388

Gotoh M[1], Takeda M[2], Nishizawa O[3], Yoshida M[4], Takahashi S[5], Masumori N[6]

1. *Urology Department, Nagoya University Graduate School of Medicine,* ***2.*** *Department of Urology, University of Yamanashi, School of Medicine,* ***3.*** *Department of Urology, Shinshu University School of Medicine,* ***4.*** *Department of Urology, National Center for Geriatrics and Gerontology,* ***5.*** *Department of Urology, Nihon University School of Medicine,* ***6.*** *Department of Urology, Sapporo Medical University School of Medicine*

COMBINATION THERAPY WITH IMIDAFENACIN AND TAMSULOSIN IS EFFECTIVE AND SAFE FOR BPH PATIENTS WITH PERSISTENT OAB SYMPTOMS AFTER TAMSULOSIN MONOTHERAPY REGARDLESS OF PROSTATE SIZE; SUB-ANALYSIS OF ADDITION STUDY

Hypothesis / aims of study

Several reports have indicated that combination therapy with an alpha1-blocker and an anticholinergic agent is effective in benign prostate hyperplasia (BPH) patients with storage symptoms who are unresponsive to alpha1-blocker monotherapy. On the other hand, treatment of BPH with an anticholinergic drug increases the risk of urinary retention and increases post-void residual urine (PVR). Imidafenascin (IMI) is a newly developed anticholinergic drug that is commercially available in Japan. Recently, we evaluated the efficacy of imidafenacin 0.2 mg/day combined with tamsulosin (TAM) 0.2 mg/day in overactive bladder (OAB)/BPH patients who did not respond to alpha1-blocker monotherapy (ADDITION study [1]. In this report, we assessed the efficacy and safety of combination therapy with IMI and TAM in OAB/BPH patients using ADDITION Study[*2] data stratified by prostate volume (PV).

Study design, materials and methods

In this randomized, open-labeled, parallel-group, multicenter study, Japanese OAB/BPH patients aged 50 years or older were randomly assigned to a TAM monotherapy group or IMI+TAM combination group. Efficacy was assessed using the overactive bladder symptom score (OABSS), a frequency volume chart (FVC) and international prostate symptom score (IPSS) before and after therapy. The OABSS [2,3] is a psychometrically validated symptom questionnaire designed to comprehensively quantify OAB symptom severity for four symptoms, daytime frequency, nocturnal frequency, urgency and urgency incontinence, based on the total score ranging from 0 to 15 points. For the IPSS, changes in score were evaluated by calculating the total, voiding and storage scores. QOL was assessed using the IPSS-QOL and BPH impact index (BII). Evaluation of these parameters was conducted at baseline (week 0), after 4, 8 and 12 weeks of combination treatment. Data were divided by PV into two groups (large PV group; PV ≥30 mL and small PV group; PV <30 mL) with reference to the TIMES Study[*1]. Statistical analysis of quantitative continuous variables and comparison of the groups were performed using the mixed effect model.

