

CHANGES OF MUSCARINIC AND PURINERGIC RECEPTOR EXPRESSION IN UROTHELIUM OF RATS WITH DETRUSOR OVERACTIVITY INDUCED BY BLADDER OUTLET OBSTRUCTION

Hypothesis / aims of study

Benign prostatic hyperplasia (BPH) is one of the most common causes of bladder outlet obstruction (BOO), and the patients with BPH would experience not only voiding symptoms but also storage symptoms such as urgency and frequency. Urothelium is involved in sensory mechanisms and can release chemical mediators. Therefore, the urothelium plays an important role in manifestation of overactive bladder symptoms [1], and changes of various receptor expressions in urothelium may have important pathophysiological role. Among the various receptors existing on urothelium, muscarinic and purinergic receptors have been proposed as the key factors in micturition mechanism [2, 3]. This study was undertaken to investigate the changes of urothelial muscarinic and purinergic receptors in rats with BOO, and whether these changes in distribution and expression are related with detrusor overactivity.

Study design, materials and methods

A total of 30 Sprague-Dawley rats weighing approximately 250-300 g were used for this study and divided into two groups: 10 control and 20 BOO groups. Control group consisted of sham operated animals. Partial BOO was induced for 3 weeks. 3 weeks after BOO, the cystometrography (CMG) was carried out, and contraction pressure, interval of contraction, presence of non-voiding contraction were checked to validate the manifestation of detrusor overactivity in BOO group. The bladders of each group were dissected out after CMG and weighed. Immunofluorescence staining was performed to localize M2, M3 muscarinic receptors and P2X3 purinergic receptor in a portion of the bladder. The remaining portion of the bladder was dissected into urothelium and smooth muscle layer under the microscopy. The expression of the M2, M3 muscarinic receptors and P2X3 purinergic receptors in both layers were analyzed by performing reverse transcriptase polymerase chain reaction (RT-PCR).

Results

On CMG, significant decrease in contraction interval and increase in contraction pressure of the BOO group compared with control group were noted, and the data was revealed to show that BOO induced detrusor overactivity. On immunofluorescence staining, muscarinic and purinergic receptors were localized in both urothelium and suburothelial layer in control and BOO groups. The expression of both M2 and M3 muscarinic receptors were apparently increased in urothelial layer of BOO group compared to control group. Also, the expression of P2X3 purinergic receptor was increased in urothelial layer of BOO group compared to control group, but less apparent than muscarinic receptor expression. The expression of both muscarinic and purinergic receptor in muscular layer showed no apparent difference between two groups. In urothelial layer, the RT-PCR analysis demonstrated that the levels of both M2, M3 muscarinic receptor and P2X3 purinergic receptor mRNA were significantly increased in BOO group compared to control group. In muscular layer, only the mRNA expression of M3 muscarinic receptor was increased in BOO group compared to control group. However, the mRNA expression of M2 muscarinic and P2X3 purinergic receptors showed no significant difference between two groups in muscular layer.

Interpretation of results

We observed that the increased expression of M2, M3 muscarinic and P2X3 purinergic receptor in urothelial layer are associated with detrusor overactivity after bladder outlet obstruction. These results support a role for muscarinic and purinergic mechanisms in urothelial sensory function. Also, it is likely that the alterations of these receptors could have an impact on sensory signaling and involve in development of overactive bladder symptoms. Therefore, the muscarinic and purinergic receptor in urothelial layer may be a potential target for pharmacotherapeutic intervention in bladder storage disorders.

Concluding message

The present data demonstrate that the changes of muscarinic and purinergic receptors in urothelium may be related to overactive bladder symptom and detrusor overactivity after bladder outlet obstruction.

References

1. Urology 64:7-11, 2004.
2. Br J Pharmacol 129:416-419, 2000
3. J Urol 171:448-452, 2004.

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