DEVELOPMENT AND VALIDATION OF A CLINICALLY-RELEVANT CHRONIC MODEL OF INTERSTITIAL CYSTITIS / BLADDER PAINFUL SYNDROME

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Objective

Interstitial cystitis / bladder painful syndrome (IC/BPS) is a chronic inflammatory disease characterized by visceral pain and urinary symptoms. A main limitation in IC/BPS understanding is the lack of appropriate preclinical model. Cyclophosphamide (CYP) is commonly used as an experimental model for IC/BPS in rodent. However, the proposed models are mainly acute and very aggressive, contrasting with what occurred in clinic, and often associated with severe toxicity. In addition, only few of them recapitulate the 3 hallmark symptoms of IC/BPS: bladder inflammation, pain and dysfunction. Our aim was to develop and validate a chronic model of CYP-induced IC/BPS in rats that would share key features of the human disease.

Methods

Female rats (Sprague-Dawley)

von Frey Testing

Signals

CYP (40 mg/kg, i.p.) or saline (5 mL/kg, i.p.)

Gabapentin (100 mg/kg, p.o.), or saline (10 mL/kg, p.o.)

Results

Bladder pain

Alloodynia

Hyperalgesia

Histological characteristics

Vesical vascular permeability

Voiding frequency (12h recording)

Conclusions

We developed and validated a new chronic model of IC/BPS in female rat. This model recapitulates the key features of human non-ulcerative IC/BPS, which accounts for more than 80% of IC patients. These include sustained visceral pain and mild inflammatory response in bladder tissue characterized by edema, focal urothelial injury and absence of massive infiltrate or tissue hemorrhage. In accordance with the human situation, bladder pain and inflammation are associated with urinary frequency.

This new model is of significant value for better understanding pathophysiological mechanisms and evaluating new therapies for IC/BPS.

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