Efficacy of terazosin for overactive bladder symptoms and sexual function in patients with overactive bladder and symptomatic benign prostatic hyperplasia: a prospective multicenter trial

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Objective: This study is to evaluate the efficacy of terazosin in the treatment of overactive bladder (OAB) symptoms and sexual dysfunction in patients with symptomatic benign prostatic hyperplasia (BPH) and OAB.

Methods: Of 200 men aged 50-80 years with symptomatic BPH, an International Prostatic Symptom Score (IPSS) ≥8 accompanied by OAB symptoms, 185 patients completed treatment with terazosin 2-5 mg once daily for 8 weeks. Patients were asked to complete a voiding diary, the International Index of Erectile Function (IIEF) questionnaire, and the IPSS at baseline, 4 and 8 weeks.

Results: 8-week terazosin treatment improved OAB symptoms as well as reducing IPSS (19.8 to 12.7) and IIEF (34.4 to 37.4) scores. OAB symptoms improved significantly, irrespective of symptom severity by the IPSS, but the IIEF score only increased in patients with severe symptoms.

Conclusions: Additional studies are needed to further evaluate the placebo effect. However, terazosin monotherapy is effective in patients with symptomatic BPH and OAB, and may increase sexual function in patients with severely symptomatic BPH. **(J Korean Continence Soc 2008;12:36-41)**

Key Words: Prostatic hyperplasia, Adrenergic alpha-antagonists, Erectile function, Overactive bladder

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Introduction

Benign prostatic hyperplasia (BPH) is the most prevalent urological diagnosis in men presenting with urinary symptoms in primary care, with the risk and severity of symptoms increasing with age (1). The most common symptoms are related to voiding, whereas the most bothersome are related to storage (2), with the latter characterized as overactive bladder (OAB), including urgency usually associated with frequency and nocturia (3). The storage symptoms are probably caused by bladder instability secondary to obstruction, such as bladder wall hypertrophy and collagen disposition (4). These findings suggest that relief or severity changes in voiding symptoms may reduce OAB symptoms. Previous studies, however, have analyzed changes in the frequency of urge episodes, not the severity of urgency per se, although there have been assessments of OAB symptoms in BPH patients.

Recent various treatment strategies for BPH may affect sexuality, with α1-adrenoceptor blockers shown to improve sexual function and quality of life in men with concomitant BPH (5,6).

Terazosin, an α1-adrenoreceptor blocker with equal affinity for the 3 subtypes (A, B and D) of α1-adrenoreceptors used, has been used as first-line treatment for LUTS in patients with BPH. In the present study, we evaluated the effects of terazosin on OAB symptoms and LUTS related sexual function in men with symptomatic BPH and OAB.

Materials and Methods

Patients

The study population consisted of men aged 50-80 years, complaining of LUTS caused by symptomatic BPH between January 2005 and February 2006. Preoperative evaluations included a medical history, physical examination, urinary analysis, urine culture, digital rectal examination (DRE), serum PSA level, 3-day voiding diary including Indevus Urgency Severity Scale (IUSS) (7), uroflowmetry, and, post-void residual (PVR) measurement. Patients were also asked to complete the International Index of Erectile Function (IIEF) questionnaire and the International Prostatic Symptom Score (IPSS) questionnaire.

Patients eligible for enrollment were required to have moderate to severe LUTS (IPSS ≥8) and maximum urinary flow rate (MFR) of less than 15 ml per second (volume voidied ≥150 ml) with or without erectile dysfunction. Patients also had an average daytime frequency of 8 or more times, nocturia more than once per night and urgency (2 or more urgency episodes ≥grade 2 per day) with or without urge incontinence.

In their voiding diaries, patients recorded the volumes of every voluntary micturition and marked the level of urgency for each. Urgency severity was measured with the IUSS, a 4-point validated scale rating patient perception of urgency severity at each void. The urgency severity score was defined as the urgency number divided by the number of voids.

Patients with suspicious results on the DRE and/or serum PSA concentrations of 4 ng/ml or more underwent prostate biopsy with a minimum of 6 cores. Those with negative results were enrolled. Exclusion criteria included severe liver or heart disease, history of neurogenic bladder, DM, CVA or orthotopic hypotension, clean intermittent catheterization, PVR of 200 ml or more, acute or chronic urinary infection, interstitial cystitis or use of α-adrenoreceptor antagonists for hypertension. Patients were also excluded if they lacked an ability to communicate and did not understand the requirements of the study, or if they voided more than 3000 ml per day.

Trial Protocol

Patients were given 2 mg to 5 mg terazosin once daily for 8 weeks. LUTS including OAB symptoms and erectile function using 3-day voiding diary, IPSS and IIEF were assessed at baseline, 4 and 8 weeks. Free uroflowmetry, including PVR, and systolic and diastolic blood pressure were measured at each visit. Terazosin dose was increased to 5 mg once daily in patients with IPSS changes of less than 4 after 4 weeks.

