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THE CORRELATION BETWEEN PROSTAGLANDIN E2, BLADDER OUTLET OBSTRUCTION, AND REACTIVATION OF C-FIBERS IN THE HUMAN BLADDER

Hypothesis / aims of study

Although overexpression of prostaglandin E2 (PGE2) in the urinary bladder of animal experimental models with bladder outlet obstruction (BOO) is involved in the micturition reflex through activation of c-fibers, there are few reports on the correlation between PGE2 in the human bladder, BOO, and reactivation of c-fibers. In the present study, we evaluated whether PGE2 in the bladder correlated with BOO and reactivation of c-fibers.

Study design, materials and methods

A total of 46 male patients were enrolled in this study. The exclusion criteria were chronic renal failure (serum Cr level > 1.5 mg/dL), diabetes mellitus with a fasting blood glucose of 200 mg/dL or greater, urinary tract infection with white blood cell count of > 5/hpf in the urine, prostatitis, bladder cancer, and non-steroidal anti-inflammatory drugs use. Additionally, to minimize the influence of PGE2 produced in the kidney, the patients with urinary Cr level above mean + 1 standard deviation (SD) in the samples were excluded from this study. The storage symptoms included in IPSS (frequency, urgency, and nocturia) were evaluated. Free flowmetry, pressure flow study (PFS), and ice water test (IWT) were performed in all patients to evaluate the degree of BOO and reactivation of c-fibers. Urine samples at free flow and samples of delivered physiologic saline after completing IWT were taken to measure the levels of PGE2 and Cr.

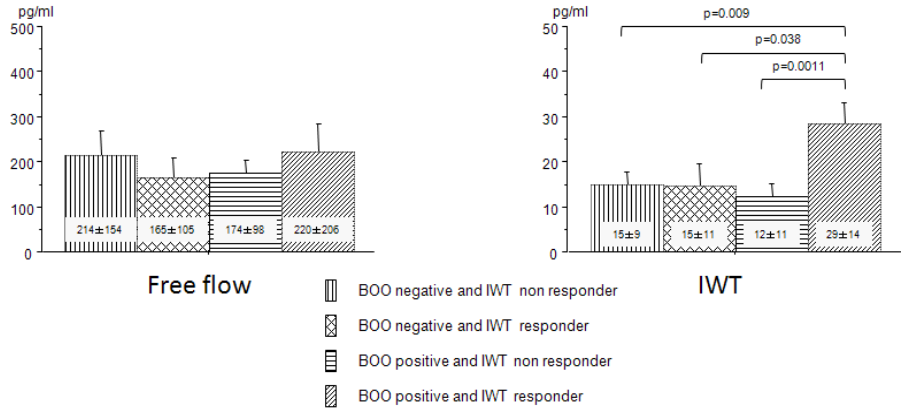
Results

Thirty-eight, and 39 patients were eligible in the free flow study and IWT, respectively. Although there was no difference in the score of urgency between IWT responders with and without BOO, the score of urgency in the IWT responders was significantly higher than that in the IWT non-responders (Table 1). The Cr and PGE2 concentrations in free flowmetry were about ten-fold higher than those in the delivered physiological saline collected after completing IWT. There was a positive correlation between PGE2 and Cr concentration in free flowmetry ($p > 0.05$, $r = 0.33$) but not in IWT. There was no difference in the PGE2 concentration in free flowmetry among the patient groups divided according to BOO and response to IWT. However, the concentration of PGE2 in IWT in the patients with BOO and positive response to IWT was the highest among the groups (Fig. 1). There was a positive correlation between BOO and the PGE2 concentration in IWT ($p = 0.012$, $r = 0.38$), but not in free flowmetry.

Table 1. Characteristics of patients divided according to Bladder outlet obstruction and the response to Ice water test

	A	B	C	D	
	BOO negative IWTnon-responder	BOO negative IWTresponder	BOO positive IWTnon-responder	BOO positive IWTresponder	p
Mean age ± SD(y.o)	63 ± 16.8	69 ± 4.4	70.1 ± 10.5	67.1 ± 8.6	n.s
Frequency	0.5 ± 1.3	3.2 ± 1.3	1.7 ± 1.4	2.5 ± 1.9	A vs.B:p=0.002,A v.s,D,p<0.005
Urgency	0.5 ± 1	4.8 ± 0.4	1.5 ± 1.2	3.8 ± 1.1	A vs.B:p<0.0001,A v.s,C,p<0.03,A v.s,D,p<0.001, B v.s,C,p<0.0001, C v.s,D,p<0.0001,
Nocturia	1.4 ± 1.4	2.7 ± 0.6	2 ± 1.2	2.7 ± 1.5	A v.s,D,p<0.003
Bladder outlet obstruction index	13 ± 15	13 ± 25	66 ± 22	77 ± 17	A v.s,C,p<0.0001,A v.s,D,p<0.0001, B v.s,C,p<0.0001, B v.s,D,p<0.0001,
Bladder contractility index	106 ± 37	111 ± 29	119 ± 27	124 ± 24	n.s
Mean first diseire to void(ml)	221 ± 125	131 ± 41	167 ± 108	138 ± 25	n.s
Mean maximum desire to void(ml)	479 ± 168	245 ± 56	340 ± 98	275 ± 80	A vs.B:p<0.0007,A v.s,C,p<0.007,A v.s,D,p<0.0004
Mean bladder volume at the response of IWT(ml)		86 ± 33		80 ± 19	n.s
Mean maximum pressure of the response of IWT(mmH_2O)		52 ± 27		58 ± 28	n.s

Fig.1 The concentration of PGE2 in samples.



Interpretation of results

1. In this study, there was a positive correlation between PGE2 and Cr concentration in free flowmetry but the difference in the PGE2 concentration was not significant in free flowmetry among the patient groups divided according to BOO and response to IWT.

This phenomenon suggested that temporary urine was an improper sample to evaluate PGE2 in the bladder because it had a potential to involve PGE 2 produced in the kidney to a great degree.
2. The concentration of PGE2 in IWT in the patients with BOO and positive response to IWT was the highest. There was a positive correlation between BOO and the PGE2 concentration in IWT. In other words, BOO had a potential to induce PGE2 production, and the increase in PGE2 may reactivate c-fibers in the human bladder as well as in the animal experimental models with BOO.

Concluding message

In the human bladder, BOO induce PGE2 production, and the increase in PGE2 may cause urgency by the micturition reflex through activation of c-fibers.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Review boad in Nara medical university**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**