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Research Article

COMPARISON OF THE EFFICACY AND SAFETY OF TAMSULOSIN (0.4 mg) V/S (and) FINASTERIDE FOR SHORT-TERM TREATMENT OF PATIENTS WITH SYMPTOMATIC BENIGN PROSTATIC HYPERPLASIA

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ABSTRACT

Objective: To evaluate the comparative efficacy and safety of tamsulosin 0.4mg once daily verses finasteride in men with symptomatic benign prostatic hyperplasia.

Patients and method: In this randomised study, 69 patients were enrolled. Of these 51 were receive tamsulosin 0.4 mg and 18 patients were receive finasteride 5 mg once daily for 12 weeks. The primary outcome measures (mean changes in total and /or individual I-PSS score, prostate volume and life style questionnaire) were compared from baseline to 12 weeks of study.

Result: During study both drugs reduced the total and individual I-PSS scores, while tamsulosin significantly improved lower urinary tract symptoms compared to finasteride ($p \leq 0.0002$) within 3-monts of therapy, (mean change in I-PSS scores from baseline to end of the study was 16.7 VS 9.0 in tamsulosin VS finasteride respectively). Improvement in symptoms score was 82.67% in tamsulosin compare to 45.50% in finasteride. The life style questionnaire was significantly improved in tamsulosin group. The prostate volume is slightly increased (0.75ml) in tamsulosin and 1.44 ml decreases in finasteride group during study. Adverse events were similar in both groups; most common observed adverse event was dizziness (4.34%) in tamsulosin similar to finasteride ((7.14 %). While sexual disorder (2.1%) delayed ejaculation was prominent in tamsulosin group.

Conclusion: Once daily dosing of tamsulosin at bed time at a fix dose level (0.4mg) offers an efficient improvement in total and individual I-PSS score compare to finasteride. The prostate volume was increase in tamsulosin while it was decreased in finasteride group; adverse events other than ejaculatory disorder were similar similar in both groups. Tamsulosin is safe, well tolerated and significantly more effective than finasteride for short term treatment of symptomatic BPH.

Keyword: Tamsulosin; Finasteride; BPH (Benign prostatic hyperplasia); I-PSS (International-prostate symptom score); AUR (Acute urinary retention)

INTRODUCTION

The prostate is an accessory gland of the male reproductive system. It lies in the lesser pelvis bellow the neck of the urinary bladder, secretion of this gland adds bulk to the seminal fluid[1]. Benign prostatic hyperplasia is a pathological condition associated with ageing. Pathological evident of the disease appears in men between 40 and 50 years old[2]. BPH may be asymptomatic, but often becomes symptomatic from the 5th decade of life[3]. Incidence of benign prostatic hyperplasia by the age 60 year 50% and by the 8th decade of life it affects 85% of men[1]. The progression of benign prostatic hyperplasia is characterized by the a number of clinical feature such as deterioration in LUTS (which consist of obstructive and irritative symptoms, obstructive symptoms are hesitancy, poor flow, intermittent stream, dribbling, sensation of poor bladder emptying and episode of near retention while irritative system are frequency, nocturia, urgency, urge incontinence and enuresis), bladder complication, hematuria and recurrent urinary tract infection, all of these leads to a worsening the patients quality of life[4]. The cause of benign prostatic hyperplasia, are not fully understood. The DHT hypothesis infers that benign prostatic hyperplasia occurs following an age related changes in prostatic androgen metabolism, which favours accumulation of DHT[5]. It is synthesized in the prostate from circulating testosterone by the action of the enzyme 5α-reductase, type-2, this enzyme localized principally in the stromal cells; 5α-Reductase is an enzyme which, convert testosterone to DHT[6]. Inhibition of 5α- reductase was thus considered one of a potential option for DHT- mediated disorders[6]. A dynamic component related to the tone of smooth muscle fibres in the bladder neck, surgical capsule and fibromuscular stroma[7] is α adrenergic receptors. There are 2 types of α adrenergic receptors in the prostatic capsule adenoma, and bladder neck, designated as α1 and α2. The action of the α2 receptors is same as α1 but the receptor which predominantly mediating the contractile properties of the human prostatic adenoma is the α1 types[8]. α-receptor blockers have been proven to decrease the tone of prostatic capsule and (adenoma), decreasing the pressure in the prostatic part of the urethra and bladder neck without affecting bladder pressure[9].

