

Comparison of Clinical Efficacy of Finasteride and Dutasteride as 5-alpha Reductase Inhibitor

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= Abstract =

Purpose: To compare the clinical therapeutic efficacy of finasteride and dutasteride as 5-alpha reductase inhibitor (5-ARI) in the medical treatment of benign prostate hyperplasia.

Materials and Methods: From July 2007 to July 2010, 354 benign prostatic hyperplasia patients with combination medication : alpha blocker plus 5-ARI were enrolled. These patients were classified into a finasteride medication group (F group) and dutasteride medication group (D group) retrospectively. We initially measured the total prostate volume (TPV), prostate specific antigen (PSA), International Prostate Symptom Score (IPSS), quality of life score (QoL), maximal flow rate (Qmax), and post-void residual urine (PVR). After at least twelve months of medication, we rechecked these clinical parameters and during medication, side effects related to medication were also recorded.

Results: The F group (n=129) and D group (n=225) showed no differences in baseline characteristics for age, TPV, IPSS, QoL scores, or PSA. After medication, decreases in TPV were relatively higher in the D group than the F group (28.2% vs 20.5%). In addition, the decrease in PSA (43.6% vs 39.2%) and IPSS score (4.6 vs 3.5) were also higher in the D group. There were no significant differences in QoL score, Qmax, PVR change, or side effects between the two groups.

Conclusions: Dutasteride showed greater efficacy in reduction of TPV and PSA and in symptomatic improvement by IPSS score than finasteride. More large scale studies about the differences on clinical efficacy of finasteride and dutasteride are needed.

Key Words: Benign prostate hyperplasia, 5-alpha reductase inhibitors, Prostate volume

Introduction

Benign prostatic hyperplasia (BPH) is a senile disease that is usually accompanied by annoying lower urinary tract symptoms (LUTS) and might give rise to

acute urinary retention (AUR) and BPH related surgery. It is also known that LUTS affects quality of life in the majority of those who reach average life expectancy.

Therefore, we mainly focus on BPH-related outcomes to improve LUTS in terms of symptoms and urinary flow, to prevent unfavorable disease progression, and to optimize their management.

Knowledge of the progressive nature of BPH and risk of BPH progression is growing. Pharmacological effects on BPH continue to evolve so there are an increasing number of therapeutic choices for individual

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patients with BPH. Uncontrolled disease progression is characterized by aggravation of symptoms, deterioration of the urinary flow rate, increase in prostate volume, and the need for BPH-related surgery. Numerous factors have been shown to be linked to the risk of BPH progression.¹

Currently, most patients that visit a urologist for LUTS are given empirical treatment with an alpha-adrenergic blocker medication either with or without a 5-alpha reductase inhibitor (5-ARI). Especially successful treatment outcomes have been reported after long-term use of 5-ARIs.²

Finasteride selectively inhibits the Type 2 isoenzyme of 5-alpha reductase (5AR), which controls the conversion of testosterone to dihydrotestosterone (DHT), while dutasteride inhibits both Type 1 and Type 2 5AR. Differences and similarities of the overall outcomes of these 2 agents, in terms of pharmacologic effect, safety, and efficacy, can be inferred from short-term comparative trials. Head-to-head clinical studies to analyze pharmacologic parameters, time to onset of clinical effect, and short-term clinical efficacy and safety of dutasteride and finasteride are available.³ However, well designed trials must be evaluated as well in order to validate the clinical efficacy and safety of these 2 agents. The goal of this study is to describe these two agents' differences and similarities of in the way they affect prostate size, flow rate, and symptoms of BPH patients after 12 months of treatment.

Materials and Methods

Medical records of patients presenting with LUTS between July 2007 and July 2010 were reviewed. Those diagnosed with BPH after adequate initial baseline studies and who received at least three months of combination medication (alpha blocker plus 5-ARI) treatment were eligible for the study. 5-ARI monotherapy patients were not included. Patients had bladder surgery, urethral surgery, previous prostate surgery, or medical disease (cerebrovascular diseases, uncontrolled diabetic mellitus), prostate malignancy were excluded. Patients were also excluded if they were receiving any treatment known to affect vesico-urethral

function. In the end, 354 BPH patients with combination medication were enrolled retrospectively.

