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EFFECT OF DUTASTERIDE ON BLADDER WALL HYPETROPHY IN PATIENTS WITH BENIGN PROSTATIC OBSTRUCTION : A 24-WEEK OPEN-LABEL, SINGLE-ARM PILOT STUDY

Hypothesis / aims of study

Bladder outlet obstruction (BOO) secondary to benign prostatic hyperplasia has been shown to cause bladder hypertrophy and increased bladder weight [1]. We may evaluate BOO and bladder function by measuring bladder wall thickness and bladder weight using ultrasound [2].

We assume that the prevention of BPH progression by 5α-reductase inhibitor (5ARI) may be result of bladder function protection by the reduction of prostate size and BOO. To our knowledge, there have been no studies evaluating the effects of a 5ARI on bladder function. Therefore, we evaluated the effects of 5ARI on bladder function by the evaluation of bladder wall hypertrophy and lower urinary tract symptoms (LUTS).

Study design, materials and methods

This study was prospective and open label. Primary objective was to explore the efficacy of Dutasteride in reducing bladder wall hypertrophy from baseline to 6 months of treatment in male patients with benign prostatic obstruction. Secondary objective was to evaluate the efficacy of Dutasteride on improving LUTS, number of micturitions and urgency episodes, and urodynamic parameters from baseline to 6 months of treatment. The tolerability, safety, patient perception and quality of life from baseline to 6 months of treatment were evaluated.

Inclusion criteria were as follows: 1) Age ≥50 and <80 years old, 2) Presence of LUTS for at least 3 months, 3) International Prostate Symptom Score (IPSS) ≥ 15, 4) BOO confirmed by pressure-flow study ; BOO index (BOOI) ≥20, 5) prostate volume measured by transrectal ultrasonography (TRUS) ≥ 30ml and < 100ml. Patients were treated with 0.5mg Dutasteride once a day for 6 months. At baseline and after 6 months of Dutasteride treatment, we measured ultrasound estimated bladder weight (UEBW) and bladder wall thickness with using a battery-powered 3D hand-held ultrasound system, the BladderScan® BVM 6500 device (Diagnostic Ultrasound, Bothell, WA). UEBW divided by body surface area (BSA) which was statistically significant parameter correlating with BOO was evaluated [3]. We assessed the efficacy of Dutasteride by comparing IPSS score, Quality of life (QoL) score, maximum urine flow rate, residual urine volume, prostate volume, and serum PSA level between baseline and after 6 months of treatment. Changes in number of micturitions/24h, volume voided/micturition from baseline to 6 months of treatment were evaluated. The correlation of BOOI with UEBW, UEBW/BSA, and bladder wall thickness was analyzed by the Spearman's test. BOOI was calculated by PdetQmax-2Qmax of pressure flow study.

Results

A total of 37 patients were enrolled in this study and 7 patients dropped out, therefore 30 patients completed the 6-month study and evaluated. The mean age of the patients was 68 years (range 56-79) and mean duration of disease was 41.9 ± 35.6 months. Mean BOOI was 43.03 ± 14.20 in the pressure-flow study performed at baseline. The mean UEBW was 47.10 ± 7.79 g before treatment and 50.07 ± 5.39 g after treatment; this difference was not significant. Also, the change of mean UEBW/BSA and bladder wall thickness were not significant. Total, voiding and storage scores of IPSS, QoL score were significantly improved after the Dutasteride treatment for 6 months. Serum PSA level and prostate volume was significantly decreased. Maximum urine flow rate was increased significantly. There was no significant difference in post-void residual urine volume before and after treatment.

Interpretation of results

Our study showed a statistically significant improvement in maximum flow rate and IPSS scores with the significant reduction of the prostate volume and serum PSA level after 6 months Dutasteride treatment; however, there was no significant change in UEBW, UEBW/BSA, or bladder wall thickness.

This observation may be explained by 1) UEBW or bladder wall thickness is not an useful parameter to predict BOO; 2) 6-month treatment of Dutasteride is not sufficient to show a change in bladder wall hypertrophy in spite of the prostate volume reduction.

Concluding message

Treatment of BPH patients with dutasteride for 6 months significantly improved maximum urine flow rate, IPSS, prostate volume, and serum PSA, but had no significant difference on UEBW, UEBW/BSA, and bladder wall thickness. Considering the short study period and small sample size of this study, a large, multicenter, long-term study is warranted to confirm the validity of these results.

Table. The change of bladder weight and thickness and voiding parameters according to the treatment of Dutasteride (mean ± S.D)

	Baseline	6 months later	*p*-value

Ultrasound estimated bladder weight (g)	47.10 ± 7.79	50.07 ± 5.39	0.2591
UEBW/BSA (g/㎡)	26.47 ± 4.30	28.21 ± 3.53	0.2533
Bladder wall thickness (mm)	2.41 ± 0.48	2.30 ± 0.31	0.3014
Maximal flow rate (ml/sec)	8.89 ± 2.50	11.68 ± 4.66	0.0182
Post-void residual urine (ml)	96.07± 62.47	74.63 ± 73.94	0.9801
IPSS			
Total scores	20.23 ± 5.56	10.90 ± 5.87	<0.0001
Voiding scores	12.53 ± 3.86	5.97 ± 4.16	<0.0001
Storage scores	7.70 ± 2.72	4.93 ± 2.77	<0.0001
Quality of life score	4.67 ± 1.03	2.70 ± 1.37	<0.0001
PSA (ng/ml)	3.54 ± 4.08	1.27 ± 0.72	<0.0001
Prostate volume (ml)	44.72 ± 16.58	37.48 ± 12.85	<0.0001
Bladder diary variables			
Micturations per 24h	8.78 ± 1.94	8.79 ± 2.29	1.0000
Nocturnal micturitions	1.47 ± 1.02	1.42 ± 1.11	1.0000
Urgency episodes per 24h	1.46 ± 3.50	2.69 ± 4.06	0.0209
Functional bladder capacity	295 ± 72.40	310.44 ± 104.22	0.2804

UEBW; ultrasound estimated bladder weight
UEBW/BSA; ultrasound estimated bladder weight/body surface area
IPSS_total scores; international prostate symptom scores item 1-7
IPSS_voiding scores; international prostate symptom scores item 1,3,5,6
IPSS_storage scores; international prostate symptom scores item 2,4,7
PSA : prostate specific antigen

References

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Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**ClinicalTrials.gov** **NCT00827814**
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	**Samsung Medical Center Institutional Review Board**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**