349

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UROTHELIAL DYSFUNCTION AND CHRONIC INFLAMMATION IN THE PATIENTS WITH BLADDER OUTLET OBSTRUCTION AND DIFFERENT BLADDER DYSFUNCTION

Hypothesis / aims of study

The time-course study shows that bladder dysfunction following bladder outlet obstruction (BOO) changes from compensation (hypersensitive bladder, HSB), detrusor overactivity (DO) to decompensation (detrusor underactive, DU). Previous studies have shown increased urothelial cell apoptosis and suburothelial inflammation in patients with bladder storage problems, such as interstitial cystitis, ketamine-related cystitis and recurrent urinary tract infection. The aim of this study was to investigate the urothelial inflammation and urothelial cell apoptosis in patients with bladder outlet obstruction with different bladder dysfunction.

Study design, materials and methods

The bladder biopsy specimens were obtained from 30 male patients with BOO proved by urodynamic study. These patients were scheduled to undergo transurethral resection of the prostate (TURP). Of them, 8 patients had HSB, 12 patients had DO and 10 patients had DU. Immunofluorescence staining of the adhesive protein E-cadherin, tryptase (to assess mast cell activity) and TUNEL staining (to assess urothelial apoptosis) were performed in all the bladder specimens.

Results

The mean age of the patients was 69.1±11.9 years old. Table 1 showed that patients with BOO and DU had significantly lower voided volume, Qmax and Pdet than patients with HSB and DO. Patients with DO had significantly larger prostate compared with patients with DU and HSB. Table 2 showed that a significantly lower distribution of E-cadherin in BOO patients with DO and DU bladder tissues compared with that of BOO with HSB (11.2±7.7 versus 23.8±14.4, p= 0.03; 9.2±9.6 versus 23.8±14.4, p= 0.03) and the control group. The tryptase signal was significantly stronger than the control in all BOO groups, but DO group was significantly higher than that of HSB group (19.1±6.1 versus 13.6±5.1, p=0.04). TUNEL staining revealed a significantly higher apoptotic cell count in the BOO with DO (3.5±2.6) and DU (4.0±3.4) groups compared with that of HSB (0.6±1.0) (p=0.027) or the controls (0.85 ± 1.3) (p= 0.004).

Interpretation of results

It has been demonstrated that E-cadherin is associated with bladder sensation and barrier function. The defective urothelial junction protein may increase bladder permeability which contributes to the uninhibited bladder contraction. In addition, the expression of mast cell activity was significantly greater in BOO with DO specimens compared with BOO with HSB specimens, indicating that chronic inflammation of the bladder in BOO with DO patients was more severe than that in BOO with HSB patients. Interestingly, the E-cadherin, mast cell activity and urothelial apoptosis were similar between BOO patients with DO and DU. These findings may indicate chronic inflammation and dysfunction of junction proteins persistently affect the transition of bladder function from HSB to DO to DU.

Concluding message

Our preliminary results suggested that impairment of junctional protein of urothelial cells, chronic inflammation and urothelial cell apoptosis might be associated with different stages of bladder dysfunction after BOO due to BPH. Our study provides a new focus for clinical care and future study to prevent bladder decompensation after long-term outlet obstruction.

Table 1. The prostate size and urodynamic findings in BOO patients with HSB, DO and DU

	BOO & HSB (N=8)	**BOO & DO (N=12)**	**BOO & DU (N=10)**
Voided volume (mL)	246 ± 102	152 ± 81	30 ± 66
Qmax (mL/s)	6.9 ± 3.0	7.6 ± 4.2	0.6 ± 0.8
PVR (mL)	114 ± 80	78 ± 100	388 ± 149
Pdet (cmH_2O)	63 ± 49	59.7 ± 26.0	14.6 ± 21.2
TPV (mL)	49.9 ± 31	78.5 ± 29.3	31.4 ± 10.8
TZI	0.43 ± 0.15	0.46 ± 0.1	0.26 ± 0.15

DO: detrusor overactivity, DU: detrusor underactivity, HSB: hypersensitive bladder, Pdet: maximal detrusor pressure, PVR: post-voided residual, Qmax: maximal urinary flow rate, TPV: total prostate volume, TZI: transitional zone index.

Table 2: Expression of E-cadherin, mast cell and TUNEL in the bladder specimens of the controls and BOO patients with HSB, DO and DU

	Control (N=10)	**BOO+HSB (N=8)**	**BOO+DO (N=12)**	**BOO+DU (N=10)**	**P value ***	**P value#**
E-cadherin	27.7 ± 10.4	23.8 ± 14.4	11.2 ± 7.7	9.2 ± 9.6	0.014	0.001
Tryptase	4.16 ± 2.68	13.6 ± 5.1	19.1 ± 6.1	12.5 ± 11.4	0.142	0.000
TUNEL	0.85 ± 1.31	0.6 ± 1.0	3.5 ± 2.6	4.0 ± 3.4	0.027	0.004

* Analysis among BOO subgroups, # analysis among the BOO and control groups; BOO: bladder outlet obstruction, HSB: hypersensitive bladder, DO: detrusor overactivity, DU: detrusor underactivity.

Disclosures
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