—**Report on Experiments and Clinical Cases**—

The Short-Term Effects of Terazosin in Japanese Men with Benign Prostatic Hyperplasia

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Abstract

We evaluated the short-term efficacy of terazosin for treating symptomatic benign prostatic hyperplasia (BPH). Thirty men, aged 52 to 83 years (mean: 69.2 years) complaining of obstructive urinary symptoms due to BPH who had not received any prior treatment for their symptoms were orally administered 2 mg/day of terazosin. Symptoms (the total IPSS and the obstructive and irritative symptom scores) and objective parameters (peak flow rate [Qmax] and prostatic volume) were evaluated before treatment and after 1, 2, and 4 weeks of treatment. The mean total IPSS and the mean symptom scores for weak stream and nocturia were significantly decreased after only 1 week of treatment, while the mean scores for emptying, frequency, and urgency were significantly decreased after 2 weeks of treatment. However, the mean scores for intermittency and hesitancy did not decrease significantly at any time during treatment. Regarding objective parameters, the mean Qmax was significantly improved after 1 week of treatment, but the mean prostatic volume remained almost unchanged after 4 weeks. In conclusion, short-term terazosin therapy not only improved Qmax but also alleviated symptoms including irritative symptoms. (J Nippon Med Sch 2001; 68: 181—185)

Key words: prostate, benign prostatic hyperplasia, clinical effect, terazosin

Introduction

Lower urinary tract symptoms (LUTS) secondary to symptomatic benign prostatic hyperplasia (BPH) are common in elderly men. BPH has both a static (anatomical) component caused by the enlarged prostate gland and a dynamic component related to increased smooth muscle tone in the prostatic urethra secondary to noradrenaline released from sympathetic nerve endings acting on the α 1-adrenoceptor (AR). α 1-AR antagonists (α 1-blockers) can produce a significant improvement in symptoms and urine flow in patients with LUTS due to BPH by reducing dynamic obstruction. Therefore, α 1-blockers have become a first-line option among various medical therapies. Terazosin is one of the most widely used and investigated α 1-blockers for the management of mild to moderate LUTS related to BPH in Japan[1-8]. However, the changes in obstructive and irritative symptoms and objective parameters after 1 week of treatment have not been widely determined in Japan. Evaluating what kind of symptoms an α 1-blocker improves after 1 or 2 weeks of treatment is practically very helpful when selecting one α 1-blocker to be administered for new-visiting outpatients with various symp-

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Table 1 IPSS questionnaire scores for benign prostatic hyperplasia

Question	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	About always
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating ? (Incomplete emptying)	0	1	2	3	4	5
2. Over the past month, how often have you had to urinate again less than two hours after you finished urinating ? (Frequency)	0	1	2	3	4	5
3. Over the past month, how often have you found you stopped and started again several times when you urinated ? (Intermittency)	0	1	2	3	4	5
4. Over the past month, how often have you found it difficult to postpone urination ? (Urgency)	0	1	2	3	4	5
5. Over the past month, how often have you had a weak urinary stream ? (Weak stream)	0	1	2	3	4	5
6. Over the past month, how often have you had to push or strain to begin urination ? (Hesitancy)	0	1	2	3	4	5
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning ? (Nocturia)	none	1 time	2 times	3 times	4 times	5 or more times
						Total IPSS = sum of questions (subscores) 1 to 7

toms. Therefore, we assessed the clinical effects of terazosin in patients with BPH by measuring the changes in symptoms and peak flow rate at 1, 2 and 4 weeks of treatment compared with those at baseline.

Materials and Methods

Thirty patients aged 52 to 83 years (mean: 69.2 years), with normal blood pressure and LUTS due to BPH who had not received any prior treatment for their symptoms were enrolled in the present study. Criteria for enrollment included: (1) a total International Prostatic Symptom Score (IPSS) (**Table 1**) of 10 or more, or an IPSS of 3 or more for at least one symptom, and (2) a peak flow rate (Qmax) of 15 m*l*/second (s) or less, or an average flow rate of 7.5 m*l*/s or less. Patients with urological disease except BPH, as well as those taking drugs that could affect voiding, were excluded. Informed consent was obtained from all of the patients. All 30 patients were given 2 mg/day of terazosin orally for 4 weeks, because the optimal dose of this drug had been set at 2 mg/day in a multicenter dose-finding study in Japan[3].

The total IPSS, the scores for obstructive symptoms (such as incomplete emptying, intermittency, weak stream, and hesitancy), the scores for irritative symptoms (such as frequency, urgency and nocturia), and the Qmax value were compared with the baseline data at 1, 2, and 4 weeks after the start of administration. Prostatic volume was estimated by transrectal ultrasonography and evaluated before treatment and after 4 weeks of treatment. Safety was assessed at baseline and at 1, 2, and 4 weeks after treatment to check whether this treatment could be continued. Statistical analysis was performed using Wilcoxon's paired test and $p < 0.05$ was considered to indicate a significant difference.

