects of antifibrotics to widely used medications for BPH and derive the relative benefits of including pirfenidone and halofuginone for the management of LUTS.