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DIFFERENT EXPRESSIONS OF THE BLADDER INFLAMMATION, APOPTOSIS AND BARRIER PROTEINS IN PATIENTS WITH BLADDER OUTLET OBSTRUCTION, INTERSTITIAL CYSTITIS, SPINAL CORD INJURY, RECURRENT URINARY TRACT INFECTION AND KETAMINE CYSTITIS SUGGEST A SIMILAR PATHOPHYSIOLOGY IS INVOLVED IN DIFFERENT BLADDER CONDITIONS

Hypothesis / aims of study

Lower urinary tract symptoms (LUTS) comprise storage, voiding and post-micturition symptoms affecting the lower urinary tract and may be associated with chronic inflammation. There are many lower urinary tract dysfunctions (LUTD), such as bladder outlet obstruction (BOO), interstitial cystitis (IC), spinal cord injury (SCI), and recurrent urinary tract infection (UTI), may similar LUTS. Previous studies have suggested that the molecule mechanism of interstitial cystitis (IC) involved urothelial dysfunction, activation of mast cell, and chronic inflammation. Recent studies also demonstrated that higher apoptotic cell numbers and lower E-cadherin expression in IC patients were associated with chronic inflammation of bladder wall. We hypothesized that the inflammatory reaction, apoptosis, and urothelial junctional dysfunction might also exit in the other LUTDs. The aim of this study was to measure the infiltration of mast cell, apoptosis cell numbers, and E-cadherin expression in patients with BOO, IC, SCI, recurrent UTI, and ketamine cystitis (KC).

Study design, materials and methods

Bladder tissue were obtained from 17 patients with IC/BPS proven by cystoscopic hydrodistension, 10 patients with BOO, 10 patients with SCI, 10 patients with recurrent UTI, and 10 patients with KC. Another 10 patients with stress urinary incontinence without irritative symptoms served as normal patients. The bladder specimens were investigated by immunofluorescence (IF) staining of E-cadherin for urothelial junction and TUNEL assay for urothelial apoptosis. Mast cell activation was also performed for mucosa inflammation by IF using tryptase. The results of IF were quantified by calculating the percentage of positive cells per area unit. Statistical analysis was performed using Mann-Whitney test and p value small than 0.05 was considered as significance.

Table 1. Expression of E-cadherin, TUNEL and mast cell activation in LUTS disease patients

	KC	IC	Recurrent UTI	BOO	SCI	Control
E-cadherin	11.0 ± 11.3	25.1 ± 16.3	26.2 ± 5.0	42.8 ± 14.3	44.4 ± 18.8	42.4 ± 16.7
Mast cell	7.8 ± 3.7	4.6 ± 3.0	2.4 ± 1.2	5.1 ± 2.0	3.7 ± 2.7	1.3 ± 1.2
TUNEL	4.2 ± 1.5	2.4 ± 1.7	1.9 ± 2.4	1.2 ± 1.1	2.4 ± 1.4	0.08 ± 0.3

Table 2. The comparative results in the mast cell activation (non-asterisks) and TUNEL (asterisks) between all LUTD and control groups. The numbers indicate p values between groups

	KC	IC	Recurrent UTI	BOO	SCI	Control
KC	Nil	0.02	0.00	0.05	0.00	0.00
IC	0.01*	Nil	0.01	0.67	0.39	0.00
Recurrent UTI	0.02*	0.51*	Nil	0.00	0.21	0.03
BOO	0.00*	0.06*	0.41*	Nil	0.19	0.00
SCI	0.01*	0.98*	0.53*	0.03*	Nil	0.02
Control	0.00*	0.00*	0.03*	0.00*	0.00*	Nil

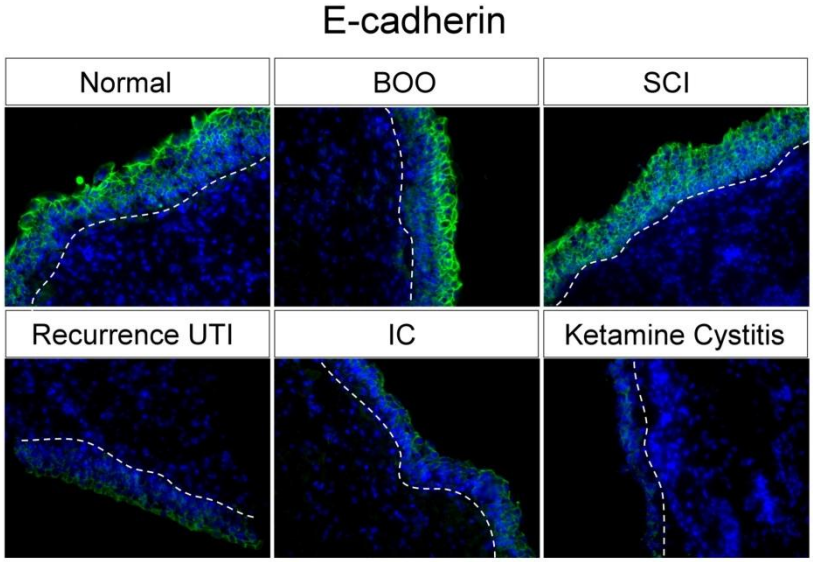
Fig. 1. Immunofluorescence staining of E-cadherin in the normal control and LUTD bladders.

Results

Significantly decreased expression of E-cadherin in patients with IC, KC, and recurrent UTI was found compared to those with normal, SCI, and BOO, respectively (25.1±16.3 v 11.0±11.3 v 26.2±5.0 v 42.4±16.7 v 44.4±18.8 v 42.8±14.3, $p<0.05$). Highly significant increase of the number of mast cells infiltration was observed in patients with KC, IC, recurrent UTI, SCI, and BOO compared with normal, respectively (7.8±3.7 v 4.6±3.0 v 2.4±1.2 v 3.7±2.7 v 5.1±2.0 v 1.3±1.2, $p<0.05$). Statistically significant increase of the number of the apoptotic cells in patients with KC, IC, SCI, recurrent UTI, BOO was observed compared with normal, respectively (4.2±1.5 v 2.4±1.7 v 2.4±1.4 v 1.9±2.4 v 1.2±1.1 v 0.08±0.3, $p<0.05$) (Table 1) (Fig. 1).

Interpretation of results

Our study revealed that urothelial dysfunction as shown by significant decrease of E-cadherin expression was present in IC, KC, and recurrent UTI, especially more severe in KC. However, there was no difference in the urothelial junction barrier between SCI, BOO, and normal controls. The increased signal of TUNEL was observed significantly in all LUTD compared to the controls. Moreover, there was also statistically significant increase of mast cells infiltration in LUTD compared to the controls. The results suggest that chronic inflammation and abnormal urothelial differentiation were present in all LUTD. However, only KC, IC, and recurrent UTI were involved in the junctional barrier dysfunction. These results indicate LUTD are associated with chronic bladder inflammation and abnormal urothelial function (Table 2).



Concluding message

LUTD may be associated with chronic inflammation and abnormal urothelial dysfunction. High apoptotic cell numbers and low expression of E-cadherin were observed in KC and IC. KC bladders had the most severe urothelial dysfunction, urothelial apoptosis and inflammation. The inflammation and increased urothelail apoptosis might be the common pathophysiology of various LUTD that caused different LUTS.

Disclosures

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