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Comparison of Tamsulosin and Finasteride for Lower Urinary Tract Symptoms Associated with Benign Prostatic Hyperplasia in Korean Patients

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Tamsulosin (0.2 mg) and finasteride (5 mg) once daily for 24 weeks were compared in a single-blind, randomized study as initial treatments for lower urinary tract symptoms associated with benign prostatic hyperplasia (BPH) in 205 Korean patients. Symptom and quality of life (QOL) assessment by the International Prostatic Symptom Score (I-PSS), maximum urinary flow rate (Q_{max}) and adverse events were analysed at 4 weeks and 24 weeks. On intention-to-treat analysis, both drugs showed similar efficacy at endpoint (decreased I-PSS, increased Q_{max} and improved QOL score; 34.7%, 23.9% and 34.1% for tamsulosin, and 30.5%, 22.2% and 23.1% for finasteride, respectively). However, tamsulosin produced significant improvements in I-PSS and Q_{max} at 4 weeks compared with finasteride (17.6% versus 10.0% and 10.9% versus 3.1%, respectively), and a superior QOL score improvement during the study. Adverse events were observed significantly more frequently among finasteride than tamsulosin patients (23 versus four). Both were equally effective in long-term treatment of urinary outflow obstruction symptoms associated with BPH in Korean patients, but tamsulosin was more effective for short-term treatment, with a better safety profile.

KEY WORDS: Tamsulosin; Finasteride; Benign prostatic hyperplasia; Korea; Lower urinary tract symptoms

Introduction

Benign prostate hyperplasia (BPH) is a common condition among elderly men and its prevalence increases with age.[1 – 5] BPH produces bothersome lower urinary tract symptoms (LUTS) that significantly impair the quality of life of these patients.[6] Traditionally, surgical intervention or watchful waiting were the only accepted treatment options for BPH. However, pharmacological therapies including α_1-adrenoceptor antagonists such as tamsulosin, terazosin, doxazosin and alfuzosin, as well as the 5α-reductase inhibitor, finasteride, are now used as first-line treatment modalities for this disorder in patients with mild-to-moderate symptoms.

Various studies with α_1-adrenoceptor antagonists have all shown comparable long-term improvements in symptom scores and urinary flow rates.[7 – 11] Among these

antagonists, tamsulosin possesses greater selectivity for α_1A-adrenoceptors than for α_1B-adrenoceptors.[12,13] This property results in tamsulosin being associated with minimal cardiovascular adverse events, such as postural hypotension, compared with other adrenoreceptor antagonists.[14,15] An alternative medical therapy for LUTS, finasteride has been found to reduce prostate size, which leads to improvement in symptoms and bladder outlet obstruction. Several reports have described its efficacy and safety in patients with BPH.[16 – 19]

Almost all reports evaluating the two agents in the management of LUTS have been undertaken in western countries, with little data available on their efficacy and safety in Asian men. Since the socio-economic, dietary and physical aspects of the Far East differ greatly from those of western countries, it is expected that the clinical aspects of BPH patients in this region would also differ from those in western countries.

This study was designed to compare the efficacy and safety of tamsulosin and finasteride in the treatment of lower urinary tract symptoms associated with BPH in a group of Korean patients.

Patients and methods

This 24-week, randomized, single-blind study was authorized by the Ethics Committee of Seoul National University Hospital. Patients were informed of the details of the study by their doctors, and their consent obtained before starting the study. Patients with moderate-to-severe symptomatic BPH were selected. BPH was diagnosed from patient history, symptoms, digital rectal examination and transrectal ultrasonic imaging. The Korean version of the International Prostatic Symptom Score (I-PSS) was used for assessment of symptoms and quality of life (QOL).[1,20] Patients aged 51 – 80 years, with a total I-PSS of > 8,[21] a maximum urinary flow rate (Q_{max}) of 5 – 15 ml/s and residual urine of < 150 ml/s were enrolled. Exclusion criteria included patients with: prostatic cancer; serum prostate-specific antibody (PSA) levels > 10 ng/ml; prostatitis; neurogenic bladder; bladder cancer; bladder stones; urethral strictures; neurological conditions that might interfere with normal voiding; and those with BPH who had undergone transurethral resection or experienced urinary retention. Also excluded were patients with marked disorders of other organs, such as cardiac, renal, or hepatic insufficiency. Patients were randomized into two groups, one receiving tamsulosin 0.2 mg and the other finasteride 5 mg once daily for 24 weeks. Efficacy and safety were measured every 4 weeks for all evaluable patients in both groups. The primary parameters for assessment of efficacy were changes in Q_{max}, and the total and QOL scores in I-PSS. Other efficacy parameters included prostate volume, which was assessed by ultrasonography. In addition, the number of patients with a clinically significant response to tamsulosin or finasteride treatment was determined, defined as those patients with a > 20% improvement over baseline in Q_{max}, or > 20% decrease in total I-PSS.[21] Adverse events considered to be possibly or probably related to study medications were recorded during the complete treatment period. Intention-to-treat (ITT) analysis was performed.