Results

1. Symptoms (Fig. 1)

(1) Obstructive symptoms

The mean (±SD) total IPSS was 17.8±8.1, before treatment. It decreased significantly to 14.7±7.2 after 1 week of treatment, and decreased further to 13.8±6.7 after 2 weeks and 12.5±7.4 after 4 weeks. The

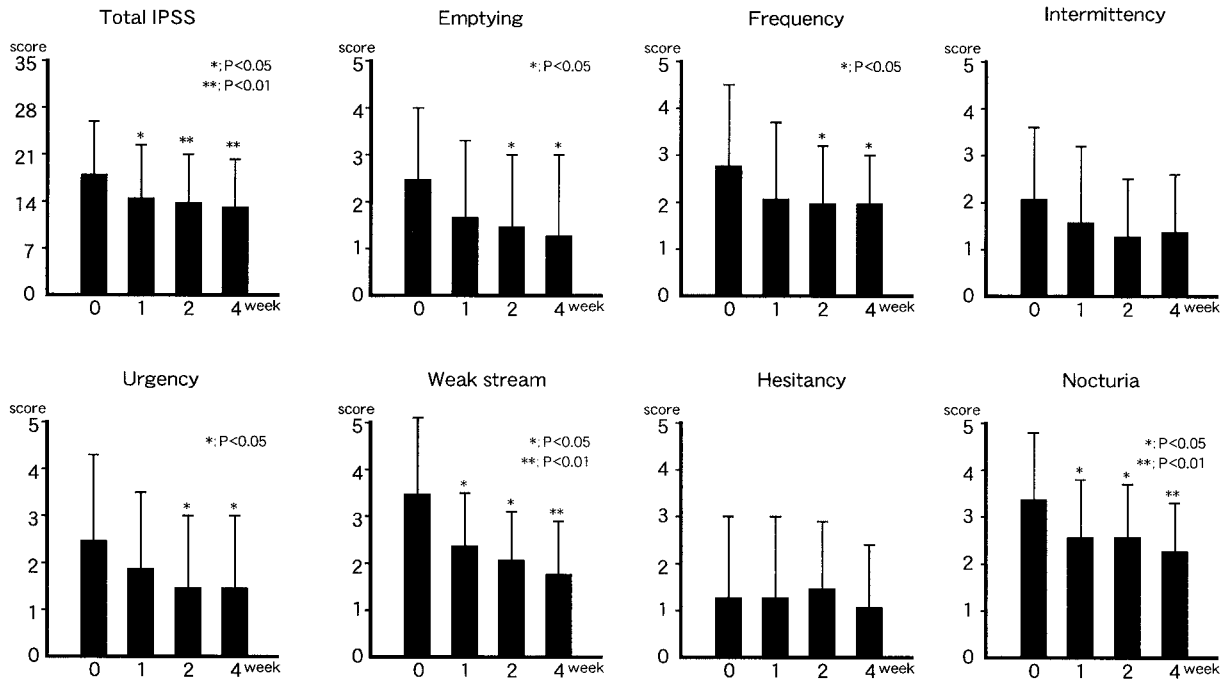

Fig. 1 The mean total IPSS and the mean scores for weak stream and nocturia were significantly decreased after only 1 week of treatment. The mean scores for emptying, frequency, and urgency were significantly decreased after 2 weeks. However, the mean scores for intermittency and hesitancy were not decreased significantly by treatment.

mean (±SD) score for emptying was 2.5±1.5 before treatment. It decreased significantly to 1.5±1.5 after 2 weeks of treatment and remained stable at 1.5±1.5 after 4 weeks. The mean baseline score for weak stream was 3.5±1.6, and this showed a significant decrease to 2.4±1.2 after 1 week of treatment and to 2.1±1.1 after 2 weeks, with a further decrease to 1.8±1.1 after 4 weeks. In contrast, the mean scores for intermittency and hesitancy did not decrease significantly during treatment.

(2) Irritative symptoms

The mean baseline scores for frequency and urgency were 2.8±1.8 and 2.5±1.9, respectively, and these scores decreased significantly to 2.0±1.2 and 1.5±1.5 after 2 weeks of treatment, and subsequently remained stable at 2.0±1.0 and 1.5±1.5 after 4 weeks. The mean baseline score for nocturia was 3.4±1.4. It showed a significant decrease to 2.6±1.2 after 1 week of treatment, remained at 2.6±1.1 after 2 weeks, and then decreased further to 2.3±1.1 after 4 weeks.

