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MECHANICAL DISTENSION OF THE URETHRA INDUCES A RELEASE OF ATP/PGE2 FROM THE EPITHELIUM

Hypothesis / aims of study

The bladder epithelium acts as a sensory organ that responds to mechanical and chemical stimulation by releasing neurotransmitters, such as acetylcholine, ATP, and prostaglandins (PGs). Researchers have hypothesized that these mediators can act on suburothelial afferent nerves and interstitial cells to modulate bladder activity during the storage phase. They have further suggested that detrusor overactivity caused by bladder outlet obstruction (BOO) may be initiated from the bladder outlet region rather than from the bladder itself (1). Pharmacological activation of urethral afferent nerves by intraurethral PGE_2 elicited an excitatory effect on micturition reflex (2). Furthermore, immunohistochemical data have indicated the presence of capsaicin-sensitive primary afferent fibers in the rat proximal urethra (3). Considering these findings, stretch-induced release of some mediators from the urethral epithelium may play an important role in the induction of detrusor overactivity in patients with BOO. In the present study, we evaluated whether the urethral epithelium was capable of synthesizing and releasing mediators in response to urethral distension.

Study design, materials and methods

Female Sprague-Dawley rats were anesthetized with halothane, and the bladder and proximal urethra were exposed through a midline abdominal incision. A catheter infusing Krebs or drug solution was inserted into the proximal urethra through the bladder and fixed at the bladder neck. A second catheter was introduced into the distal urethra and fixed at the external urethra. Urethral perfusion was carried out with 150 µL Krebs solution (baseline), and the solution was collected. Next, 150 µL of Krebs solution was maintained in the urethra for one or three minutes and then collected. ATP and PGE_2 amounts were measures with luciferin-luciferase assay and ELISA assay, respectively.

Results

The ATP releases elicited by urethral distension for three minutes increased significantly, reaching 13 times as much as those at baseline. The PGE_2 release also increased significantly, 7 times as much as those at baseline. The nonselective COX inhibitor ketoprofen significantly suppressed ATP release by 64% and PGE_2 release by 51%.

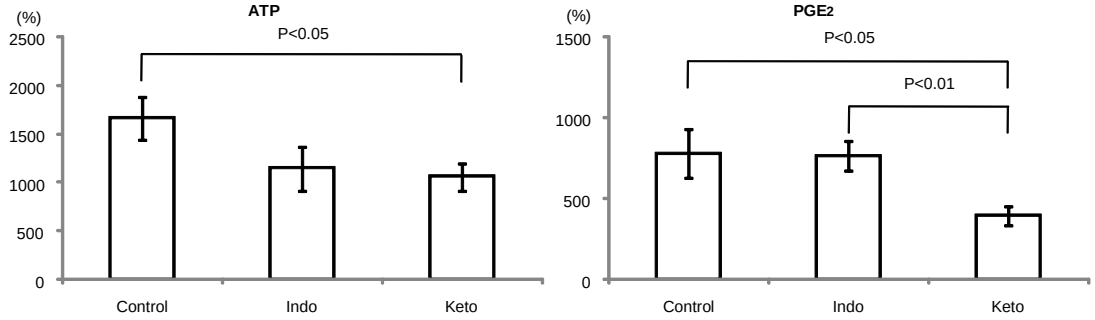

Figure: Effect of COX inhibitors on ATP and PGE_2 release from the urethra.

Interpretation of results

These results suggest that urethral epithelium has the ability to synthesize ATP and PGE_2 in response to urethral distension. There is a possibility that mediators released from the urethra participate in the development of detrusor overactivity. COX inhibitors may decrease ATP release from the urethelium. This is a hypothesis worthy of further study.

Concluding message

This animal model seems to be useful for evaluating the effect of selected drugs on mediators elicited by urethral distension.

References

1. J Urol 1994,151:1554
2. J Urol 2007,177:771
3. Neuroscience 1986,18:727

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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
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