The IPSS was composed of voiding (Q1, Q3, Q5 and Q6) and storage symptom (Q2, Q4 and Q7) scores and quality of life assessment index. The IIEF consisted of a series of 15 questions characterizing 5 major domains of sexual function: erectile function (EF, Q1-Q5 and Q15), intercourse satisfaction (IS, Q6-Q8), orgasmic function (OF, Q9 and Q10), sexual desire (SD, Q11 and Q12) and overall sexual satisfaction (OSS, Q13 and Q14).

Electronically measured MFR and voided volume were determined. Measurements were repeated if voided volume was less than 150 ml. PVR was assessed by bladder scan.

We compared OAB symptoms and sexual function between patients with moderate (IPSS: 8-19) and severe (IPSS: 20 or more) LUTS. Adverse events were recorded throughout the study.

Statistical Analyses

All statistical analyses were performed using the SPSS for windows® package, korean version 12.0 (SPSS, Chicago, Illinois). All statistical tests were two-tailed with the significance level set at 0.05. The Chi-square and Student's t tests were used to compare data from the patient groups with moderate and severe IPSS. Baseline and posttreatment values for all parameters of terazosin treatment were compared using the Wilcoxon signed ranked test and paired t-test, including urgency severity score (8)

Results

Of the 200 eligible patients with symptomatic BPH and OAB enrolled, 185 (mean age 63.5±7.7 years) completed the study. At baseline, the mean prostate volume was 32.1±10.3 cc according to DRE and the mean serum PSA level was 1.6±1.3 ng/ml.

The decrease in blood pressure was statistically significant (systolic pressure: 129.5±12.6 mmHg to 126.0±12.1 mmHg, diastolic pressure: 80.7±8.9 mmHg to 78.3±10.3 mmHg, $p<0.01$), but not clinically significant. Except for PVR (28.6±35.3ml to 23.2±37.2 ml, $p>0.05$), all IPSS scores improved significantly ($p<0.001$) at 8 weeks, including MFR (11.5±4.4 ml/s to 14.7±5.5 ml/s), total (19.8 to 12.7), voiding (11.6 to 7.5) and storage (8.3 to 5.2) scores. Terazosin-treated patients had a statistically significant decrease in OAB symptoms, including daytime frequency, nocturia, number of urgency episodes, and urgency severity score ($p<0.001$ for each) (Table 1). Daytime frequency decreased more than 25% in 48 patients (25.9%), nocturia more than 50% in 73 patients (39.5%), the number of urgency episodes more than 50% in 92 patients (59.4%) and urgency severity score more than 50% in 70 patients (37.8%) (Table 2).

The IIEF score increased significantly after treatment (34.4 to 37.4, $p=0.001$), as did the scores of all 5 domains ($p<0.05$ for each). Functional bladder capacity (FBC) increased signi-

Table 1. Changes in international index of erectile function (IIEF) and voiding parameters from baseline to 8 weeks in patients treated with terazosin

	Baseline	After treatment		*p*-value*
		4 weeks	8 weeks	
Total (1-7) IPSS	19.8±6.5	14.8±6.3	12.7±5.8	<0.001
Total IIEF score	34.4±19.9	35.8±20.7	37.4±20.3	0.001
Daytime frequency	8.4±2.4	7.7±2.1	7.4±1.9	<0.001
Nocturia	2.2±1.1	1.7±0.9	1.4±0.9	<0.001
FBS (ml)	298.3±92.6	319.0±97.1	327.5±87.9	<0.001
No. urgency (/24hrs)	3.4±3.6	2.1±2.9	1.7±2.7	<0.001
Urgency severity score	0.9±0.7	0.7±0.7	0.6±0.7	<0.001

Abbreviations: IPSS, international prostatic symptom score; FBS, functional bladder capacity; NS, nonsignificant
*between baseline and 8 weeks

Table 2. Number of terazosin-treated patients with improvements in urinary parameters

	Daytime frequency	Nocturia	No. urgency (/24hrs)	Urgency severity score
75% reduction	6 (3.2%)	24 (13.0%)	67 (43.2%)	28 (15.1%)
50-75% reduction	2 (1.1%)	49 (26.5%)	25 (16.2%)	42 (22.7%)
25-49% reduction	40 (21.6%)	46 (24.9%)	27 (17.4%)	30 (16.2%)
0-24% reduction	85 (45.9%)	45 (24.3%)	20 (12.9%)	29 (15.7%)
no change (0%)	7 (3.8%)	22 (11.9%)	9 (5.8%)	6 (3.2%)
Increase	52 (28.1%)	21 (11.4%)	16 (10.3%)	56 (30.3%)

Table 3. Characteristics of patients with moderate and severe international prostatic symptom scores (IPSS)

	Moderate IPSS (8-19)	Severe IPSS (≥20)	p-value
No. patients	98	87	
Age (years)	63.1±6.8	63.9±8.6	NS
Prostate volume (cc)	32.4±9.6	31.8±11.2	NS
Serum PSA (ng/ml)	1.6±1.4	11.2±4.0	NS
Duration (months)	33.3±73.4	34.5±37.7	NS
Blood pressure			
Systolic (mmHg)	129.9±13.1	129.1±12.0	NS
Diastolic (mmHg)	80.3±8.9	81.2±8.9	NS
MFR (ml/s)	11.7±4.7	11.2±4.0	NS
PVR (ml)	26.5±27.7	31.1±42.6	NS
Dosage (mg)			
4 weeks	2.9±1.4	2.8±1.4	NS
8 weeks	3.1±1.5	3.1±1.5	NS

Abbreviations: PSA, prostatic specific antigen; Qmax, maximum flow rate; PVR, post-void residual; NS, nonsignificant

ficantly as did mean volume voided.

