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Matsukawa Y[1], Hattori R[1], Majima T[1], Takai S[1], Gotoh M[1]
1. *Department of Urology, Nagoya University Graduate School of Medicine, Japan*

IS COMBINATION THERAPY WITH AN ANTICHOLINERGIC AGENT AND AN A1-ADRENOCEPTOR ANTAGONIST EFFECTIVE AS FIRST-LINE TREATMENT FOR PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA COMPLICATED BY AN OVERACTIVE BLADDER? A RANDOMIZED, PROSPECTIVE, COMPARATIVE, URODYNAMIC STUDY

Aims of study
Around 60% of benign prostatic hyperplasia (BPH) patients show overactive bladder (OAB) symptoms. In the treatment of BPH, α1 adrenoceptor(AR) antagonists play a primary role and relieve both voiding and storage symptoms, and are widely used as first-line drug therapy.

But it was reported that the improvement in storage symptom was poor in the patients with BPH complicated by OAB. Anticholinergics are widely used to treat OABs but are rarely administered to BPH patients because of risks such as urinary retention and deterioration in voiding function. Although several randomized studies have reported the efficacy of combination therapy (CT) with an anticholinergic agent and an α1- AR antagonist, their analyses were mainly based on symptomatic parameters. We performed a pressure-flow study (PFS) in BPH patients with OAB to compare the efficacies of CT using an anticholinergic agent and a α1-AR antagonist and monotherapy (MT) using an α1-AR antagonist.

Study design, materials and methods
We conducted a single-center, randomized, prospective study. The study group comprised 120 untreated BPH patients with urinary urgency (at least once per week), who fit the inclusion criteria; 1) international prostate symptom score (IPSS)-total ≥ 8 points, 2) IPSS-QOL ≥3 points, 3) prostate volume as measured by transabdominal or transrectal ultrasonography ≥ 20 ml, 4) maximum flow rate (Qmax) < 15 ml/sec when the voiding volume on uroflowmetry (UFM) was ≥ 100 ml, 5) postvoid residual urine volume (PVR) on UFM < 100 ml, 6) age ≥ 50 years,7) OAB symptom score (OABSS) ≥3 points.
The patients were randomly assigned to receive MT with silodosin 8mg/day or CT with silodosin 8mg/day and propiverine 20mg/day. Changes in parameter values from baseline to 8 weeks after administration were assessed using IPSS, IPSS- QOL index, and OABSS; voiding and storage functions were measured by urodynamic study(UDS).

Results
Efficacy analysis was performed using 52 and 54 patients in the MT and CT groups, respectively (Table). At baseline, no significant differences were detected in IPSS, IPSS-QOL, or OABSS between the two groups. Comparison of the baseline data obtained by UDS revealed no significant differences in bladder capacity at first desire to void (FDV), maximum cystometric capacity (MCC), Qmax, detrusor pressure at Qmax (PdetQmax), PVR, bladder obtlet obstruction index (BOOI).

After treatment, both groups showed significant improvement in mean IPSS, IPSS-QOL, and OABSS; however, the CT group showed greater improvement. In particular, the CT group showed statistically significant improvement in OABSS (P = 0.04). As for voiding and storage function, both groups showed significant improvement in PdetQmax and BOOI. The PVR decreased significantly in the MT group but increased significantly in the CT group. The FDV and MCC significantly improved only in the CT group. Detrusor overactivity observed before treatment disappeared in 69.7% (CT group) and 45.1% (MT group). The CT group showed significantly greater reduction in the rate of detrusor overactivity than the MT group (P = 0.04).

There was no patient who had urinary retention and four patients could not continue the administration due to adverse reactions such as dry mouth and constipation, and two patients was unable to undergo UDS after administration in the CT group, while three patients could not continue the administration due to adverse experience, and five patients was unable to undergo PFS after administration. There was no difference between two groups in adverse effect.

Concluding message
First-line therapy with silodosin and propiverine significantly improved the symptoms, storage function, and obstruction in BPH patients with OAB.
Combination therapy with an anticholinergic agent and an α1- AR antagonist was safe and more effective in improving storage function than monotherapy using an α1-AR antagonist in the treatment of BPH with OAB

		MT group (silodosin) N = 52	P (intra-group)	CT group (silodosin + propiverine) N = 54	P (intra-group)	P improvement (inter-group)
Age(mean)		69.6		70.4		**ns**
Prostate volume (ml)		47.1		45.6		**ns**
IPSS	**Before**	18.3		18.5		
	After	12.8	<0.01	11.5	<0.01	**ns**

QOL-index	**Before**	4.9		4.9		
	After	3.6	<0.01	3.5	<0.01	**ns**
OABSS	**Before**	7.2		7.6		
	After	4.9	<0.01	4.3	<0.01	**0.04**
FDV (mL)	**Before**	118		106		
	After	141	0.06	145	<0.01	**0.04**
MCC (mL)	**Before**	238		210		
	After	269	0.05	264	<0.01	**0.04**
Qmax (mL/s)	**Before**	8.6		8.5		
	After	10.9	<0.01	9.8	<0.01	**ns**
PdetQmax (cmH_2O)	**Before**	73.3		72.5		
	After	54.9	<0.01	59.5	<0.01	**ns**
PVR(mL)	**Before**	59		44		
	After	33	<0.01	66	<0.01	**<0.01**
BOOI	**Before**	56.1		56.6		
	After	33.1	<0.01	39.9	<0.01	**ns**
DO cases	**Before**	33		33		
	After	17		10		
Disappearing rate		45.1%		69.7%		**0.04**

MT: monotherapy, CT: combination therapy, FDV: first desire to void, MCC: maximum cystometric capacity, Qmax: maximum flow rate, PdetQmax: detrusor pressure at maximum flow rate, PVR: postvoid residual urine volume, BOOI: bladder outlet obstruction index,
DO: Detrusor overactivity

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