We initially measured total prostate volume (TPV), International Prostate Symptom Score (IPSS), quality of life (QoL) score, prostate specific antigen (PSA), maximal flow rate (Qmax), and post-void residual urine (PVR). Each eligible patient was asked to fill in the IPSS questionnaire. The Qmax was measured by uroflowmetry. PVR was measured using diagnostic ultrasound. Transrectal ultrasonography was performed to calculate the prostate volume. The anteroposterior (H) and transverse (W) diameters were measured on the largest transverse image of the prostate. The horizontal distance between the proximal and most distal parts of the prostate on a midline sagittal scan was considered the longitudinal (L) diameter. The prostate volume was determined using the following formula: prostate volume = $\pi/6 \times H \times W \times L$.⁴ To minimize bias, only one examiner participated in initial and follow-up calculation of prostate volume by transrectal ultrasonography.

After routine initial baseline studies, these patients were classified into a finasteride medication group (F group) and dutasteride medication group (D group). All of the patients kept the initial prescription without any kind of drug regimen alteration. After at least twelve months of medication, we rechecked the clinical parameters described above.

To evaluate the efficacy of the two groups' treatments after more than a twelve month period, a comparative analysis was performed for TPV, PSA, Qmax, PVR, and IPSS, and Qol score. Drug-related adverse effects were also recorded as impotence, ejaculatory disorders, and decreased libido in both groups.

Data entry and statistical analyses were performed using SPSS ver. 12.0 (SPSS Inc., Chicago, IL, USA). Baseline values of the clinical factors were analyzed using the independent t-test.

Results

The patient demographics are shown in Table 1. The mean patient ages were 67.7 and 66.7 years and the average follow-up periods were 15.4 (12~19) and

Table 1. Comparison of baseline characteristics of the finasteride medication group (F group) and dutasteride medication group (D group)

Parameters	F group	D group	p-value
Patients (n)	129	225	
Age (years)	67.6±9.6	66.7±9.4	0.46
Medication period (months)	15.4±3.1	16.1±3.3	0.82
Combination medication			0.71
Alfuzosin (%)	39 (30.2%)	76 (33.7%)	
Tamsulosin (%)	90 (69.8%)	149 (66.3%)	
TPV (g)	55.0±21.1	55.8±20.1	0.43
PSA (ng/ml)	2.0±1.4	1.9±1.3	0.28
IPSS/QoL	18.9/3.2	19.1/3.3	0.62/0.90
Qmax (ml/sec)	12.1±2.7	12.4±2.1	0.61
PVR (ml)	59.8±37.5	54.0±38.2	0.14

Values are presented as number (%) or mean±standard deviation.

TPV: total prostate volume, PSA: prostate-specific antigen, IPSS: International Prostate Symptom Score, Qmax: maximum uroflow rate, PVR: post-void residual urine.

p-value < 0.05.

Table 2. Comparison of changes in clinical parameters between the finasteride medication group (F group) and dutasteride medication group (D group)

Parameters	F group	D group	p-value
Decrease in TPV (%)	10.3 g (20.5)	15.7 g (28.2)	< 0.01*
Decrease in PSA (%)	0.74 ng/ml (39.2)	0.83 ng/ml (43.6)	0.02*
Decrease in IPSS	3.5	4.6	< 0.01*
Decrease in QoL	1.4	1.5	0.73
Increase in Qmax (ml/s)	2.11	2.65	0.61
Decrease in PVR (%)	17.7 ml (29.7)	17.9 ml (33.3)	0.14

TPV: total prostate volume, PSA: prostate-specific antigen, IPSS: International Prostate Symptom Score, QoL: quality of life score, Qmax: maximum uroflow rate, PVR: post-void residual urine.

*p-value < 0.05.

16.1 (12~24) months for F group and D group respectively. F group (n=129) and D group (n=225) showed no differences in baseline characteristics for age, TPV, IPSS, QoL score, PSA, Qmax, or PVR.

