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HIGHLY EXPRESSION OF ANGIOTENSIN TYPE-1 RECEPTOR (AT1) IN THE RAT DETRUSOR MUSCLE WITH BLADDER OUTLET OBSTRUCTION

Hypothesis / aims of study

Recently, it is reported that the organ derangement is genereated by the tissue rennin-angiotensin system RAS [1]. Angiotensin is the main effector peptide RAS and exerts a variety of biological actions [2]. Angiotensin are mediated by at least two receptor subtypes, designated AT1 and AT2. AT1 receptor was considered that it may play a role in mediating cell-proliferation, hypertrophy, smooth muscle contraction and sympathetic transmission [3]. In cardiovascular disease, vascular remodeling is facilitated via the AT1 receptor in RAS.

Benign prostate hypertrophy (BPH) is the common cause of bladder outlet obstruction. Bladder detrusor muscle is sometimes occurred to fibrosis, cell growth and cellular infiltration in chronic bladder outlet obstruction. Overactivity of the local rennin-angiotensin system (RAS) might be involved in bladder remodeling. The functional role of RAS in voiding function is unknown. In this study, we investigated the expression of AT1 receptor in the rat detrusor muscle with bladder outlet obstruction model.

Study design, materials and methods

The 12-week-old female Wistar rats were used in this study. They were divided into two groups; sham operation group and partial bladder outlet obstruction (P-BOO) group. Partial bladder outlet obstruction model was induced with urethane anesthesia as follows. The urethra was intubated with a 2.9 Fr Polyethylene tube, and middle abdominal incision was performed and retropubic space developed. The bladder was exposed, and a double 4-0 silk ligature was placed loosely around the proximal urethra producing a standardized degree of obstruction, and finally the Polyethylene tube was removed. Incision was closed with surgical sutures. Sham operated rats were underwent identical surgical procedures without ligation. After 2, 4 and 8 weeks surgery, both sham operation group rats and P-BOO rats were examined cystometorical investigation. After cystometrical investigation, entire bladder was removed, and AT1 expression of each bladder was investigated by western blot analysis. We used anti-AT1R (rabbit anti-AT1, Santa Cruz) for primary antibody and anti-rabbit IgG for secondary antibody. Immunoreactivity was visualized using ECL dura (PIERCE).

Results

The weight and capacity of bladder in P-BOO were significantly increased compared with sham operation group. And the weight and capacity of bladder in P-BOO were gradually increased after surgery. The detrusor contraction in 2-weeks P-BOO was higher. However, at 8-weeks P-BOO voided pattern was overflow.

In western blot analysis, expression of the AT1 receptor was detected on detrusor muscle in both sham operation and P-BOO. Furthermore, expression of AT1 on detrusor muscle in P-BOO was higher than in sham operation. However, there was no difference in the expression of AT1 between 2, 4 and 8 weeks P-BOO.

Interpretation of results

AT1 receptor in detrusor muscle was highly expressed in partial bladder outlet obstruction. Alteration of detrusor muscle in chronic bladder outlet obstruction may be generated via AT1 receptor.

Concluding message

These data suggested that tissue rennin-angiotensin system (RAS) mediated by AT1 may involved in bladder remodeling with chronic bladder outlet obstruction

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