—Originals—

The short-term effects of tamsulosin in Japanese men with benign prostatic hyperplasia

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Abstract

We evaluated the short-term effects of tamsulosin in treating benign prostatic hyperplasia. Twenty-seven patients, aged 57 to 86 years (mean 68.4), complaining of obstructive urinary symptoms who had received no previous treatment for such symptoms were orally administered 0.2 mg of tamsulosin for 4 weeks. Symptoms (total AUA symptom score and AUA symptom subscores) and objective parameters including peak and average flow rate, and post-void residual urine rate were evaluated before and after 1, 2 and 4 weeks of treatment. The mean total AUA symptom score and the mean AUA symptom subscores for incomplete emptying and weak stream were significantly decreased after only 1 week of treatment. The mean AUA symptom subscores for intermittency, urgency and nocturia were significantly decreased after 4 weeks of treatment. The mean AUA symptom subscores for frequency and hesitancy were unchanged after 4 weeks of treatment. The mean peak and average flow rate, and post-void residual urine rate were significantly improved after only 1 week of treatment. In conclusion, tamsulosin improved not only objective parameters but also symptoms only 1 week after the start of treatment. (J Nippon Med Sch 1999; 66: 382—387)

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

Introduction

Benign prostatic hyperplasia (BPH) is the most common cause of bladder outlet obstruction (BOO) in men older than 40 years of age. One mechanism of BOO due to BPH is dynamic urethral obstruction caused by noradrenaline released from sympathetic nerve endings. α_1-adrenoceptor antagonists are correspondingly widely used in the management of BPH for patients with mild to moderate symptoms who do not require surgery, or for those awaiting surgery.

Several selective α_1-adrenoceptor antagonists such as doxazosin and terazosin have been widely investigated[1-4]. They have a rapid onset of action and are likely to produce therapeutic results within a few weeks. Tamsulosin is also a selective α_1-adrenoceptor antagonist, but differs from the above agents in the following respect: tamsulosin has greater selectivity for α_{1A}-than for α_{1B}-adrenoceptors[5].

The efficacy of tamsulosin for the treatment of BPH has already been well documented[6-9]. Lepor[8], and Narayan and others[9] reported that tamsulosin (0.4 mg/day) had a rapid onset of action, based on improvement in total AUA symptom score (**Table 1**) and peak urinary flow rate (Qmax) in a phase III multicenter placebo-controlled study in the United States. However, no clinical findings after 1 week of treatment with tamsulosin have previously been available from Japan. We therefore assessed the short-term effects of tamsulosin in patients with BPH by measuring the improvement in sympton and objective parameters 1, 2 and 4 weeks after the start of treatment with it.

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Table 1 AUA-7 Symptom index 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	Almost 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 urinate from the time you went to bed at night until the time you got up in the morning? (Nocturia)	none	1 time	2 time	3 time	4 time	5 or more times

Total AUA Symptom Score = sum of questions (subscores) 1 to 7

Material and Methods

Patients complaining of obstructive urinary symptoms due to BPH who had received no treatment for BPH such as medication, TURP or minimally invasive surgery were enrolled in the present study.

Twenty-seven patients, aged 57 to 86 years (mean 68.4) who met the following criteria for inclusion established for this study: 1) total AUA symptom score ≧10, or one of the AUA symptom subscores ≧3, 2) Qmax ≦15 m*l*/second (s) or average flow rate ≦7.5 m*l*/s, were orally administered 0.2 mg of tamsulosin for 4 weeks. Patients with prostatic cancer, bladder neck constriction, bladder stones, bladder diverticulum, urethral stenosis, neurogenic disorders or who were being administered drugs affecting voiding function were excluded. Informed consent was obtained from all patients.

Symptoms (total AUA symptom score and AUA symptom subscores) and objective parameters including Qmax, average flow rate, and post-void residual urine (PVR) rate [PVR volume/(voided volume + PVR volume) ×100%] were evaluated before and 1, 2 and 4 weeks after the start of administration.

Prostatic volume was estimated before and after treatment by transrectal ultrasonography, using the following formula: prostatic volume (cm^3) = $\pi/6 \times$ prostatic width (cm) ×height (cm) ×length (cm).

Statistical analysis was performed using Wilcoxon's paired and unpaired tests and $p<0.05$ was considered to indicate a significant difference.