Results

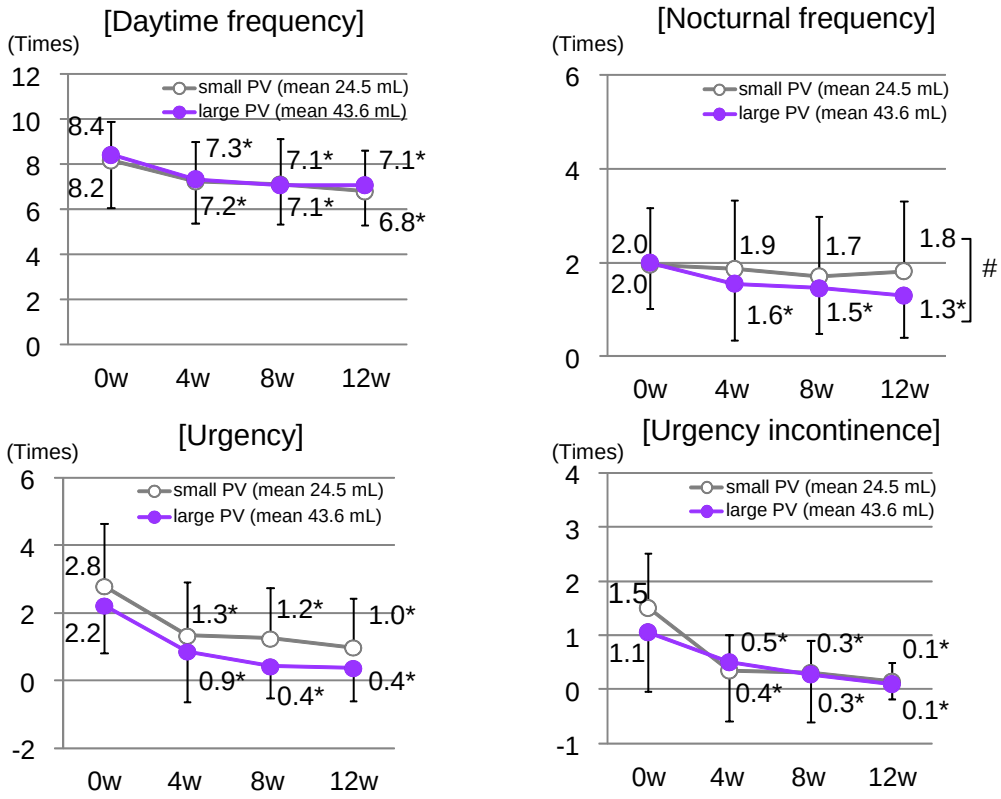
A total of 308 patients were enrolled. In the IMI+TAM group (n=151), the numbers of patients in the large and small PV groups were 88 and 63, respectively. Mean PV size in the large and small PV groups was 43.6±14.9mL and 24.5±2.8mL, respectively. The ratio of patients with nocturnal polyuria (nocturnal polyuria index ≥33%) was 40.3% in the large PV group and 55.0% in the small PV group, and the difference was statistically significant (p=0.0431). The parameters daytime frequency, nocturnal frequency, urgency and urgency incontinence in FVC and OABSS were significantly improved at week 4, 8 and 12 in both groups, except nocturnal frequency in the small PV group (Fig. 1). In inter-group comparison, the improvement of nocturnal frequency assessed by FVC and OABSS was significantly greater in the large PV group than in the small PV group (Fig. 1). IPSS total score, storage and voiding sub-score were significantly reduced after combination treatment in both groups. In addition, IPSS-QOL and BII were significantly improved after combination treatment in both groups. The changes of IPSS, IPSS-QOL and BII were not significantly different between the two groups. Although mean PVR significantly increased in the large PV group (from 15.5mL to 22.3mL), the increase of PVR was clinically minimal and no urinary retention was observed.

Interpretation of results

In the large and small PV groups, the combination therapy significantly improved all OAB symptoms (daytime frequency, nocturnal frequency, urgency and urgency incontinence), IPSS, IPSS-QOL and BII. Only the decrease of nocturnal voiding was significantly greater in the large PV group than in the small PV group. The significantly greater ratio of patients with nocturnal polyuria in the small PV group might have contributed to the difference in improvement of nocturia between the two groups.

Concluding message

This study demonstrated that IMI and TAM combination therapy is effective and safe in BPH patients with persistent OAB symptoms after tamsulosin monotherapy, regardless of PV size.



Mean ± SD Mixed effects model; * 0w vs 4w・8w・12w, # smaller PV vs larger PV $p<0.05$

Fig. 1
Effects of IMI+TAM combination therapy on daytime frequency, nocturnal frequency, urgency and urgency incontinence assessed by FVC.

References
1. Takeda M: International Continence Society 42nd annual meeting; #440, 2012
2. Homma Y, et al. Urology, 2008; 68: 318
3. Gotoh M, et al. Urology, 2011; 78: 768

Disclosures
Funding: none **Clinical Trial:** Yes **Public Registry:** No **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** Ethics Committee, Nagoya University Graduate School of Medicine **Helsinki:** Yes **Informed Consent:** Yes