

Original article

# Beneficial Effect of Increasing the Dose of Tamsulosin to 0.4 mg in Japanese Patients with Benign Prostatic Hyperplasia

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## Abstract

**Objective:** Tamsulosin is often administered at a dose of 0.2 mg in Japan, Korea, and elsewhere in Asia, while a dose of 0.4 mg is more common in the West. In order to determine the higher dose might also be appropriate in the North-East Asian setting, we studied whether the effect of increasing the dose to 0.4 mg in Japanese patients who had dysuria associated with benign prostatic hyperplasia.

**Patients and Methods:** Twenty-two cases with a voiding volume  $\geq 100$  ml assessed by uroflowmetry out of 31 patients with benign prostatic hyperplasia and an IPSS (International Prostate Symptom Score)  $\geq 8$  whose symptoms were controlled with 0.2 mg of tamsulosin were entered into this study. We evaluated IPSS and QOL (quality of life) score, urinary flow parameters and residual urine volume before and 4 weeks after increasing the dose of tamsulosin.

**Results:** Statistical analyses performed using the Wilcoxon test showed no significant alteration in IPSS total score or QOL score with the increased dose, but Qmax (maximum urinary flow rate) improved from  $10.1 \pm 5.5$  ml/s to  $12.1 \pm 6.5$  ml/s ( $p = 0.013$ ), and residual urine volume improved from  $37.6 \pm 26.4$  ml to  $22.2 \pm 24.3$  ml ( $p = 0.012$ ). Two of the 31 patients complained of new symptoms; 1 complained of breast pain and the other complained of dizziness.

**Conclusions:** From the lack of side effects of more than moderate grade in the present study, increasing the dose of tamsulosin might be recommended before switching patients to other drugs.

**Key words:** alpha-1 blockers, benign prostatic hyperplasia, tamsulosin

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## Introduction

Benign prostatic hyperplasia (BPH) is a common disease in elderly men. Pharmacological therapy with alpha-1 adrenoceptor antagonists is considered to be the first-line treatment, for example, treatment with tamsulosin, which selectively blocks alpha-1a adrenoceptors. For lower urinary tract symptoms associated with benign prostatic hyperplasia, such  $\alpha 1$ -blockers are generally used as the initial treatment, tamsulosin, naftopidil and silodosin being the examples currently most widely used in Japan. If first-line therapy with tamsulosin, for example, does not achieve a satisfactory response, either a switch to another  $\alpha 1$ -blocker or an increase in the dose may be considered. Regarding the latter, although Japanese studies have been conducted to assess the effectiveness of dose increase in the same patients, the numbers involved were very low<sup>1,2)</sup>.

While Tamsulosin is most commonly administered at a dose of 0.4 mg in the West, 0.2 mg is more often applied in Japan, Korea, and elsewhere in Asia, to take into account body size. However, this may influence efficacy, and therefore, the present study of the effects of increasing the dose to 0.4 mg in Japanese patients who had dysuria associated with benign prostatic hyperplasia was conducted.

## Patients and Methods

From August 2008 to December 2009, 31 patients with BPH who had been treated with 0.2 mg of Tamsulosin for more than 4 weeks and had an IPSS of 8 or more agreed to an increase in the dose and were prospectively enrolled in the present study. A total of 22 patients with a voiding volume  $\geq 100$  ml assessed by uroflowmetry were ultimately evaluated. The patients' ages ranged from 63 to 82 years (mean 71.8). BPH was diagnosed from clinical history, subjective and objective symptoms, digital rectal examination

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**Table 1** The characteristics of the patients before increasing the dosage (22 cases with a voiding volume  $\geq 100$  ml by uroflowmetry)

