

RELATIONSHIP BETWEEN ACETYLCHOLINE AND ATP RELEASES AND BLADDER SMOOTH MUSCLE FUNCTION IN PARTIAL OUTLET OBSTRUCTION IN RATS

Hypothesis / aims of study

It has been reported that partial bladder outlet obstruction (BOO) leads to hypertrophy and alteration in contraction of bladder smooth muscle. Acetylcholine (ACh) and ATP have been known to play an important role on contraction of urinary bladder. However, there is little available information about the relationship between neurotransmitters (ACh and ATP) releases and bladder smooth muscle function in BOO. Therefore, using muscle bath technique, we investigated the changes in ACh and ATP releases and bladder smooth muscle contractility in BOO rats.

Study design, materials and methods

Partial bladder outlet obstruction (BOO) was performed by ligating the proximal urethra over 1mm angio-catheter in adult female SD rats. Sham operated rats were served as controls. Rats were sacrificed 2 weeks, 3 months and 6 months after introducing BOO. Smooth muscle strip was dissected from the body of urinary bladder. Each strip was suspended in organ bath filled with Krebs-Henseleit solution, and tension development was recorded. Microdialysis probe was inserted into the strip, and Ringer solution was perfused into the probe at a constant flow rate. The contractions induced by carbachol, ATP, KCl (80 mM) and electrical field stimulation (EFS; supramaximal voltage, 0.3 msec duration, 2.5 - 40 Hz and 3 sec train) were evaluated. Furthermore, using microdialysis technique, we collected the dialysate during EFS, and measured the amount of ACh and ATP in the dialysate fraction by HPLC with ECD and luciferine-luciferase assay, respectively. In addition, isolated bladder specimens were immunohistochemically stained for rabbit polyclonal S-100 antibodies in both BOO and control rats.

Results

Bladder weight was gradually increased after introducing BOO. There were not significant changes in KCl-induced contractile response through the experimental period in both groups. Carbachol-induced contractile response did not change until 3 months after introducing BOO, however it was significantly reduced in 6 months, as compared with the control. There was significant increase in ATP-induced contractile response at 2 weeks and 3 months after introducing BOO. However, the contractile response induced by ATP was returned to the control values at 6 months after BOO. EFS-induced contractile responses in bladder strips of BOO rats were gradually decreased during experimental period, and were significantly decreased in 6 months, as compared with the control rats. ACh and ATP releases from bladder strip were not significantly different between groups until 2 weeks after introducing BOO. However, ACh and ATP releases in BOO rats were gradually decreased in 3 to 6 months, and they were significant lower than that of the control group in 6 months. Immunohistochemical staining of S-100 showed the significant decreased number of the positive neuron in bladder of BOO rats in 6 months, as compared with the control rats.

Interpretation of results

The present data show the gradual decreases in ACh and ATP releases from the bladder strips in BOO rat, which may relate to the decreased number of S-100 positive neuron in immunohistochemical staining. The denervation supersensitivity may contribute to the increased contractile responses induced by ATP in bladder strips in BOO rats in 2 weeks and 3 months. The decreased number of neurons and the decreased releases of ACh and ATP may cause the decrease in EFS-induced contractile responses in bladder strips of the chronic phase of BOO rats.

Concluding message

The present data suggest that the changes in the number of neuron and ACh and ATP releases in bladder may contribute to bladder smooth muscle functions in BOO rats.