When we classified the patients into groups with moderate (8-19) and severe (≥20) IPSS, we observed no significant intergroup differences in mean age, serum PSA level, duration, uroflowmetry, blood pressure or dose of terazosin at 4 and 8 weeks (Table 3). At baseline, the patients with moderate IPSS had milder OAB symptoms, including daytime frequency (7.6 vs. 9.2, p<0.001) and number of urgency episodes (2.8 vs. 3.9, p=0.034), than those with severe IPSS (Table 4). However, there were no significant differences in nocturia and urgency severity score. In the groups with moderate and severe IPSS, daytime frequency (7.6 to 6.9 vs. 9.2 to 7.8), nocturia, FBC and mean voided volume improved significantly after terazosin treatment (all p<0.011), showing that symptom improvement was independent of IPSS severity. Similarly, in both groups, the number of urgent episodes and urgency severity score were decreased significantly by terazosin treatment (p<0.001).

Pre-treatment sexual function, as scored by the IIEF, did not differ significantly between the two groups (p=0.068). In patients with moderate IPSS, total IIEF score and scores in all IIEF domains did not change significantly after 8 weeks of terazosin treatment. In contrast, total IIEF score increased significantly in patients with severe IPSS (31.6 to 36, p= 0.001), as did scores in 4 of the 5 domains, EF (12.9 to 14.8, p=0.001), IS (5.3 to 6.2, p=0.003), OF (4.4 to 5.1, p=0.008) and SD (4.6 to 5.1, p=0.001), the only exception being OSS (Table 4).

Adverse events included dizziness in 8 patients, asthenia in

Table 4. Changes in overactive bladder (OAB) symptoms and international index of erectile function (IIEF) score in patients with moderate (8-19) and severe (≥20) international prostatic symptom score (IPSS) after treatment with terazosin

	OAB symptoms	Baseline	After treatment	p-value
Moderate IPSS (8-19)	Daytime frequency	7.6±2.1	6.9±1.8	0.003
	Nocturia	2.1±0.9	1.3±0.9	<0.001
	FBS (ml)	325.1±93.9	349.3±89.8	0.009
	No. urgency (/24hrs)	2.8±3.5	1.3±1.9	<0.001
	Urgency severity score	0.8±0.7	0.5±0.6	<0.001
Severe IPSS (≥20)	Daytime frequency	9.2±2.5	7.8±1.8	<0.001
	Nocturia	2.3±1.2	1.5±0.9	<0.001
	FBS (ml)	271.2±83.4	304.3±80.4	<0.001
	No. urgency (/24hrs)	3.9±3.7	2.1±3.2	<0.001
	Urgency severity score	0.9±0.7	0.7±0.8	<0.001
	IIEF domain	Baseline	After treatment	p-value
Moderate IPSS (8-19)	Total (1-15)	36.9±19.3	38.6±19.7	NS
	EF (1-5,15)	15.4±8.8	15.9±9.4	NS
	IS (6-8)	5.9±3.9	6.4±4.0	NS
	OF (9,10)	5.4±3.6	5.6±3.5	NS
	SD (11,12)	5.2±2.3	5.4±2.1	NS
	OSS (13,14)	5.1±2.4	5.4±2.2	NS
Severe IPSS (≥20)	Total (1-15)	31.6±20.3	36.0±20.9	0.001
	EF (1-5,15)	12.9±9.0	14.8±9.3	0.001
	IS (6-8)	5.3±4.1	6.2±4.4	0.003
	OF (9,10)	4.4±3.6	5.1±3.5	0.008
	SD (11,12)	4.6±2.1	5.1±2.2	0.001
	OSS (13,14)	4.5±2.5	4.8±2.5	NS

Abbreviations: FBS, functional bladder capacity; MVV, mean voided volume; EF, erectile function; IS, intercourse satisfaction; OF, orgasmic function; SD, sexual desire; OSS, overall sexual satisfaction; NS, nonsignificant

6, orthostatic hypotension in 4, headache in 3, somnolence in 2 and hemospermia in 1.

Conclusion

As our study did not include randomized controlled trials, additional studies will be needed to further evaluate the placebo effect in sexual function and LUTS during terazosin therapy in patients with symptomatic BPH.

We were unable to demonstrate the placebo effect, however, we found that terazosin monotherapy is effective in patients with symptomatic BPH and OAB. In addition, terazosin monotherapy may increase sexual function in patients with severely symptomatic BPH.

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