

DETRUSOR OVERACTIVITY AND CONNEXIN EXPRESSION IN PATIENTS WITH BLADDER OUTLET OBSTRUCTION DUE TO BENIGN PROSTATIC HYPERPLASIA

Hypothesis / aims of study

Bladder outlet obstruction is a common medical disorder which leads to rearrangements of smooth muscle and epithelial cells of the bladder wall and to alterations in their function. Detrusor overactivity and storage symptoms are frequently associated with bladder outlet obstruction and this may be related with increased electrical coupling. Connexins (Cx) constitute a family of transmembrane proteins that form gap junction channels allowing metabolic and electrical coupling of cellular networks. This study was performed to evaluate the changes of connexin 26 (Cx26) and connexin 43 (Cx43) expression in bladder and whether these changes are related to detrusor overactivity in patients with bladder outlet obstruction due to benign prostatic hyperplasia (BPH).

Study design, materials and methods

The study groups included 36 male patients who have bladder outlet obstruction due to BPH and received transurethral resection of prostate (TUR-P). The pre-operative evaluation included history taking, urinalysis, international prostatic symptom score (IPSS), transrectal sonography, PSA, and urodynamic study. On the basis of the urodynamic results, the patients were divided into two groups according to the presence of detrusor overactivity (DO): DO(+) and DO(-) group. The cases that the maximal bladder capacity was less than 200ml or that have uninhibited detrusor contraction were defined as DO(+) group. The symptoms, IPSS (voiding and storage symptom score), prostate size, PSA value, and urodynamic parameters were compared in two groups. The bladder mucosal biopsy was performed in the posterior wall of the bladder from all patients during TUR-P. The expressions of Cx26 and Cx43 mRNA in two groups were analysed by reverse transcriptase polymerase chain reaction (RT-PCR). To localize both Cx26 and Cx43 proteins, immunohistochemical staining was performed.

Results

14 (38.9%) of the 36 patients presented detrusor overactivity in urodynamic study. From the analysis of symptom, the incidence of urge incontinence in DO(+) group was higher than that of DO(-) group ($P < 0.05$). However, the number of nocturia, prostate volume, PSA value, and IPSS were not different between DO(+) and DO(-) groups. The maximum bladder capacity and PdetQmax were low in DO(+) group compared with DO(-) group on urodynamic study ($P < 0.05$). However, the Qmax and residual volume were not significantly different between DO(+) and DO(-) groups. In the RT-PCR, the Cx26 and Cx43 mRNAs were detectable in all tissue. The RT-PCR analysis demonstrated that the levels of both Cx26 and Cx43 mRNA were significantly increased in DO(+) group compared with DO(-) group ($P < 0.05$). The immunohistochemical staining showed that the Cx26 and Cx43 were localized in the mucosal layer, especially Cx26 in urothelium and Cx43 in suburothelial area, respectively. The staining intensity of Cx26 and Cx43 were increased in DO(+) group compared with DO(-) group.

Interpretation of results

The expressions of the connexins in mucosal layer are modulated under conditions of detrusor function in bladder outlet obstruction. We observed that the expression of both Cx26 and Cx43 increased at both transcript and protein levels in DO(+) group. The elevated level of connexins can lead to the formation of larger or more gap junctions in the mucosal layer. Therefore, these gap junctions may provide pathways for cell-to-cell communication, and result in activation of sensory transduction.

Concluding message

The present data demonstrate that the increased Cx26 and Cx43 levels in mucosal layer may be related to overactive bladder symptom and detrusor overactivity in patients with bladder outlet obstruction due to BPH.