The A-blockers used were selective alpha blockers: alfuzosin (10 mg) and tamsulosin (0.2 mg). In the F group, there were 39 (30.2%) alfuzosin (10 mg) patients and 90 (69.8%) tamsulosin (0.2 mg) medication patients. In the D group, there were 76 (33.7%) alfuzosin (10 mg) medication patients and 149 (66.3%) tamsulosin 0.2 mg medication patients, and there were no statistically significant differences between the two groups.

In the F group and D group, the mean prostate volumes were 55.0 (±21.1) g and 55.8 (±20.1) g, and the

mean PSA levels were 2.0 (±1.4) and 1.9 (±1.3) ng/mL, respectively. The changes in the clinical parameters after medication for twelve months are shown in Table 2. The decreases in the TPV were 15.7g (28.2 %) in the D group, which was relatively higher than the 10.3 g (20.5%) in the F group. In addition, the decrease in PSA (0.83 ng/ml [43.6%] versus 0.74 ng/ml [39.2%], respectively), and the IPSS score (4.6 versus 3.5, respectively) were also higher in the D group than the F group. There were no significant differences in the changes of QoL score, Qmax increment, or PVR reduction between the two groups. These remarkable differences in clinical findings are confirmed by Fig. 1 and 2. In Table 3, the reported overall side effects were similar in the F group (9.3%) and the D group

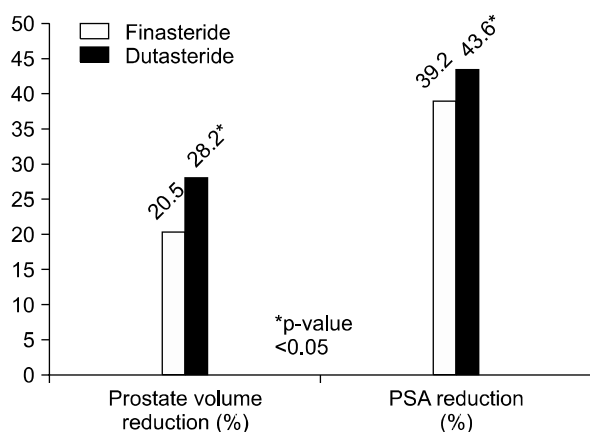


Fig. 1. Comparison of changes in prostate volume and prostate specific antigen (PSA) after finasteride and dutasteride medication.

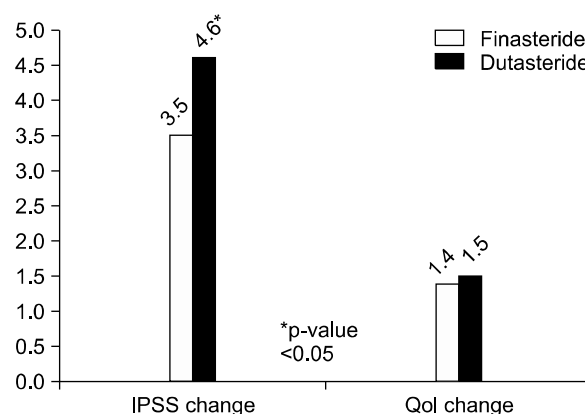


Fig. 2. Comparison of changes in International Prostate Symptom Score (IPSS) and quality of life (QoL) score after finasteride and dutasteride medication.

Table 3. Comparison of side effects between finasteride medication group (F group) and dutasteride medication group (D group)

Parameters	F group, % (n)	D group, % (n)	p-value
Impotence	4.7 (6)	4 (9)	0.32
Decreased libido	2.3 (3)	2.7 (6)	0.51
Ejaculatory disorder	1.6 (2)	1.8 (4)	0.64
Gynecomastia	0.8 (1)	0.4 (1)	0.40
Others	0 (0)	0.9 (2)	0.14
Total	9.3 (12)	9.8 (22)	0.61

p-value < 0.05.

(9.8%) during the medication period. The most common side effect was impotence, and other side effects showed no differences between the two groups.