METHOD & STUDY DESIGN

This short-term (12 weeks) clinical study was conducted in Department of Pharmacology, S.S. Medical College and associated Sanjay Gandhi Memorial Hospital Rewa, M.P. India; with aim to compare the efficacy and safety of tamsulosin o.4 mg versus fenasteride 5mg once daily in patients with BPO. A total of 69 men were enrolled in the study, 51 patients take tamsulosin and 18 were on fenasteride regimen. Patients were on I-PSS scoring system with the total score is more than 3 points; I-PSS scoring system is based on seven items: Sensation of not completely emptying of bladder; Increase frequency of micturition (within two hour); Stopped and started again several times when urinating; Difficulty to postpone urination; Weak urinary stream; Strain during urination; Number of urinate during night.

Inclusion criteria

Male patients above 40 years with enlarge prostate size and LUTS including hesitancy, poor stream and terminal dribbling.

Exclusion Criteria

Patients are excluded in this study with a consistent residual urine volume >200 ml., history of previous bladder neck, prostate or pelvic region surgery, other condition which would affect micturition including neurological bladder disorder, bladder neck stenosis, urethral stricture, prostate cancer, bladder stone etc. History of hypersensitivity to α-adrenoceptor antagonists and take any other investigational drugs within the previous 3-months. All urological therapy had to be avoided until the end of the trial.

Study Design

Men treated with these drugs as modified–release preparation one daily after dinner; patients were assessed at enrolment, and after 2,

4, 8 and 12-weeks. At visit-1 (enrolment visit); total\individual I-PSS score as well as vital signs, laboratory evaluation and H\O any recent or concomitant medication has been taken, the size of prostate was estimated by rectal palpation and abdominal ultrasound. At each visits; total\individual I-PSS and adverse events were assessed and vital signs were monitored.

Assessment of Efficacy

Parameters for efficacy were total and individual I-PSS score and urinary flow rate, significant response was defined as those with a ≥ 25% decrease in total I-PSS score. Efficacy assessments were made on patients who received treatment from baseline to complete 3-month and attend regular follow-up. Safety assessments includes; monitoring of the occurrence of adverse events, vital signs and laboratory determinations.

Statistical method

Within-group changes from baseline were assessed using the paired student t test. The significance level set at $P \leq 0.05$.

RESULTS

A total of 69 men were enrolled in the study. The men assigned to the tamsulosin and finasteride was similar in term of age, baseline demographic characteristics and symptoms, shown in table 1.

Table 1: Basic Parameters, including Age, Occupation and I-PS Score grade of BPH patients

Age Group.		**Tamsulosin**		**fenasteride (5mg)**		**Grand Total**	
S. No	In Years	No.	%	No.	%	No.	%
1.	40-49	02	3.92	00	00	02	2.89
2.	50-59	08	15.68	02	11.11	10	14.49
3.	60-69	23	45.09	09	50.00	32	46.37
4.	70-79	14	27.45	06	33.33	20	28.98
5.	80-89	04	7.84	01	5.55	05	7.24
Total		51	100	18	100	69	100
	Occupation						
1.	Govt. Servant	23	45.09	09	50.00	32	46.37
2.	Sedentary Worker	11	21.56	05	27.78	16	23.18
3.	Heavy Worker	12	23.52	03	16.67	15	21.73
4.	Businessmen	05	9.80	01	5.56	06	8.69
Total		51	100	18	100	69	100

During the 3 month of study, 5 (9.80%) men in tamsulosin and 4 (22.22%) in the finasteride group were discontinued the treatment, the most common reason were; lost to follow-up, lack of efficacy, adverse drug effects. Acute urinary retention developed in 1 (2.4%) men in the tamsulosin and 3 (21.42%) men in the finasteride group during the study. 10 (19.60 %) patients in the tamsulosin and 03 (n=18) in finasteride group were enrolled in catheterized state (at 1st visit of study) and most of them remove their catheter within 15-25 days of treatment. Two men (4.3%) in the tamsulosin and 2 (11.11%) in finasteride group underwent supra- pubic prostatectomy surgery, as shown in table 2.