	Mean $\pm$ SD	Minimum	Maximum
Age	71.8 $\pm$ 6.5	63	82
Prostate volume (ml)	41.6 $\pm$ 40.2	10	167
Total IPSS score	14.7 $\pm$ 5.7	8	27
Voiding symptoms subscore	5.7 $\pm$ 3.5	1	12
Weak stream	2.7 $\pm$ 1.4	1	5
Intermittency	1.5 $\pm$ 1.5	0	5
Straining	1.7 $\pm$ 1.6	0	5
Storage symptom subscore	6.2 $\pm$ 3.7	0	12
Day time frequency	2.9 $\pm$ 1.5	0	5
Night time frequency	2.9 $\pm$ 1.4	0	5
Urgency	1.6 $\pm$ 1.5	0	5
Sense of residual urine	2.2 $\pm$ 1.7	0	5
QOL	4.0 $\pm$ 1.1	2	6
Qmax (ml/s)	10.1 $\pm$ 5.5	3.8	29.6
Residual urine volume (ml)	37.6 $\pm$ 26.4	0	100

IPSS, International Prostate Symptom Score; QOL, quality of life; Qmax, maximum urinary flow rate. The minimum value for prostatic volume was 10 ml. This case showed middle lobe enlargement.

and transabdominal ultrasonography to determine the prostate volume. Any patients with other conditions causing urinary symptoms or a reduced urinary flow rate (e.g., cystitis, prostatitis, lithiasis, urothelial malignancies, a neurogenic bladder, a history of surgical treatment for BPH, drug treatment affecting urination such as anticholinergic agents, and urethral stricture) were excluded. The baseline characteristics of the patients are shown in Table 1.

All subjects received an increase in the dose of tamsulosin from 0.2 mg to 0.4 mg, but this was discontinued, reduced or changed to another drug if adverse events were encountered. Urinary symptoms were assessed using the IPSS and a QOL score. These two, together with uroflow variables (maximum urinary flow rate [Qmax] and postvoiding residual urine volume), were assessed before and 4 weeks after increasing the dose. Postvoiding residual urine was measured mainly using transabdominal ultrasonography. The voiding symptom subscores (sum of the scores for question 1, emptying; 3, intermittency; 5, weak stream; and 6, hesitancy) and the storage symptom subscores (sum of the scores for question 2, voiding frequency; 4, urgency; and 7, nocturia), together with the total IPSS score, were assessed.

Changes with the increased dosage for each variable were analyzed using the Wilcoxon signed-rank test, with a  $p$  value  $< 0.05$  considered significant.

## Results

### *Changes of subjective and objective symptoms by increased dosage of tamsulosin*

No change in the IPSS total score or QOL scores was apparent between the two time points or when each category of the IPSS was separately evaluated (Figure 1).

