

LONG-LASTING BREACHES IN THE BLADDER PERMEABILITY BARRIER LEAD TO INTERSTITIAL CYSTITIS IN THE RAT

Hypothesis / aims of study

It has been hypothesized that a defect in the glycosaminoglycan (GAG) layer of the bladder results in the characteristic symptoms of pain, frequency, urgency and nocturia experienced by patients with interstitial cystitis (IC). An increase in bladder mucosal permeability can be reproduced by the intravesical administration of protamine sulfate (PRO); however, the influence of PRO after administration into the bladder disappears within 5 days (Am J Physiol 283: F242, 2002). We developed a chronic animal model of selective urothelial injury using PRO, which seems to resemble IC in humans.

Study design, materials and methods

Insertion of a polyethylene catheter through the bladder dome was performed in female Sprague-Dawley rats. The other end of the catheter was connected to a Model 2002 Micro-Osmotic Pump (Alzet Co., Palo Alto, California) fixed in the abdominal wall for continuous delivery of PRO (1 or 10 mg/ml, 12 µl daily) or vehicle for 2 weeks. The urinary frequency (UF) and voided volume (VV) were measured in the metabolic cage for 2 weeks. The Group 4 rats received a high dose (10 mg/ml) of PRO for 2 weeks and were followed for an additional 2 weeks without PRO. The bladder samples were removed after the experiments and processed for light microscopic investigations and prostaglandin E2 (PGE2) determinations. The PGE2 content was determined spectrophotometrically using EIA Kit Monoclonal LCP-45 (Cayman).

Results

UF was markedly increased and VV was reduced in rats treated with a high dose (10 mg/ml) of PRO for 2 weeks, but UF and VV was not changed in rats treated with vehicle or a low dose (1 mg/ml) of PRO. UF was further increased in rats treated with a high dose of PRO and followed for an additional 2 weeks. Histological sections in rats treated with a high dose of PRO demonstrated a loss of the upper layer of urothelial cells and an increased number of mast cells. The PGE2 level in the bladder wall was significantly elevated in rats treated with a high dose of PRO and followed for an additional 2 weeks.

Interpretation of results

These results suggest that chronic urothelial injury leads to an increase in UF and a decrease in VV. An increased PGE2 level in the bladder wall is likely to relate to the long-lasting IC symptoms.

Concluding message

This model will be useful in defining the mechanisms to induce IC and in investigating therapeutic modalities.