Results

1. Symptoms (Fig. 1)

The mean (±standard deviation (SD)) total AUA symptom score at baseline was 17.4±8.2, and significantly decreased to 13.4±6.6 after 1 week of treatment, 11.9±6.3 after 2 weeks and 10.3±7.0 after 4 weeks. The mean (±SD) AUA symptom subscore for incomplete emptying at baseline was 2.4±2.1, and significantly decreased to 1.6±1.6 after 1 week of treatment, remained stable at 1.7±1.7 after 2 weeks, and further decreased to 1.3±1.3 after 4 weeks. The mean (±SD) AUA symptom subscore for weak steam at baseline was 4.0±1.4, and significantly decreased to 2.9±1.8 after 1 week of treatment, further decreased

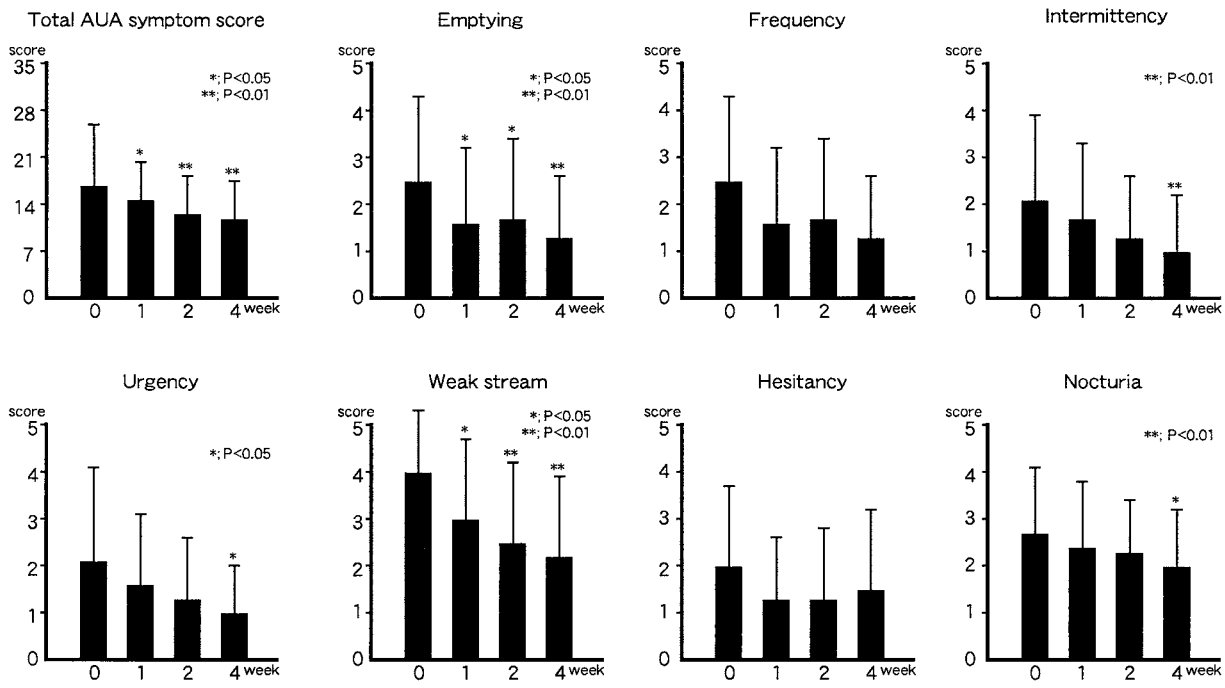

Fig. 1 The mean total AUA symptom score, and the mean AUA symptom subscores for incomplete emptying and weak stream at baseline were significantly decreased after 1 week of treatment. The mean AUA symptom subscores for intermittency, urgency and nocturia at baseline were significantly decreased after only 4 weeks of treatment. The mean AUA symptom subscores for frequency and hesitancy at baseline were decreased (but not to significant extents) after 4 weeks of treatment

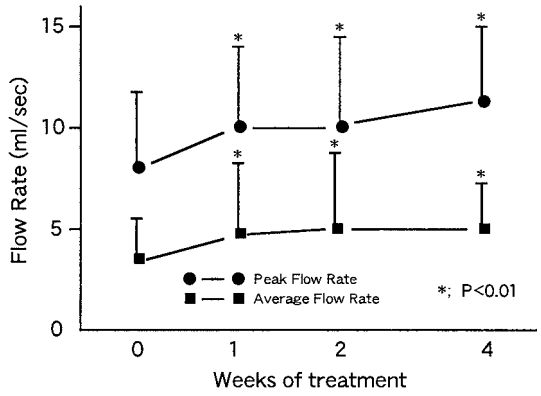

Fig. 2 The mean peak flow rate and average flow rate at baseline were significantly improved after 1 week of treatment, and improved further after 2 and 4 weeks.

