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EVALUATION OF COMBINATION THERAPY (75 MG/DAY NAFTOPIDIL PLUS 30 MG/DAY URAPIDIL) IN PATIENTS WITH BPH/LUTS POORLY RESPONDING TO ALPHA1 BLOCKER MONOTHERAPY

Hypothesis/aims of study
Benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) are primarily treated with alpha1 blockers. There has been a recent increase in the types of alpha1 blockers available, facilitating the adoption of therapeutic strategies such as switching one drug to another and increasing the drug dose level. However, some cases fail to respond to any type of alpha1 blocker (non-responders to alpha1 blocker monotherapy). The present study was undertaken to evaluate the efficacy of combining alpha1 blocker therapy with urapidil in the cases poorly responding to alpha1 blocker monotherapy.
Study design, materials and methods
The study involved patients satisfying all of the following requirements: (1) patients with poor responses to oral treatment with tamsulosin hydrochloride (0.2 mg/day) or silodosin (8 mg/day) who had a quality of life score (QOL-S) rated with the international prostate symptom sore (IPSS) of 3 or higher despite 8-week or longer treatment, and (2) patients failing to show improvement 8 weeks after switching of the previous drug to naftopidil (75 mg/day). Twenty-five patients (mean age: 70 ± 6.5 years) were enrolled to the study. Urapidil (30 mg/day) was added to the naftopidil therapy in these 25 patients. Subjective symptoms were evaluated using IPSS and overactive bladder symptom score (OABSS). As objective symptoms, urinary flow parameters and residual volume were evaluated. The evaluation was made at the start and 8 weeks after the start of urapidil treatment.

Results
Table 1 shows the time course of subjective symptoms. The total IPSS improved significantly after the start of combination therapy compared to that before the start of the combination therapy. Of the IPSS subscores, the scores on daytime frequancy and nocturia improved significantly. QOL-S also improved significantly in 56% of all patients. The total OABSS and OABSS subscores decreased after the start of the combination therapy, although none of these changes was statistically significant. Table 2 shows the time course of objective findings. Urinary flow analysis revealed that maximum flow rate (Qmax), mean flow rate (Qave), and voided volume (VV) improved significantly. Post-void residual volume (PVR) did not change significantly.

Table.1 Time course of subjective symptoms

		0W	8W	P
IPSS	1.Imcomplete emptying	2.2 ± 1.6	2.0 ±1 .6	P=0.41
	2. Frequancy	2.9 ± 1.5	2.2 ± 1.3	P = 0.023
	3. Intermittency	2.0 ± 1.7	1.9 ± 1.8	P=0.66
	4. Urgency	1.6 ± 1.6	1.6 ± 1.8	P=0.87
	5. Weak stream	2.3 ± 1.6	2.2 ± 1.4	P=0.73
	6. Straining	2.3 ± 1.7	1.7 ± 1.5	P=0.22
	7. Nocturia	3.0 ± 1.4	2.7 ± 1.3	P = 0.036
	Total	16.4 ± 6.7	14.2 ± 7.2	P = 0.037
	QOL-S	4.3 ± 1.0	3.6 ± 1.3	P < 0.001
OABSS	Q-1	0.8 ± 0.6	0.8 ± 0.7	P=1.0
	Q-2	2.5 ± 0.9	2.4 ± 1.0	P=0.26
	Q-3	2.0 ± 1.6	1.7 ± 1.7	P=0.43
	Q-4	1.2 ± 1.7	1.0 ± 1.5	P=0.08
	Total	6.4 ± 3.15	5. 8 ± 2.9	P=0.17

Table.2 Time course of objective parameters

		0W	8W	P
Urinary flow	VV (ml)	175.9 ± 78.9	215.5 ± 84.0	P = 0.003
	Qmax (ml/s)	11.8 ± 6.8	13.9 ± 5.9	P = 0.003
	Qave (ml/s)	5.9 ± 3.2	7.3 ± 3.4	P = 0.012
	PVR (ml)	26.1 ± 28.8	19.6 ± 27.3	P=0.29

Interpretation of results

Some investigators reported that treatment with multiple alpha1 blocker subtypes in an alternating fashion manifested efficacy to some extent [1]. However, responses to alpha1 blocker monotherapy are limited. In the present study, combination therapy using multiple alpha1 blockers resulted in the alleviation of subjective and objective symptoms even in poor responders to alternating alpha1 blocker monotherapy. We believe that improvement of QOL-S in 56% of the patients with BPH/LUTS (disease affecting the QOL) following combined naftopidil-urapidil therapy is noteworthy. Following recent clinical introduction of a 5alpha reductase inhibitor in Japan, we now have various options for the treatment of BPH/LUTS, but the efficacy of existing methods sometimes remains unclear for small-size prostates. Combination therapy using multiple alpha1 blockers is promising as a valid means of treatment for small-sized prostates or cases requiring rapid manifestation of efficacy.

Concluding message

Some cases of BPH/LUTS fail to respond well to alpha1 blocker monotherapy, and physicians find it difficult to treat such cases. In future, it is desirable to identify an optimum combination of drugs for combination therapy using multiple alpha1 blockers for patients with BPH/LUTS.

References

1. BJU Int. 2006:97:747-751

Specify source of funding or grant	**None**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Nagasaki university hostital**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**