2. Objective parameters (Fig. 2)

The mean (±SD) Qmax showed a significant increase from 8.6±4.0 m*l*/s at baseline to 10.8±5.3 m*l*/s after 1 week of treatment. It improved further to 12.4±6.2 m*l*/s after 2 weeks, and then remained stable at 12.5±4.5 m*l*/s after 4 weeks. The baseline prostatic volume was 30.6±13.1 cm^3 (mean±SD) and it showed minimal change after 4 weeks of treatment (30.0±14.2 cm^3).

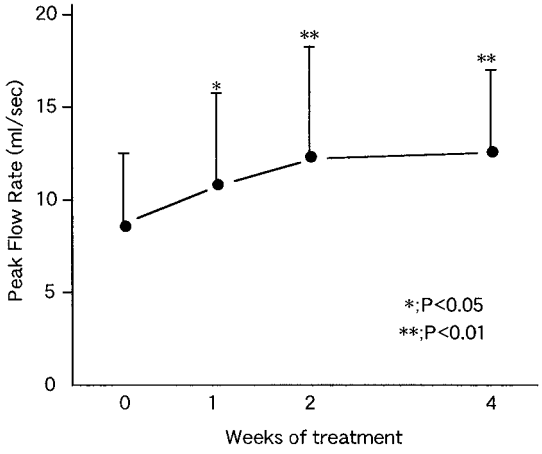

Fig. 2 The mean peak flow rate (Qmax) was significantly increased after 1 week of treatment, and it improved further after 2 and 4 weeks.

Discussion

Until recently, the treatment for patients with BPH has usually been surgical, but medicinal treatment has become available with the development of α 1-blockers such as terazosin, tamsulosin, and urapidil. However, the changes in obstructive and irritative symptoms and objective parameters after 1 week of treatment have not been widely determined in Japan. Therefore, we prospectively assessed the clinical effects of terazosin in Japanese patients with LUTS due to BPH based on the changes in symptoms and Qmax after 1, 2, and 4 weeks of treatment compared with those at baseline. Placebo controlled study is necessary to evaluate the clinical effect of α 1-blockers. However, a placebo group could not be included in the present study, because it was difficult to from the practical point of view to select a placebo group from our general outpatient population.

Lepor and others[9] investigated the effect of terazosin on BPH in a randomized placebo-controlled multicenter study. Only a dose of 10 mg/day produced a significant difference of Qmax compared with placebo after 6 weeks of treatment. However, the patients in the present study exhibited a significant improvement in Qmax after only 1 week of treatment at 2 mg/day. Nakamura and others[2] also investigated the effect of terazosin (2 mg/day) on Qmax for 1 week of treatment and reported that a significant improvement in Qmax was showed after only 2 days of treatment. Thus, the dose of terazosin and the duration of treatment necessary to achieve improvement seem to be lower and earlier in Japan than in Europe, which may be related to the lower dose of the drug required to maintain an effective blood level in Japanese compared with caucasians.

Concerning subjective symptoms, as Eri and others[10] reported, the average ratio of the percent improvement in obstructive versus irritative symptoms seems to be 2.0 with α-blocker therapy, indicating a better response for obstructive symptoms. Lepor and others[11] reported that 5 mg/day of terazosin improved the mean obstructive and irritative symptom scores by 63% and 35%, respectively. In a multicenter, randomized, double-blind, placebo-controlled Canadian study, Elhilali and others[12] found that the mean improvement in the irritative symptom score was less marked and was only significant after 6 weeks of administration. Conversely, terazosin significantly improved all three irritative symptoms after 2 weeks of treatment in the present study. Some clinical observations[13,14] also support the concept of a direct effect of α-blockers on the bladder, such as a more marked decrease in irritative than in obstructive symptoms and the fact that the irritative symptoms are often relieved rapidly. Furthermore, in small uncontrolled studies, α 1-blockers have been shown to increase bladder capacity and decrease uninhibited detrusor contraction in patients with detrusor hyperreflexia[15], as well as abolishing detrusor instability in BPH patients[16].

Although α 1-blockers lower blood pressure, these changes are smaller in patients with normotension than in those with hypertension. Also, for the normotensive patients in the present study terazosin at a daily dose of 2 mg did not appear vasodilatory events during the 4 weeks of treatment despite the no dose-titration phase, which makes it difficult to evaluate a correlation between change in blood pressure and clinical improvements.

In conclusion, we found that terazosin significantly improved not only Qmax after 1 week of treatment but also all irritative symptoms after 2 weeks without adverse events. We previously found that tamsulosin, another α 1-blocker, could only improve nocturia among the irritative symptoms after 4 weeks of treatment[17]. Therefore, in Japanese men with LUTS due to BPH, terazosin (2 mg/day) therapy may improve irritative symptoms more rapidly than tamsulosin. From these findings, terazosin may be more suitable for new outpatients with BPH whose main complaints are irritative rather than obstructive symptoms.

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