to 2.5 ± 1.8 after 2 weeks, and was stable at 2.1 ± 1.8 after 4 weeks. The mean (± SD) AUA symptom subscores for intermittency, urgency and nocturia at baseline were 2.1 ± 1.8, 2.1 ± 2.0 and 2.7 ± 1.4, respectively, and significantly decreased to 1.0 ± 1.2, 1.0 ± 1.0 and 2.0 ± 1.2 after 4 weeks of treatment. The mean (± SD) AUA symptom subscores for frequency and hesitancy at baseline were 2.1 ± 1.8 and 2.0 ± 1.7, respectively, and decreased (but not to significant extents) to 1.8 ± 1.4 and 1.5 ± 1.7 after 4 weeks of treatment.

2. Objective signs

The mean (± SD) Qmax significantly improved from 7.8 ± 3.5 m*l*/second(s) at baseline to 9.8 ± 3.5 m*l*/s after 1 week of treatment, and improved further to 10.0 ± 3.8 m*l*/s after 2 weeks, and 11.1 ± 3.5 m*l*/s after 4 weeks (**Fig. 2**). The mean (± SD) average flow rate significantly improved from 3.5 ± 2.1 m*l*/s at baseline to 4.8 ± 3.5 m*l*/s after 1 week of treatment, and improved further to 5.0 ± 3.8 m*l*/s after 2 weeks, and 4.9 ± 2.4 m*l*/s after 4 weeks (**Fig. 2**). The mean (± SD) PVR rate (%) at baseline was 30.9 ± 32.3 and significantly decreased to 10.5 ± 12.1 after 1 week of treatment, and stabilized at 8.8 ± 12.7 after 2 weeks, and 10.5 ± 12.1 after 4 weeks (**Fig. 3**). The mean (± SD) prostatic volume (cm^3) at baseline (34.6 ± 15.1) remained nearly unchanged after 4 weeks of treatment (33.0 ± 14.8).

Table 2 Pretreatment parameters in groups A and B divided by fourth-week results

Parameters	Group A (n = 15)	Group B (n = 12)	p Value
Peak flow rate (ml/s)	8.1 ± 4.4	9.3 ± 2.3	N.S.
Average flow rate (ml/s)	3.7 ± 2.4	6.0 ± 2.1	$p < 0.05$
Residual urine rate (%)	42.5 ± 33.9	8.1 ± 9.3	$p < 0.05$
Total AUA symptom score	21.8 ± 5.7	13.6 ± 8.0	$p < 0.05$
Prostatic volune (cm^3)	45.0 ± 15.0	25.0 ± 13.0	$p < 0.05$
Decrease in total AUA symptom score after one week of treatment	9.7 ± 7.6	1.1 ± 3.3	$p < 0.005$

Group A: Total AUA symptom score decreased by 25% or more from pretreatme-n t to 4th week of treatment, Group B: Total AUA symptom score decreased by less than 25% from pretreatment to 4th week of treatment, N.S.: Not significant.

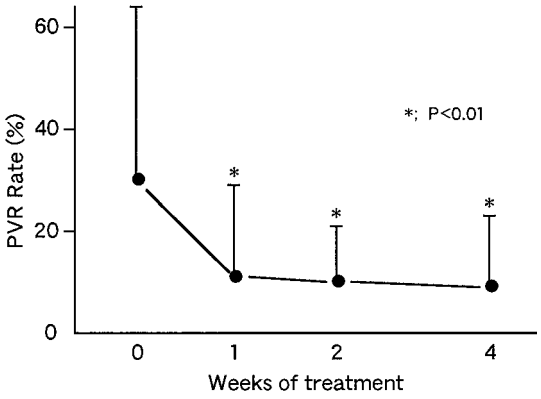

Fig. 3 The mean post-void residual urine (PVR) rate (%) at baseline was significantly decreased after 1 week of treatment, and stabilized after 2 and 4 weeks.