Discussion

BPH is a complex disease that is progressive in elderly men. BPH is usually associated with annoying LUTS; progressive disease can also result in complications such as AUR and BPH-related surgery.⁵

First-line pharmacologic treatment options for men with symptomatic LUTS include the alpha-blockers and the 5-ARIs: finasteride or dutasteride.⁶ By blocking the conversion to DHT crucial in the initial development and normal growth of the prostate, reduced concentration of DHT inside the prostate arouses the degeneration of the prostate glandular tissue. Two isoforms of 5ARs have been discovered: type 1 with mi-

nor expression and activity in the prostate, but predominant in extraprostatic tissues, such as the skin or liver, and type 2 with predominant expression and in the prostate.^{7,8}

Finasteride has proven to selectively block the Type 2 isoenzyme, while dutasteride blocks both forms of the enzyme. Though dutasteride and finasteride are both 5-ARIs, their pharmacologic and clinical efficiency are somewhat different. It was clearly demonstrated that serum DHT suppression was significantly greater with dutasteride (94.7%) than with finasteride (70.8%).⁹

These findings raise the question of whether the pharmacologic differences in DHT suppression of a selective versus a dual inhibitor of 5AR results in clinically significant differences in the management of BPH. However, the studies of differences and similarities between these 2 agents in the way they affect

prostate size, urinary flow rate, voiding symptoms, risk of progression, and safety are limited.¹⁰

Prostate volume is perhaps the most extensively studied of the risk factors for BPH progression and symptomatic relief.¹¹ Patients with symptomatic BPH who receive dutasteride or finasteride can anticipate experiencing a significant prostate gland size decrease and improved symptoms. The Proscar Long-Term Efficacy and Safety Study (PLESS) was the first long-term placebo-controlled evaluation of 5AR inhibition in BPH. In this study, prostate volume decreased in the finasteride group (-18%) in the first year. Prostate volume in the placebo group continued to have a gradual increase in average size over the course of 4 years compared to baseline ($+14\%$).¹

The Medical Treatment of Prostate Symptoms Study (MTOPS) was designed to evaluate the effect of medical therapy on overall BPH progression for over 4 years; the longest and largest trial of medical management of BPH, it randomized 3047 men with BPH and confirmed significant prostate gland volume reduction with finasteride (-16%).¹¹

On the other hand, when a larger number of patients in dutasteride trials ($n=4325$) received double-blind therapy for 2 years, the prostate volume in the dutasteride group decreased by -25.7% compared to baseline versus an increase in prostate volume of $+1.7\%$ in the placebo group.⁵

The 4-year, multicenter, randomized, double-blind, placebo-controlled, parallel group study named the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) study reported that prostate volume decreased from 45.7 ± 0.28 ml at baseline to 38.6 ± 0.31 ml at year 2 (a mean decrease of 17.4%) and 39.0 ± 0.32 ml at year 4 (a mean overall decrease of 17.5%).¹²

In a recent study of the differences in therapeutic effects and changes in the PSA level with treatment after finasteride or dutasteride, a total of 219 patients were evaluated for 1 year. The degree of PSA reduction was relatively higher in the dutasteride combination therapy group ($p=0.020$), but the volume of the prostate gland reduction was not statistically significant.¹³ In the latest multicenter, randomized, double-blind, 12-month, parallel-group study, the re-

duction was 26.7% in the finasteride group vs. 26.3% in the dutasteride group ($p=0.65$).¹⁴

Our data showed a greater decrease in the TPV after dutasteride medication than finasteride medication. The volume reduction after dutasteride of 28.2% was notably higher than previous studies but the reduction after finasteride of 20.5% seemed similar to that of dutasteride. The decrease in serum PSA showed similar results: a 43.6% decrease after dutasteride medication and 39.2% decrease after finasteride medication.

Serum PSA is easily measured in clinical practice and can therefore facilitate the identification of those men with BPH at risk for disease progression and help to guide therapeutic decisions. Although the precise relationship between PSA and prostate growth may vary from one individual to another, the PSA has a positive correlation with prostate size. Therefore, the PSA appeared to be the most significant associated factor in medication management of BPH-as good as prostate volume.¹⁵

As for symptomatic relief, dutasteride was more effective than finasteride. The results of a 3-month prospective study performed to evaluate the onset of symptom relief in men treated with dutasteride versus finasteride reported that dutasteride was associated with a significantly greater reduction in American Urologic Association (AUA) symptom scores than was finasteride. Forty-three percent ($n=52$) of patients experienced improvement over the 3-month period with dutasteride compared with 23% ($n=28$) of patients treated with finasteride.¹⁶