STATISTICAL ANALYSIS

Patient background characteristics among the two groups and differences in subjective and objective changes between the baseline and treatment periods were analysed using Student's *t*-test. Analysis of variance (ANOVA) and Duncan's multiple-range test were used to review inter- and intra-group differences. The appearance rate of adverse events between the groups was analysed by

Fisher's exact test. All statistics were analysed using the PC-SAS program (SAS Institute, Inc., Cary, NC, USA). Statistical differences were considered significant at $P < 0.05$.

Results

Two hundred and five patients were enrolled and randomized to the two treatment groups ($n = 103$ in the tamsulosin group, $n = 102$ in the finasteride group). Patient demographics and baseline characteristics for prostate volume and PSA levels are shown in Table 1. There were no differences in any patient background characteristics between the two groups. Fifty-nine patients (31 in the tamsulosin group, 28 in the finasteride group) were excluded from analysis or withdrew during the study. The reasons for exclusion and withdrawal are shown in Table 2.

The mean prostate volume measured by transrectal ultrasonography was decreased significantly at 24 weeks (25.7 ± 10.5 ml) compared with baseline (30.9 ± 13.7 ml) in the finasteride group ($P < 0.05$, paired Student's *t*-test).

EFFICACY

The efficacy data refer to the ITT population. I-PSS scores in the tamsulosin and finasteride groups were 19.9 ± 7.2 and 19.0 ± 7.2 during the pre-treatment stage, respectively. The scores at 4 weeks after treatment were 16.4 ± 7.9 and 17.1 ± 7.3 in the tamsulosin and finasteride groups, respectively. The

TABLE 1:
Baseline characteristics of patients with benign prostatic hyperplasia included in the comparative study of tamsulosin and finasteride

Characteristic	Tamsulosin	Finasteride
Age (years)	64.9 ± 6.8	64.4 ± 7.2
Weight (kg)	65.7 ± 6.6	66.1 ± 6.6
Height (cm)	167.7 ± 4.7	168.1 ± 4.1
Prostate volume (ml[a])	28.7 ± 13.1	30.9 ± 13.7
Prostate-specific antigen level (ng/ml)	1.8 ± 1.7	2.2 ± 2.1

Data expressed as mean ± SD.
Differences not significant for any comparison (Student's *t*-test).
[a]Estimated by transrectal ultrasonography.

TABLE 2:
Reasons for patient exclusions and withdrawals from the study

	Tamsulosin (*n*)	Finasteride (*n*)
Enrolled patients	103	102
Exclusion:		
Failure to return for follow-up	25	19
Withdrawal:		
Dissatisfaction	5	3
Adverse event	1	6
Total no. of exclusions and withdrawals	**31**	**28**

I-PSS scores improved significantly compared with baseline at 4 weeks after treatment in both groups ($P < 0.01$, paired *t*-test). There was a mean reduction of 3.5 (17.6%) on tamsulosin, and 1.9 (10.0%) on finasteride in I-PSS scores from baseline to evaluation at 4 weeks. The improvement in I-PSS scores at 4 weeks on tamsulosin was significantly superior to that on finasteride ($P < 0.05$, ANOVA and Duncan's multiple-range test; Table 3). The I-PSS scores at 24 weeks after treatment were 13.0 ± 7.1 and 13.1 ± 7.6 in the tamsulosin and finasteride groups, respectively. There was a mean reduction in I-PSS scores from baseline to I-PSS scores at 24 weeks of 6.9 (34.7%) on tamsulosin, and 5.8 (30.5%) on finasteride. These differences before and after treatment were significant in both groups ($P < 0.05$, paired *t*-test; Table 3). There were no significant differences in I-PSS scores between the two treatment groups at 24 weeks after treatment (ANOVA and Duncan's multiple-range test; Table 3).

