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# EFFECTS OF WITHDRAWING DUTASTERIDE ON SERUM TESTOSTERONE AND LOWER URINARY TRACT SYMPTOMS

Hypothesis / aims of study

The CombAT study proved that the significant improvement of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia(BPH) continued for about 18 months after administration of either dutasteride or combination therapy [1]. After this period, the patients' symptoms remained stable, but further significant improvements were not observed. Dutasteride is a type of drug which reduces prostate volume (PV) and relieves symptoms. If treated with dutasteride for a mid to long term period, the PV reduction rate is gradually reduced. For this reason, we assume that dutasteride withdrawal might be possible**,** if temporary. Symptoms following withdrawal of dutasteride have not been well clarified in BPH patients. We have evaluated (2015 ICS abstract No. 595) the withdrawal of dutasteride at the 3 month interval for the short term of six months. The result was no observed deterioration of LUTS. Few studies have focused on the change of PV and symptoms after withdrawal of dutasteride. Jeong YB et al reported the withdrawal of dutasteride for a one year interval [2]. However, there are almost no studies which investigate the relationship between LUTS and testosterone level following withdrawal of dutasteride. Therefore, we further evaluated the outcome for a year with an increased number of patients compared to our data two years ago.

Study design, materials and methods

A total of 47 BPH patients who have been treated with dutasteride for over two years and are stable were entered in the study. Forty-three patients had been treated with combination therapy of dutasteride and α-blocker, and four patients had been treated with monotherapy of dutasteride. We examined the total International Prostate Symptom Score (IPSS-T), voiding sub-score (IPSS-V), storage sub-score (IPSS-S), quality of life (IPSS-QOL), PV, serum prostate specific antigen (PSA), total testosterone (TT), and residual urine(RU) every three months for a year after stopping administration of dutasteride. Primary endpoints were the change of PV from baseline numbers. Secondary endpoints were the change of IPSS-T, IPSS-V, IPSS-S, IPSS-QOL, serum PSA, TT and RU. We also classified the patients into two groups according to the deterioration of IPSS-V(Group A) and IPSS-S(Group B)scores at 12 months compared to the baseline.

Results

Following the withdrawal of dutasteride, IPSS-T, IPSS-V, IPSS-S and IPSS-QOL did not significantly deteriorate in all 47 BPH patients. The PV and serum PSA levels increased, and serum TT decreased significantly at the 12 month follow up. The number of patients in Groups A and B was 12 and 15, respectively. Each study parameter at the discontinuation of dutatsteride had no significant difference between the two groups [Table1]. PV and PSA increased significantly in both groups (PV: Group A; 27.4±13.9→42.3±18g $P<0.01$, Group B; 32.8±12.7→45.8±18g $P<0.01$, PSA: Group A; 2.17±2.6→6.1±3.6 $P<0.01$, Group B; 2.64±2.7→5.9±3.5 $P<0.01$), but the significant decrease of TT was specific to Group B at 12 months [Figure1]. Eight patients withdrew from this study. Two patients suffered from acute urinary retention (AUR) at the 6 and 9 month study periods. One and 2 patients complained of severe voiding and storage symptoms, respectively. Three patients did not respond to follow up.

Interpretation of results

The withdrawal of dutasteride could be accomplished with no significant symptom deterioration in the majority of patients during the one year study period. IPSS-S might be influenced by a decrease of testosterone following the withdrawal of dutasteride based on the findings of the TT decrease in Group B. IPSS-V in Group A was considered to be affected only by PV and not by TT. In contrast, a previous study reported significant improvements in overactive bladder symptom score (OABSS) in the TT-elevated group, whereas no significant change was noted in the non-elevated group [2]. Another study reported that among patients with overactive bladder (OAB), dutasteride significantly improved urgency and urgency incontinence**,** especially in those who had lower OABSS, urgency incontinence scores and TT at the baseline [3]. Based on this evidence, TT is likely to contribute to improvement of storage symptoms. To date there are few studies regarding the deterioration of storage symptoms accompanied by a decrease of TT after withdrawal of dutasteride. However, this study has limitations because of its small sample size and necessitates further detailed discussion. Future studies including more patients are needed to confirm our findings.

Concluding message

To our knowledge, this is the first prospective study addressing withdrawal of dutasteride in Japanese patients. This study suggested that deterioration of storage symptoms was affected by the decrease of TT after the withdrawal of dutasteride. These findings provide further insights into the management of BPH/LUTS patients who have been treated with dutasteride. Almost all patients could safely undergo withdrawal of the dutasteride treatment; however, medical professionals should carefully monitor patients for events such as AUR.

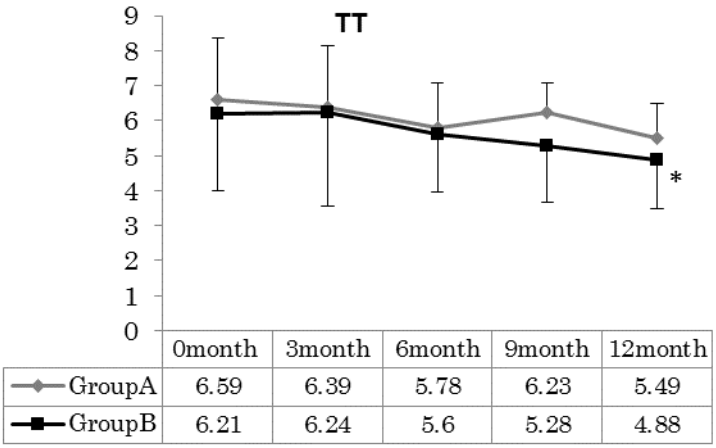
| Table1 | GroupA (n=12) | GroupB (n=15) | p-value |
|---|---|---|---|
| Age | 73 ± 7.78 | 75.8 ± 7.31 | 0.25 |
| PV | 27.4 ± 13.9 | 32.8 ± 12.7 | 0.271 |
| TT | 6.59 ± 1.77 | 6.21 ± 2.22 | 0.849 |
| PSA | 2.17 ± 2.6 | 2.64 ± 2.71 | 0.525 |
| IPSS-T | 7.5 ± 6.59 | 7.86 ± 6.45 | 1 |
| IPSS-V | 3.41 ± 3.63 | 4.86 ± 4.74 | 0.655 |
| IPSS-S | 4.08 ± 3.54 | 3 ± 2.12 | 0.708 |
| IPSS-QOL | 2.58 ± 1.38 | 2.6 ± 1.35 | 0.815 |
| PVR | 33.1 ± 42.4 | 40.2 ± 43.1 | 0.624 |

Data were indicated as Mean ± SD

Mann-Whitney U test was conducted to compare each variables between two groups. $P < 0.05$ was considered as statistically significance

**Figure1**

Mean changes from baseline of TT were analyzed using the Wilcoxon signed-rank test. P<0.05 was considered as statistical significance.




| | 0month | 3month | 6month | 9month | 12month |
|---|---|---|---|---|---|
| GroupA | 6.59 | 6.39 | 5.78 | 6.23 | 5.49 |
| GroupB | 6.21 | 6.24 | 5.6 | 5.28 | 4.88 |


References

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Disclosures

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