

THE FUNCTIONAL ROLE OF EP4 RECEPTORS IN THE RAT URINARY BLADDER WITH BLADDER OUTLET OBSTRUCTION: A POSSIBLE COUNTERACTIVE MECHANISM AGAINST DETRUSOR OVERACTIVITY.

Hypothesis / aims of study

In our previous study, one of prostaglandin E2 receptor subtypes, EP4 are largely expressed in the rat urinary bladder mucosa and detrusor with bladder outlet obstruction (BOO), while they are few in controls assessed by RT-PCR, and immunohistochemistry.

We investigate the functional role of EP4 receptors in the rat urinary bladder with outlet obstruction.

Study design, materials and methods

Materials

7 weeks-old female Sprague-Dawley rats were used for this study.

Partial BOO models have been made with 2mm-polyethylene tube covered to urethra for 4-7weeks.

Isometric contraction

Approximately 10x5mm bladder strips were suspended in a 5ml organ bath filled with Krebs solution at 37C .

The effect of 100μM ONO-AE1-329 (ONO; EP4 selective agonist) on 50 mM KCL-induced muscle contraction was evaluated in 5 controls and 6 BOOs.

Filling cystometry

Cystometry with continuously saline infusion was performed to examine the effect of intravesical 10μM EP4 agonist administration on micturition in urethane-anesthetized 5 control rats and 6 BOO.

Results

EP4 agonist significantly relaxed KCL-induced contraction of bladder strips from rats with BOO, while no reaction was observed in controls (figure 1). Additionally, a significant correlation was found between the relaxant effect of EP4 agonist and whole bladder weight which may represent BOO grade (figure 2).

Intravesical EP4 agonist perfusion caused significant prolongation of intercontraction intervals without alteration of micturition pressure (figure 3). while it did not affect on these parameters in control rats.

Effect of EP4 agonist on the high K⁺-induced contraction of bladder strips with BOO

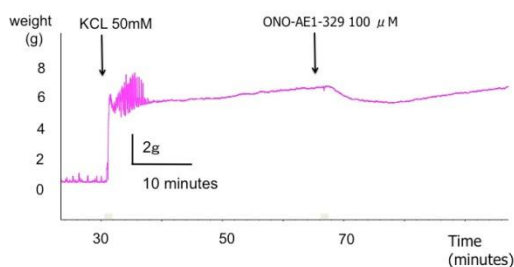


Figure 1

Relationship between the relaxant effect of EP4 agonist and whole bladder weight

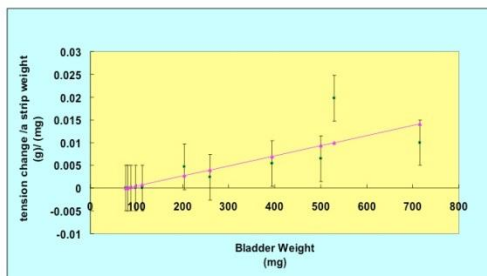


Figure 2

Cystometric investigations in bladder with outlet obstruction

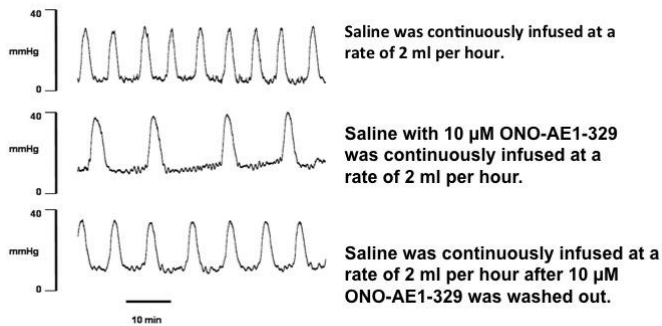


Figure 3

Interpretation of results

These results in functional investigations indicate that EP4 receptor expressed in the obstructive bladder can function in detrusor smooth muscle and the afferent pathway.

The change of detrusor muscle tone by EP4 receptor activation may affect on bladder afferent excitability.

In addition, EP4 expressed in obstructed bladder epithelium may be involved in suppression of bladder afferent activity according to the cystometric investigations.

Concluding message

Activation of EP4 receptors strongly expressed in BOO bladders may be involved in the suppression of the detrusor muscle excitability and the afferent activity. This might be a compensatory mechanism for counteracting the deterioration of storage function in the BOO bladder.

References

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Disclosures

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