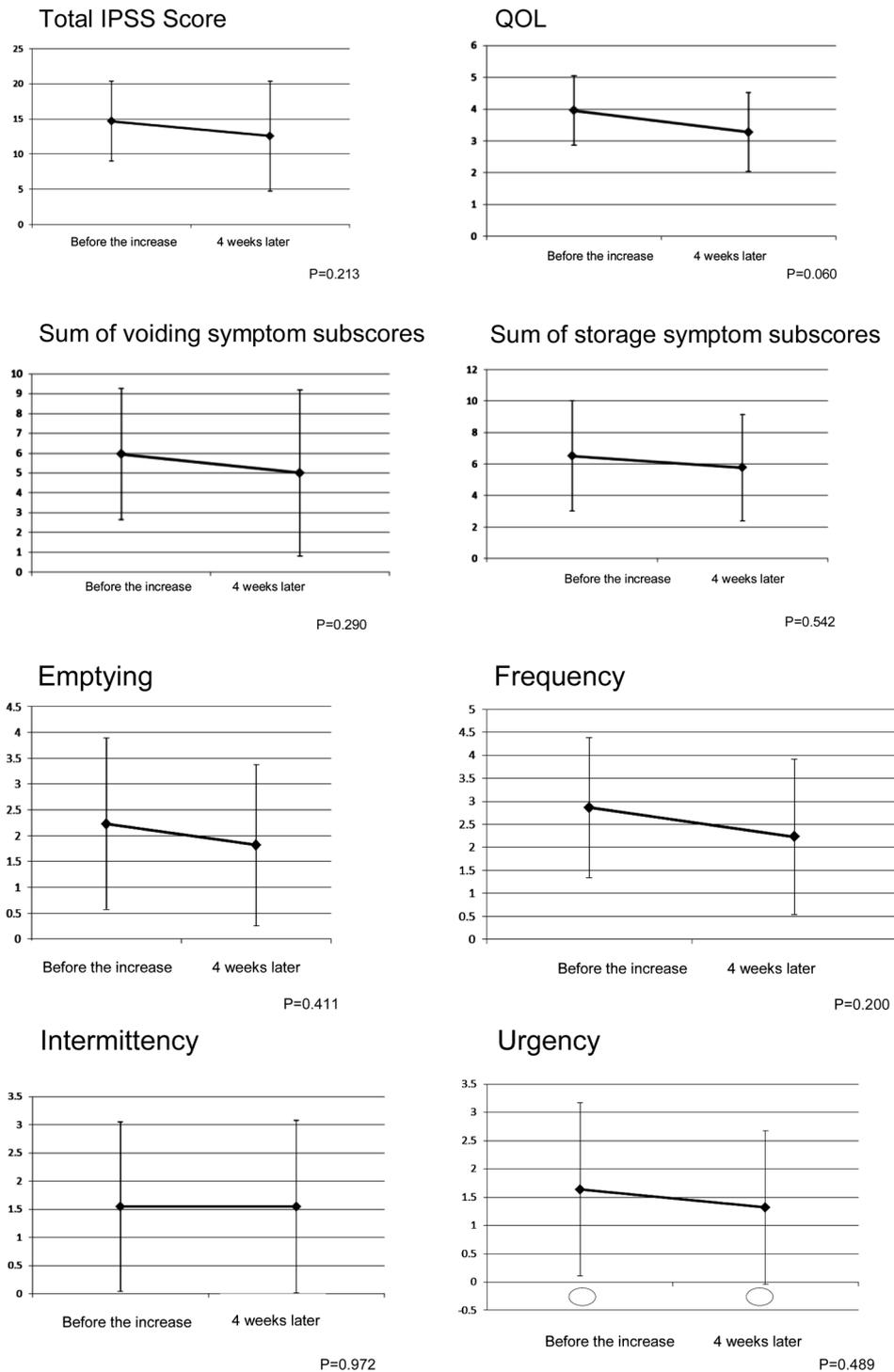
Regarding objective symptoms, Qmax improved from  $10.1 \pm 5.5$  ml/s to  $12.1 \pm 6.5$  ml/s ( $p = 0.013$ ). Moreover, mean residual urine volume decreased from  $37.6 \pm 26.4$  ml to  $22.2 \pm 24.3$  ml ( $p = 0.012$ ) (Figure 2).

### *Adverse events*

Two of the 22 patients dropped out from the tamsulosin therapy because of new adverse events, one for breast pain, and the other for dizziness. The patient with breast pain also complained of breast swelling, and the symptoms were thought to be mild gynecomastia. Both the breast pain and dizziness symptoms were disappeared soon after stopping the tamsulosin therapy.

## Discussion

The present study showed that with a Japanese group of BHP patients, increase in the dosage of tamsulosin from 0.2 to 0.4 mg did not lead to adverse side effects of more than moderate grade and was associated with improvement in both residual urine volume and Q max. We previously re-



**Figure 1** Change in IPSS category after increasing the dosage.

ported that increasing the dose of naftopidil to 75 mg led to significant improvement of the nocturia score in patients for whom the effect of a 50 mg dose was insufficient<sup>3</sup>.