Mean Q_{max} in the tamsulosin and finasteride groups measured before treatment were 9.2 ± 2.5 ml/s and 9.6 ± 2.9 ml/s, respectively. Values after treatment for 4 weeks and 24 weeks were 10.2 ± 2.8 ml/s and 11.5 ± 3.2 ml/s, and 9.9 ± 3.2 ml/s and 11.7 ± 4.3 ml/s in the tamsulosin and finasteride groups, respectively. There was a mean increase in Q_{max} of 1.0 ml/s (10.9%) and 2.2 ml/s (23.9%) on tamsulosin, and 0.3 ml/s (3.1%) and 2.2 ml/s (22.2%) on finasteride from baseline to evaluation at 4 weeks and 24 weeks, respectively. The Q_{max} improved significantly compared with baseline at 24 weeks after treatment in both groups ($P < 0.05$, paired *t*-test; Table 3). There were no significant differences in Q_{max} between the two treatment groups at 24 weeks after treatment (ANOVA and Duncan's multiple-range test, Table 3). However, at 4 weeks, finasteride did not show significant improvement in Q_{max} compared with baseline. In comparison, tamsulosin was associated with significant improvement ($P < 0.05$, Table 3). There was a significant difference in Q_{max} improvement after 4 weeks of treatment between the two groups ($P < 0.05$, ANOVA and Duncan's multiple-range test; Table 3).

Table 3:
Mean and percentage change from baseline of International Prostatic Symptom Score (I-PSS), quality of life (QOL) score and maximum urinary flow rate (Q_{max}) at 4 weeks and 24 weeks of treatment

		Tamsulosin		Finasteride		*P*-value (between groups)[c]
		Mean	Change from baseline (%)	Mean	Change from baseline (%)	
I-PSS score	Baseline	19.9 ± 7.2		19.0 ± 7.2		
	4 weeks	16.4 ± 7.9	–3.5 (17.6)[b]	17.1 ± 7.3	–1.9 (10.0)[b]	< 0.05
	24 weeks	13.0 ± 7.1	–6.9 (34.7)[a]	13.1 ± 7.6	–5.8 (30.5)[a]	NS
QOL score	Baseline	4.1 ± 1.0		3.9 ± 1.2		
	4 weeks	3.5 ± 1.2	–0.6 (14.6)[a]	3.6 ± 1.1	–0.3 (7.7)[a]	< 0.05
	24 weeks	2.6 ± 1.2	–1.4 (34.1)[a]	2.9 ± 1.4	–0.9 (23.1)[a]	< 0.05
Q_{max} (ml/s)	Baseline	9.2 ± 2.5		9.6 ± 2.9		
	4 weeks	10.2 ± 2.8	1.0 (10.9)[a]	9.9 ± 3.2	0.3 (3.1)[NS]	< 0.05
	24 weeks	11.5 ± 3.2	2.2 (23.9)[a]	11.7 ± 4.3	2.2 (22.2)[a]	NS

Statistical significance within groups (paired Student's *t*-test,), as follows: [a]$P < 0.05$ versus baseline; [b]$P < 0.01$ versus baseline; [NS], not significant ($P > 0.05$). [c]Statistical significance between groups (ANOVA and Duncan's multiple-range test) is as shown in the extreme right-hand column; NS, not significant ($P > 0.05$).

Mean QOL scores in the tamsulosin and finasteride groups measured before treatment were 4.1 ± 1.0 and 3.9 ± 1.2, respectively. Values after treatment at 4 weeks and 24 weeks were 3.5 ± 1.2 and 2.6 ± 1.2, and 3.6 ± 1.1 and 2.9 ± 1.4 in the tamsulosin and finasteride groups, respectively. There was a mean decrease in QOL score of 0.6 (14.6%) and 1.4 (34.1%) on tamsulosin, and 0.3 (7.7%) and 0.9 (23.1%) on finasteride from baseline to evaluation at 4 weeks and 24 weeks, respectively. The QOL score improved significantly compared with baseline at 4 weeks and 24 weeks after treatment in both groups ($P < 0.05$, paired *t*-test; Table 3). However, tamsulosin showed significant improvement in QOL score compared with finasteride after 4 weeks and 24 weeks of treatment ($P < 0.05$, ANOVA and Duncan's multiple-range test; Table 3).

