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CORRELATION BETWEEN ALPHA1-ADRENORECEPTOR SUBTYPE MRNA EXPRESSION LEVEL AND EFFICACY OF NAFTOPIDIL FOR BPH PATIENTS

Hypothesis / aims of study
Three subtypes of alpha1-adrenoreceptors (alpha1-ARs) have been identified by both pharmacological and molecular cloning techniques. Some reports that the alpha1A-AR and alpha1D-AR subtypes are the predominant subtype compared with alpha1B-AR in the prostate. However, these expression levels seem to vary with each patient. We examined the quantified each alpha1-AR subtype mRNA in BPH tissue obtained by prostate biopsy and correlation of the efficiency of subselective alpha1D-blocker, naftopidil in the management of benign prostatic hyperplasia (BPH).

Study design, materials and methods
A total of 28 men 50 years old or older (mean age; 67.9+/-6.9 years) with lower urinary tract symptoms secondary to untreated BPH who had undergone a transperineal ultrasound prostate biopsy were enrolled in this study. Four biopsy specimens were obtained from the transition zone, and real-time RT-PCR was performed using these samples to examine the expression level of alpha1A-AR and alpha1D-AR. Judging from the results of real-time RT-PCR, the patients were grouped into alpha1A-AR-dominant patients (n=12) and alpha1D-AR-dominant patients (n=16). After biopsy, they were treated with 50 mg naftopidil for 12 weeks and were evaluated for the efficacy (I-PSS, QoL index, Qmax and PVR) of naftopidil at 12 weeks. We examined the correlation between alpha1A-AR and alpha1D-AR mRNA expression level and efficacy of naftopidil. Informed consent was obtained from all patients before this study.

Results
Naftopidil significantly relieved lower urinary tract symptoms and significantly increased Qmax from baseline. Naftopidil improved IPSS, QoL index and Qmax in alpha1D-AR-dominant patients with a significance differences in comparison with the alpha1A-AR dominant patients.

Interpretation of results
Subselective alpha1D-blocker, naftopidil was shown to provide significant advantage in the treatment of alpha1D-AR-dominant BPH patients.

Concluding message
This study confirmed that the expression level of each alpha1 AR subtype mRNA can be a predictor of the efficiency of naftopidil in the management of BPH.

	alpha1A-AR dominant			1D-AR dominant		
	baseline	3-month	P value	baseline	3-month	P value
Total IPSS	16.8 (7.8)	8.3 (5.4)	0.001	12.4 (7.3)	6.2 (4.2)	0.002
Voiding frequency	3.3 (1.7)	1.8 (1.1)	0.04	2.2 (1.8)	1.3 (1.4)	NS
Urgency	1.3 (2.0)	0.7 (1.2)	NS	1.1 (1.1)	0.5 (0.7)	0.01
Nocturia	2.3 ((1.2)	1.5 (1.2)	NS	2.1 (1.4)	1.5 (1.5)	0.05
Intermittency	1.8 (2.3)	1.3 (1.4)	NS	1.8 (1.8)	0.9 (1.3)	0.05
Weak stream	2.7 (2.0)	1.5 (1.5)	NS	2.3 (2.1)	1.2 (1.4)	0.01
Hesitancy	2.3 (2.3)	0.8 (0.9)	NS	1.1 (1.9)	0.3 (0.5)	NS
Emptying	3.3 (0.8)	0.8 (1.0)	0.001	1.8 (1.7)	0.6 (0.7)	0.01
QOL	3.9 (1.5)	2.8 (1.8)	0.05	3.4 (1.0)	2.3 (1.2)	0.0004
Qmax	9.3 (3.31)	13.1 (6.4)	0.03	8.5 (3.1)	13.5 (7.1)	0.005