3. Pretreatment parameters predicting improvement of symptoms after 4 weeks of treatment (Table 2)

Pretreatment values of various parameters for patients were divided into two groups according to the degree of improvement in symptoms after 4 weeks of treatment. Fifteen patients whose total AUA symptom score was decreased by 25% or more from baseline after 4 weeks of treatment and 12 patients whose total AUA symptom score was decreased less than 25 %from baseline after 4 weeks of treatment were defined as good responders (Group A) and poor responders (Group B), respectively. The mean (± SD) total AUA symptom score at baseline for group A (21.8 ± 5.7) was significantly higher than that for group B (13.6 ± 8.0). The mean (± SD) Qmax (m*l*/s) at baseline for group A (8.1 ± 4.4) did not differ from that for group B (9.2 ± 2.3), whereas, the mean (± SD) average flow rate (m*l*/s) at baseline for group A (3.7 ± 2.4) was significantly lower than that for group B (6.0 ± 2.1). The mean (± SD) PVR rate (%) at baseline for group A (42.5 ± 33.9) was significantly higher than for group B (8.1 ± 9.3). The mean (± SD) prostatic volume (cm^3) at baseline for group A (45.0 ± 15.0) was significantly larger than that for group B (25.0 ± 13.0). The mean total AUA symptom score for group A had already significantly decreased after 1 week of treatment.

Discussion

Tamsulosin, a superselective α_{1A}-adrenoceptor antagonist, has been extensively studied for treatment of BPH. Large clinical trials in the United States and Europe have provided evidence that tamsulosin is effective in relieving urinary symptoms and improving Qmax, and that it has a rapid onset of action[7–9]. However, no clinical findings after 1 week of treatment with tamsulosin have previously been available from Japan. We therefore prospectively assessed the short-term effects of tamsulosin in patients with BPH based on symptom and objective parameters after 1, 2 and 4 weeks of treatment.

Lepor[8], and Narayan and others[9] reported that patients treated with tamsulosin at doses of 0.4 or 0.8 mg/day exhibited significant improvement in total AUA symptom score after only 1 week of treatment, compared with placebo-treated patients. In the present study, patients treated with tamsulosin at 0.2 mg/day exhibited significant improvement in total AUA symptom score, compared with baseline score, by 1

week after treatment initiation. AUA obstructive subscores other than hesitancy were significantly better than baseline values at week 4 of treatment. However, the only AUA obstructive subscores with significant improvement at week 1 of treatment were incomplete emptying and weak stream, and intermittency improved significantly after 4 weeks of treatment. These findings show that tamsulosin does not improve all AUA obstructive subscores in a short period of time.

Concerning irritative symptoms, subscores for urgency and nocturia were improved significantly, while no improvement was noted in frequency, at week 4 of treatment. In a placebo-controlled study of tamsulosin at doses of 0.4 and 0.8 mg/day, Narayan and others[9] reported that no improvement of irritative symptoms was observed in patients in the 0.4 mg/day group at any time during the treatment period, but was observed in patients in the 0.8 mg/day group after 5 weeks of treatment and later. Rapid improvement of irritative symptoms may be more difficult to obtain than that of obstructive symptoms with tamsulosin.

On the other hand, as Lepor[8], and Narayan and others[9] reported, tamsulosin promptly improved objective findings: Qmax, average flow rate and PVR rate were significantly better than baseline values after 1 week of treatment or later.

Regarding prediction of the effectiveness of α_1 blockers for patients with BPH before treatment, Lepor and others[10] reported that prostatic volume, Qmax, PVR and type of symptoms at baseline were not indicative of therapeutic effects of terazosin. However, there have been studies demonstrating that patients with low flow rate, those with relatively severe symptoms, and those with a predominance of obstructive symptoms tend to respond well to α_1 blockers[11-14]. We also attempted to find predictive indicators of therapeutic effects of tamsulosin by evaluating differences in baseline characteristics between good responders and poor responders. From the present study we found that good responders had lower average flow rate, higher PVR rate, higher total AUA symptom score, and larger prostatic volume at baseline than did poor responders. Moreover, the mean total AUA symptom score for good responders was already significantly decreased after only 1 week of treatment.

In conclusion, tamsulosin improved symptoms and objective parameters including Qmax, average flow rate, and post-void residual urine rate after only 1 week of treatment. Patients with relatively severe symptoms, and those with a predominance of obstructive symptoms, and those with low average flow rate tended to respond well to tamsulosin in a short period of time.

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