In PLESS, finasteride treatment resulted in significant improvement in symptom scores (-3.3 in the finasteride group compared to -1.0 in the placebo group).¹ In the MTOPS, the group that was administered combination medication with finasteride experienced a decrease in symptom score of 7.0 points compared to 5.0 points for finasteride, 6.0 points for doxazosin, and 4.0 points for a placebo. In another study, the symptom score decreased by -4.5 in the dutasteride group compared with -2.3 in the placebo group after 2 years of follow-up.¹¹ In another study's latest results, which were at 12 months, the mean AUA-SI scores were reduced by 5.5 in the finasteride

group and 5.8 in the dutasteride group.¹⁴ Our study may be one of more important direct comparative single center studies regarding symptomatic improvement by medication.

The most frequent drug-related adverse events, as expected, were sexual in nature. 5-ARIs are usually tolerable and have only negligible side effects. The most common adverse events are sexual dysfunction, including reduced libido, erectile dysfunction, and ejaculation disorders. However, the ejaculation disorder may related to the alpha blocker. One study revealed that fewer drug-related adverse events occurred in patients who received dutasteride than finasteride (17% of the dutasteride group compared with 20% of the finasteride-treated patients); there were no substantial differences between the two drugs.⁵ It has also been reported that dutasteride and finasteride have a comparable safety profile. In a 1-year comparative trial in men who received either dutasteride (n=813) or finasteride (n=817), the incidence of impotence (7 vs. 8%), decreased libido (5 vs. 6%), ejaculation disorders (1% in both groups), gynecomastia (1% in both groups), headache (1% in both groups), and malaise/fatigue (1% in both groups) did not differ significantly.¹⁷ Thus, generally, dutasteride and finasteride appeared to have a similar safety profile which agrees with our results.

As discussed above, it is clear that combination medication was much more effective than alpha-blocker monotherapy or a placebo.^{5,16} Moreover, there was no significant difference in the drug-related adverse events leading to medication withdrawal rates when comparing combination medication with alpha-blocker monotherapy, and drug-related adverse events diminished over time.¹⁸ Therefore, it is also important to encourage patients to stay on the drugs because they do not tend to contract serious side effects. Nor are there any notable difference in side effects between the two 5-ARI drugs.

Our short-term comparative results showed that dutasteride therapy reduced PSA and prostate volume, and reduced voiding symptoms better than finasteride. However, in our opinion, in comparing the safety and efficacy of dutasteride and finasteride, asserting con-

clusively the comparative superior ability and safety of one agent over the other is no longer defensible.

We have some limitations to our study. First, firm conclusions cannot be made from this study because it examined the first year of what should be very long-term therapy. Use of two different kinds of alpha blockers could be one of the problems. Next, this study design was nonrandomized and retrospective single institutional in nature. Moreover, differences in reduction of the risk of BPH progression like AUR and BPH-related surgery were not estimated. In fact, we expect either agent to result in similar developments in terms of symptom progression in the follow-up study. Because we just report weak evidence suggests a minor difference in the efficacy of the drugs in a small number of studies in a relatively short-term follow-up period. Nevertheless, the current evidence, including the results of this study, suggest that both 5-ARI agents are effective. Our data would be helpful as a short term comparative study of the superiority of dutasteride over finasteride in prostate size, PSA reduction, and possible symptomatic benefits. More studies on the potential clinical implications and differences in the use of the two 5-ARIs will be necessary in the future.

Conclusions

Dutasteride showed more efficacy than finasteride in reduction of TPV, PSA, and in symptomatic improvement by IPSS score. However, dutasteride and finasteride appeared to have a similar safety profiles. This short term comparative study of dutasteride superiority over finasteride contributes new data, but a strong confirmation of the superior ability of one agent over the other cannot be made. More large scale studies on the potential clinical efficacy and differences of finasteride and dutasteride are needed.

