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TREATMENT OF SYMPTOMATIC OVERACTIVE BLADDER IN MEN WITH TAMSULOSIN: A PROSPECTIVE MULTICENTER TRIAL

Hypothesis / aims of study

Recent work has suggested that several sympathetic-mediated mechanisms, including over-stimulation or up-regulation of α receptors in the bladder and spinal cord, may cause detrusor overactivity (1). α1 receptors influence lower urinary tract function not only through the direct effect on smooth muscle but also at the level of the spinal cord, ganglia, and nerve
terminals. Therefore pharmacological manipulation of α receptors could be used to treat overactive bladder (OAB) symptoms. There is evidence that α1-adrenergic receptor antagonists might be effective for OAB, but the clinical result is rare. We evaluated the efficacy of tamsulosin, an α1A/ α1D-selective adrenergic antagonist, in male patients with OAB in 8-week prospective, multicenter trial.

Study design, materials and methods

Male patients (aged 42–78 years) who had suffered from symptoms of OAB for at least 3 months were included in 8-week therapy with 0.2 mg tamsulosin once daily. Subjects were required to have an average frequency of ≥8 voids/24 h and have experienced at least three episodes of urgency or urge incontinence during the 3-day voiding diary period. Also International Prostatic Symptom Score (IPSS) should above 12. Those who had voided volume over 3L per day, neurogenic voiding dysfunction, and took antimuscarinic agents were excluded. Before commencing treatment patients were evaluated by digital rectal examination, PSA, voiding diary, IPSS, Bother Score, and pressure-flow study. Patients recorded micturition frequency, voided volume, frequency of urgency, severity of urgency using a voiding diary during run-in period and weeks 8 (directly preceding clinic visits). In the voiding diary patients marked the level of urgency associated with every voluntary micturition. The Urinary Sensation Scale (5 urgency levels) was used to measure urgency, and urgency was defined as ≥ level 3. Reevaluation with voiding diary, IPSS, Bother Score, uroflowmetry, and postvoid residuals (PVR) was performed after 8 weeks of treatment. Efficacy variables included change from baseline in the mean number of urgency, severity of urgency, micturition frequency, uroflow parameters, and score of symptom questionnaire. All results variables were tested with paired- t test, mixed model, GEE (Generalized Estimating Equations) method and Wilcoxon's signed rank test.

Results

A total of 81 male patients were enrolled and 70 patients completed the treatment. The efficacy analysis included all patients who received at least one dose of study drug and who had efficacy data available from the baseline and at least one on-treatment visit (n=81). Detrusor Overactivity (DO) was present in 32% (26/81) of patients. Bladder Outlet Obstructive Index (BOOI) was <20 in 18 patients (22%), 20-40 in 43 patients (53%) and > 40 in 20 pateints (25%). After 8 weeks of medication the number of urgency episodes per day was reduced from baseline by 51.3% (Table 1). Severity of urgency was significantly decreased from 2.42 to 2.01. Tamsulosin treatment significantly decreased micturition frequency, urge incontinence episode, total IPSS score, and Bother score ($p<0.0001$). In IPSS score, both of storage and voiding scores were decreased ($p<0.0001$). There were statistically significant improvement in maximum flow rate and PVR ($p<0.001$). There was no significant change in total voided urine volume a day and blood pressure. Compared with patients without DO, the changes from baseline in the daytime frequency was significantly higher in patients with DO ($p<0.05$). The changes from baseline in severity of urgency, total score of IPSS, Bother score, and maximum flow rate was significantly higher in patients with BOOI score ≥20 than patients with BOOI score<20 ($p<0.05$) (Table 2). Improvement rate of other efficacy variables were similar in the subgroups by the BOOI score or presence of DO.

Interpretation of results

Tamsulosin (0.2mg once daily) improved OAB symptoms significantly including urgency as well as voiding symptoms in men after 8-week treatment. Tamsulosin had more beneficial effects on severity of urgency, maximum flow rate and IPSS in OAB patients with bladder outlet obstruction. The presence of detrusor overactivity did not affect the treatment outcomes with tamsulosin for the patients of OAB.

Concluding message

Tamsulosin significantly improved urgency, other symptoms of OAB, and voiding symptoms. α-adrenergic antagonist appears to have therapeutic effect in the treatment of the OAB in men with or without BOO, but greater effects in BOOI score ≥20.

Table 1. Overall changes in efficacy parameters (n=81).

	Baseline (mean±SD)	Treatment (mean±SD)	p-value
Frequency (No/24-h)	11.09 ± 2.28	9.37 ± 2.12	$p < 0.0001^{*}$
Urgency (No/ 24-h)	5.20 ± 4.45	2.53 ± 3.41	$p < 0.0001^{\dagger}$

Urgency grade	2.41 ± 0.82	2.01 ± 0.76	p < 0.0001†
Urge incontinence (No/ 24-h)	0.23 ± 0.93	0.01 ± 0.07	p = 0.00293†
Functional bladder cap. (ml)	324.20 ± 121.75	324.32 ± 111.36	p = 0.95836†
Maximum flow rate (ml/sec)	11.69 ± 5.99	14.38 ± 6.93	p = 0.00002*
Post-void residual (ml)	37.74 ± 26.89	28.67 ± 25.29	p = 0.00341*
IPSS (Total)	20.45 ± 6.51	13.49 ± 5.76	p < 0.0001*
Storage symptom	9.19 ± 3.01	5.89 ± 2.59	p < 0.0001*
Voiding symptom	11.26 ± 5.00	7.59 ± 3.96	p < 0.0001*
Bothersome score	4.34	3.14	p < 0.0001‡

*: Paired t-test, †: Wilcoxon signed rank test, ‡: Generalized Estimating Equations method

Table 2. Comparison between the subgroups according to the severity of bladder outlet obstruction.

	AG number < 20		AG number ≥ 20		
	Baseline	8-week tx.	Baseline	8-week tx.	p-value
Frequency (24-h)	10.93 ± 2.79	9.39 ± 1.90	11.14 ± 2.14	9.37 ± 2.20	0.50630*
Urgency (No/24h)	5.43 ± 5.64	3.87 ± 4.62	5.13 ± 4.10	2.15 ± 2.91	0.07880*
Urgency grade	2.38 ± 0.87	2.25 ± 0.83	2.42 ± 0.82	1.95 ± 0.73	0.03026*
PVR (ml)	38.00 ± 26.34	23.83 ± 22.61	37.66 ± 27.25	30.05 ± 26.01	0.61000*
AUASS (sum)	16.53 ± 4.05	13.00 ± 5.31	21.40 ± 6.66	13.61 ± 5.90	0.0486†
Storage score	8.33 ± 2.61	6.00 ± 2.88	9.40 ± 3.09	5.87 ± 2.54	0.4431†
Voiding score	8.20 ± 4.23	7.00 ± 3.85	12.00 ± 4.91	7.74 ± 4.00	0.0324†
Bothersome score	4.05	3.55	4.42	2.98	0.0072‡

*: Percentage change, †: numeric change, ‡: Generalized Estimating Equations method

References:
1) Prostate. 1997;30:205–215.

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HUMAN SUBJECTS: This study did not need ethical approval because Because of recommended and usual clinical treatment in men but followed the Declaration of Helsinki Informed consent was obtained from the patients.