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## ADD-ON EFFECTS OF DUTASTERIDE IN MEN WITH SYMPTOMATIC BENIGN PROSTATIC HYPERPLASIA RESISTANT TO ALPHA-BLOCKER MONOTHERAPY, SPECIAL FOCUS ON ULTRA-SHORT TERM EFFECT

### Hypothesis / aims of study

Alpha-blockers are commonly used and generally effective in men with benign prostatic hyperplasia (BPH). However, some men complain of persistent lower urinary tract symptoms (LUTS). 5 $\alpha$ -reductase inhibitors (5-ARI) reduce prostatic volume and improve LUTS in men with BPH. 5-ARI provides the relief of voiding symptoms, and also is as effective as alpha-blockers for control of storage symptoms [1].

5-ARI typically takes four to six months to achieve the prostate shrinkage [2]. LUTS improvement by 5-ARI appears to occur in advance of prostate volume reduction. Thus, other factors (ex. increased testosterone) than prostate volume reduction may be associated with the early effect of 5-ARI on LUTS [3].

We examined the add-on effects of dutasteride in men with no LUTS improvement by alpha-blocker monotherapy, especially focused on its ultra-short term effect on LUTS.

### Study design, materials and methods

A total of 39 men with clinical diagnosis of BPH who had been treated by alpha-blocker for over 8 weeks, but did not obtain the LUTS improvement were enrolled in a prospective, open-label, single-arm and multicentre study. They had the prostate volume of 30 cm<sup>3</sup> or greater (as measured by transabdominal ultrasonography) and the International Prostate Symptom Score (IPSS) of 12 points or greater or QOL index of 4 points or greater despite alpha-blocker treatment. The effects of dutasteride 0.5mg daily in combination with alpha-blocker were evaluated for 24 weeks. The efficacy endpoints included changes in the IPSS, Overactive Bladder Symptom Score (OABSS), total prostate volume (PV), serum PSA, and post-void residual urine volume (PVR). The assessments were made at baseline, 2 weeks, 1, 2, 3, 6 months for IPSS, OABSS, and at baseline, 3 and 6 months for PSA, PV, and PVR.

Wilcoxon signed-ranks test was used for statistical analysis.

The study was carried out in compliance with the Helsinki Declaration. Local or regional ethics committees and institutional review boards approved the protocol.

### Results

At the baseline (alpha-blocker treatment), means of total symptom score, storage symptom subscore and voiding symptom subscore of IPSS, QOL index, and OABSS were 19.0, 7.4, 11.6, 4.1, and 6.4. Mean PV, PSA and PVR were 60.4cm<sup>3</sup>, 4.9 ng/mL, and 53mL.

Statistically significant improvements of IPSS were noted at 2nd week of dutasteride treatment ( $p = 0.0003$ ) and continued throughout week 24 with a 7.5-points decrease, and reduction of voiding subscore was much more significant ( $p = 0.0001$ ) than that of storage subscore ( $p = 0.053$ ) at 2nd week (Fig. 1). Storage symptom subscore of IPSS ( $p = 0.04$ ), QOL index ( $p = 0.01$ ), and OABSS ( $p = 0.04$ ) were significantly improved at 4th week of treatment.

At the 24th week, prostate volume and PSA was decreased by 24 % and 56 % on the average. PVR reduced from 53 to 23mL.

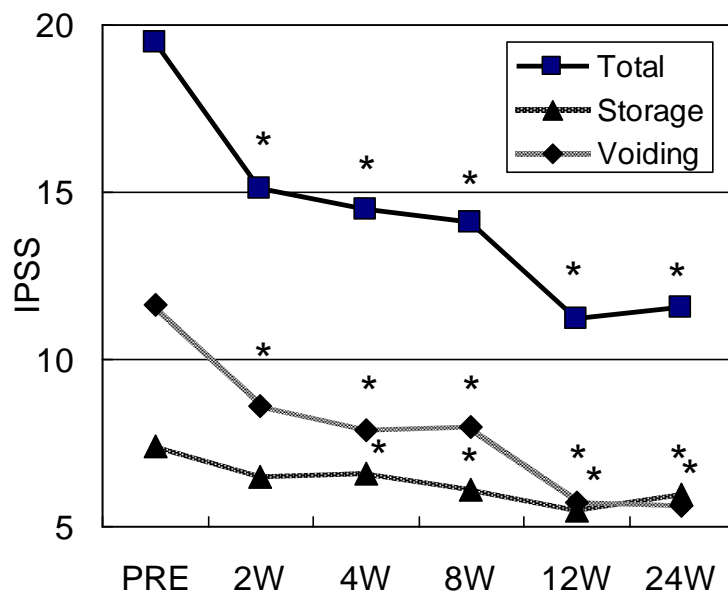
### Interpretation of results

Dutasteride add-on therapy improved rapidly LUTS in patients with BPH who did not show enough improvement with alpha-blocker monotherapy. At 2nd week of dutasteride treatment, voiding symptoms were significantly improved, while storage symptom showed a significant improvement at the 4th week.

### Concluding message

Dutasteride add-on therapy is beneficial in patients with BPH who do not get sufficient improvement with alpha-blocker treatment. Voiding symptoms may be ameliorated earlier than storage symptoms with dutasteride. This preceding effect on voiding symptoms may give some hints for the mechanisms by which dutasteride achieve an early effect on LUTS.

Fig. 1. IPSS, storage symptom subscore, and voiding symptom subscore after dutasteride add-on therapy. (\*: significant difference from the baseline values)



References

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Disclosures

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