REFERENCES

- 1) McConnell JD, Bruskewitz R, Walsh P, Andriole G, Lieber M, Holtgrewe HL, et al. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign

- prostatic hyperplasia. Finasteride Long-Term Efficacy and Safety Study Group. *N Engl J Med* 1998;338:557-63
- 2) Emberton M, Cornet EB, Bassi PF, Fourcade RO, Gómez JM, Castro R. Benign prostatic hyperplasia as a progressive disease: a guide to the risk factors and options for medical management. *Int J Clin Pract* 2008;62:1076-86
 - 3) Roehrborn CG, Boyle P, Nickel JC, Hoefner K, Andriole G; ARIA3001 ARIA3002 and ARIA3003 Study Investigators. Efficacy and safety of a dual inhibitor of 5-alpha-reductase types 1 and 2 (dutasteride) in men with benign prostatic hyperplasia. *Urology* 2002;60:434-41
 - 4) Kim CI, Chang HS, Kim BK, Park CH. Long-term results of medical treatment in benign prostatic hyperplasia. *Urology* 2006;68:1015-9
 - 5) Nickel JC. Comparison of clinical trials with finasteride and dutasteride. *Rev Urol* 2004;6 Suppl 9:S31-9
 - 6) Jacobsen SJ, Jacobson DJ, Girman CJ, Roberts RO, Rhodes T, Guess HA, et al. Natural history of prostatism: risk factors for acute urinary retention. *J Urol* 1997;158:481-7
 - 7) Carson C 3rd, Rittmaster R. The role of dihydrotestosterone in benign prostatic hyperplasia. *Urology* 2003;61(4 Suppl 1):2-7
 - 8) Iehlé C, Délos S, Guirou O, Tate R, Raynaud JP, Martin PM. Human prostatic steroid 5 alpha-reductase isoforms-a comparative study of selective inhibitors. *J Steroid Biochem Mol Biol* 1995;54:273-9
 - 9) Clark RV, Hermann DJ, Cunningham GR, Wilson TH, Morrill BB, Hobbs S. Marked suppression of dihydrotestosterone in men with benign prostatic hyperplasia by dutasteride, a dual 5alpha-reductase inhibitor. *J Clin Endocrinol Metab* 2004;89:2179-84
 - 10) Gravas S, Oelke M. Current status of 5alpha-reductase inhibitors in the management of lower urinary tract symptoms and BPH. *World J Urol* 2010;28:9-15
 - 11) McConnell JD, Roehrborn CG, Bautista OM, Andriole GL Jr, Dixon CM, Kusek JW, et al; Medical Therapy of Prostatic Symptoms (MTOPS) Research Group. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003;349:2387-98
 - 12) Andriole GL, Bostwick DG, Brawley OW, Gomella LG, Marberger M, Montorsi F, et al; REDUCE Study Group. Effect of dutasteride on the risk of prostate cancer. *N Engl J Med* 2010;362:1192-202
 - 13) Choi YH, Cho SY, Cho IR. The different reduction rate of prostate-specific antigen in dutasteride and finasteride. *Korean J Urol* 2010;51:704-8
 - 14) Nickel JC, Gilling P, Tammela TL, Morrill B, Wilson TH, Rittmaster RS. Comparison of dutasteride and finasteride for treating benign prostatic hyperplasia: the Enlarged Prostate International Comparator Study (EPICS). *BJU Int* 2011;108:388-94
 - 15) Choi H, Chang YS, Kim JB, Kang SH, Park HS, Lee JG. Analysis of initial baseline clinical parameters and treatment strategy associated with medication failure in the treatment of benign prostatic hyperplasia in Korea. *Int Neurourol J* 2010;14:261-6
 - 16) Haggerty JA, Ginsberg PC, Metro MJ, Harkaway RC. A prospective, comparative study of the onset of symptomatic benefit of dutasteride versus finasteride in men with benign prostatic hyperplasia in clinical practice. *J Urol* 2004;171:356-9
 - 17) Andriole GL, Kirby R. Safety and tolerability of the dual 5alpha-reductase inhibitor dutasteride in the treatment of benign prostatic hyperplasia. *Eur Urol* 2003;44:82-8
 - 18) Barkin J. Review of dutasteride/tamsulosin fixed-dose combination for the treatment of benign prostatic hyperplasia: efficacy, safety, and patient acceptability. *Patient Prefer Adherence* 2011;5:483-90