With regard to tamsulosin, the standard dose is specified as 0.2 mg in the dosage and administration instructions in Japan, but this can be increased or decreased according

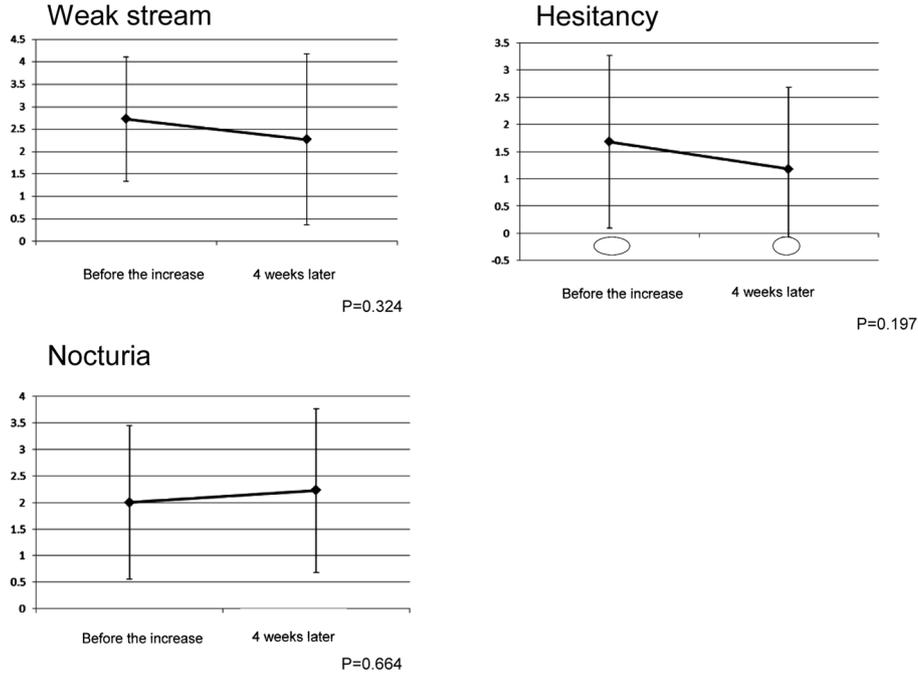


Figure 1 continued

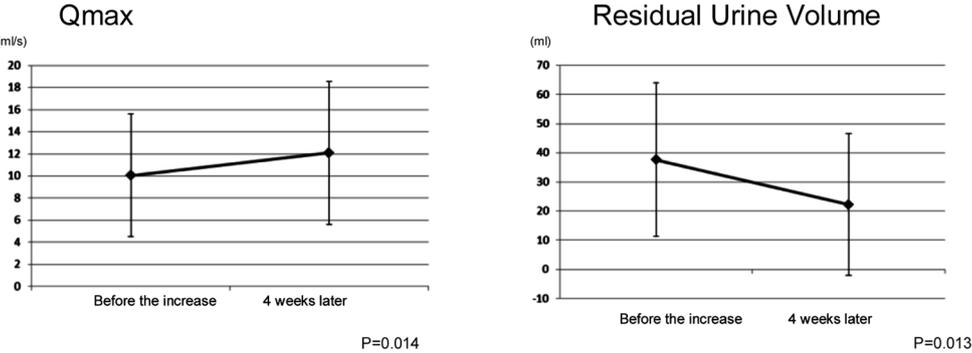


Figure 2 Change in Qmax, maximum urinary flow rate and residual urine volume after increasing the dosage.

to the age and symptoms of the patient. However, only Kobayashi et al. have previously reported a study on the effect of raising the dose to 0.4 mg in the same patients, and their study was published in 2009<sup>4)</sup>.

While significant improvement after increasing the dose of tamsulosin was noted for subjective parameters, such as the total scores of IPSS and QOL, after 8 weeks, no significant improvement of objective parameters was observed, in contrast to our study. The difference might be related to our shorter treatment period.

In case of treatment with an increased dose of tamsulosin, there was concern about possible dizziness and light-

headedness due to postural hypotension (common adverse effects of  $\alpha$ 1-blockers), but such effects occurred only in one patient.

In conclusion, it was considered that increasing the dose of tamsulosin is worth trying before switching to  $\alpha$ 1-blockers.

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