At the study endpoint, 51 (70.8%) and 35 patients (48.6%) in the tamsulosin group, and 50 (67.6%) and 37 patients (50.0%) in the finasteride group were considered to be clinical responders, according to a significant change in I-PSS scores (> 20% decrease) and Q_{max} (> 20% increase), respectively. The distribution of Q_{max} and I-PSS responders did not differ between the two groups.

SAFETY

Tamsulosin was well tolerated, with only four patients (3.9%) reporting adverse events (Table 4). In contrast, in the finasteride group, 23 patients (22.5%) reported 28 adverse events, such as decreased libido (four patients), decreased potency (15 patients), decreased ejaculatory volume (three patients), impotence (five patients) and loose stools (one patient). These side-effects were generally mild to moderate in nature. One patient (1%) in the tamsulosin group withdrew from the study due to dyspnoea, and six patients (5.9%) in the finasteride group withdrew from the study due to decreased potency. The difference in side-effect profile between the two groups was significant ($P < 0.001$; Table 4).

There were no significant changes in blood pressure or pulse rate throughout the study in either the tamsulosin or finasteride groups.

Discussion

The results of this study confirmed the efficacy of tamsulosin and finasteride in patients with BPH. At 24 weeks after drug administration, both tamsulosin and finasteride were associated with significant improvements in I-PSS scores, Q_{max} and QOL

TABLE 4:
Percentage incidence of adverse events related to tamsulosin and finasteride

	Tamsulosin *n* (%)	Finasteride *n* (%)
Enrolled patients	103	102
Patients showing adverse events[a]	4 (3.9)	23 (22.5)[d]
Adverse events	4[b]	28[c,d]
Discontinuations due to adverse events	1 (1.0)	6 (5.9)[d]

[a]As reported by individual patients.
[b]Headache (one patient), leg oedema (one), dyspnoea (one), nasal stuffiness (one).
[c]Decreased libido (four patients), decreased potency (15), decreased ejaculatory volume (three), impotence (five), loose stools (one).
[d]$P < 0.001$, significantly different from the values in the tamsulosin group (Fisher's exact test).

scores compared with baseline values. After 24 weeks of treatment, there was a decrease of 6.9 points in I-PSS score and an increase of 2.2 ml/s in Q_{max} in the patients treated with tamsulosin, compared with a decrease of 5.8 points in I-PSS score and an increase of 2.2 ml/s in Q_{max} in those receiving finasteride therapy. In an earlier study evaluating the same dose, tamsulosin was associated with significant benefits when compared with finasteride, as shown by improvements in the I-PSS score, Q_{max} and QOL scores after 4 weeks of treatment.[22]

In the current study, tamsulosin treatment resulted in a rapid onset of efficacy in terms of improvements in I-PSS score and urinary flow. Although the superiority of tamsulosin over finasteride with regard to QOL score at 24 weeks was marginal, the decrease in QOL score was statistically significant ($P < 0.05$). It was assumed that the earlier onset of improvements in subjective symptoms reported by patients receiving tamsulosin resulted in a positive impression on the patients' QOL, which persisted at 24 weeks.

A significant reduction in prostate volume was seen in the finasteride group at 24 weeks compared with the baseline value, whereas there was no significant change in prostate volume in the tamsulosin group.

In a comparison of drug safety, tamsulosin was better tolerated than finasteride. The incidence of adverse events in the tamsulosin and finasteride groups was 3.9% and 22.5%, respectively. Adverse events in the tamsulosin group included headache (one patient), leg oedema (one), dyspnoea (one) and nasal stuffiness (one), which were attributable to the α-adrenoreceptor antagonism of tamsulosin. In contrast, the majority of adverse events reported in the finasteride group were related to reduction in sexual function: decreased libido in four patients, decreased sexual potency in 15, decreased ejaculatory volume in three, impotence in five, and loose stools in one. In addition, there was a higher incidence of discontinuation due to adverse events in the finasteride group (5.9%) compared with the tamsulosin group (1.0%). The higher incidence of discontinuation in the finasteride group was attributable to the higher incidence of sexual function side-effects.

In the past, concern has been raised about cardiovascular side-effects associated with α_1-adrenoreceptor antagonists. Results from the present study confirmed the cardiovascular safety of tamsulosin and was similar to results reported in an earlier clinical study.[8] This cardiac safety profile of tamsulosin has been attributed to its more specific α_1A-adrenoreceptor antagonism. In conclusion, treatment with tamsulosin 0.2 mg once daily was associated with a quicker onset of action and better safety profile than that of finasteride 5 mg once daily in this group of Korean patients with BPH.

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