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COMPOUND X IMPROVED BLADDER FUNCTION AND HISTOPATHOLOGICAL FEATURES IN PROTAMINE SULFATE-LIPOPOLYSACCHARIDE INDUCED INTERSTITIAL CYSTITIS IN RAT BLADDER

Hypothesis / aims of study

The present study developed the interstitial cystitis (IC) rat model which represents important features of human IC bladder, such as impaired voiding function, denudated urothelium, increased inflammation, mast cell infiltration, and tissue fibrosis. Moreover, employing the IC rat model, we evaluated the therapeutic effect of Compound X, a well-known anti-fibrotic agent.

Study design, materials and methods

To make IC rat model female 8-week-old Sprague-Dawley rats were given protamine sulfate (PS, 10mg) to bladder through PE-50 catheter in order to make denudation of urothelium. After 45 minutes the bladders were emptied, washed with buffer solution and then given a second treatment with lipopolysaccharide (LPS, 750ug) for 30 minutes in order to induce inflammation. Weekly instillations of PS/LPS following this regimen over a period 5 weeks were used to induce a longer-lasting and possibly chronic injury to the urothelium. One week after final instillation of PS/LPS, 200mg/kg of Compound X (n=10, IC + Compound X) or PBS (n=10, IC) were daily intraperitoneal injection for 5 days. Ten rats were served as control.

The therapeutic effect of Compound X was examined by awake cystometry, histological and gene expression analysis after 1 week of Compound X injection.

Results

IC rat group exhibited irregular voiding frequency, decreased inter-contraction intervals, micturition volume and increased residual urine volume. Compound X treatment significantly improved most of voiding parameters by increasing the inter-contraction interval, micturition volume and decreasing residual urine volume. The bladder of IC group rats were characterized with severe denudated urothelium with inflammation, increased mast cell infiltration and tissue fibrosis. Particularly, fibrotic damage in the IC bladder was paralleled with up-regulation of Smad2, Smad3, Card10 and Tgfb2. Of note, daily intra-peritoneal injection of Compound X significantly not only improved the bladder voiding parameters but also reversed the histological and gene expression alternations characteristic for IC bladder.

Interpretation of results

The functional parameters of Compound X treated rats showed nearly normalized level of control rats in terms of micturition interval, bladder capacity, micturition pressure and number of non-voiding contractions. Furthermore inflammation and fibrosis of the bladder improved in the Compound X treated rats.

Through integrative data analysis, we identified Compound X is a novel finding that may have new treatment in IC rat model.

Concluding message

We demonstrated that Compound X therapy had therapeutic effect to repair voiding function and regenerate denudated urothelium and relieve tissue fibrosis in the LPS-induced IC rat model. Through these findings, we propose Compound X therapy as a new therapeutic approach to treat IC bladder.

Disclosures

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