Table 2: Mean Parameters (Mean ± SD) of Age, Prostate Volume, PSA of BPH patients

Mean of Demographic Parameters		**Tamsulosin (0.4mg)**	**Fenasteride (5mg)**
1	Age (Mean ± SD)	67.28 ± 7.99 (n=51)	66.55 ± 7.94 (n=18)
2	Prostate Volume (Mean ± SD)	36.28 ± 24.67 (n=15)	43.22 ± 15.13 (n=9)
3	PSA (Mean ± SD	3.41 ± 3.98 (n=2)	2.42 ± 0.45 (n=2)
4	Development of AUR during study	01 (2.4 %) (n=46)	3 (21.42 %) (n=14)
5	No of cases enrolled in catheterized state	10 (19.60 %) (n=51)	3 (16.67 %) (n=18)
6	No of cases underwent surgery	02 (4.34 %) (n=46)	02 (14.28 %) (n=14)
7	No of cases discontinued the treatment	5 (9.80%) (n=51)	4 (22.22%) (n=18)

Total symptom score

In present study 1(n=46) patient in tamsulosin and 3 (n=14) in finasteride group were increases their total symptom scores and 2 patients in finasteride placebo group have no changes in their total symptom scores from baseline. Treatment with tamsulosin resulted in a significant decrease in total I-PSS V/S finasteride, the mean changes in total I-PSS from baseline to end of study was 16.7 points in tamsulosin and 9.0 points in finasteride group as shown in table 2. The mean change from baseline in the total I-PSS scores after 1 week of treatment with tamsulosin (p 0.44) better than that of finasteride (p 0.95). After 4 weeks of treatment changes in tamsulosin group ($P<0.0001$) was statistically significant compare to finasteride (p 0.12) and at the end (12 weeks) of study this change in total scores was more significant in tamsulosin ($p<0.0001$) V/S finasteride (p 0.01) group as shown in table 3.and figure 1.

Table 3: Efficacy of Drugs on Total I-PSS Symptom Scores in Between Baseline to 12 Weeks of Interval with Statistical Calculation

S. No.	**Total I-PSS**	**Change in total I-PSS from baseline to 12 weeks**					**P Value baseline to 12 weeks**
		Regimen	**Baseline**	**2nd Week**	**4th Week**	**8th Week**	**12th Week**	
1	TOTAL I-PSS SYMPTOM SCORES	Tamsulosin(0.4 mg)	20.20 ± 8.95	13.87 ±10.42	6.9 ± 3.54	4.62 ± 2.87	3.5 ± 1.08	P<0.0001, Significant
		Finasteride (5 mg)	19.78 ± 7.92	17.44 ± 7.72	14.22 ± 6.68	12.89 ± 5.92	10.78 ± 4.76	P 0.060, Not Sign

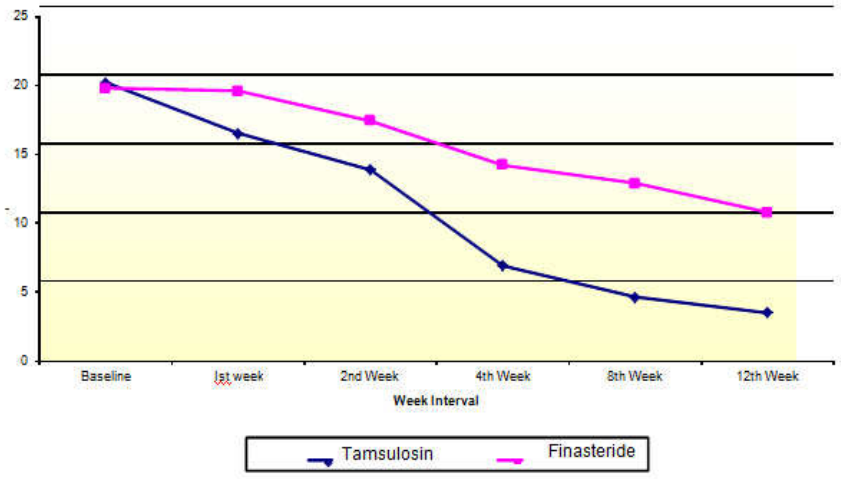

Fig. 1: Efficacy of drugs on total symptom scores

Individual I-PSS Symptom

In individual symptom scores; the mean changes in **obstructive symptoms**1 weeks after of treatment with tamsulosin is better than finasteride (*incomplete emptying symptom* scores from baseline to 1 weeks was (p 0.67), V/S (p 0.85), 4 weeks (p 0.032) V/S (p 0.11) and at the end of study this symptom score disappear in tamsulosin V/S finasteride (p 0.105) as shown in figure 1.

I*ntermittency Score* was appear significant after 2nd weeks and disappear (p=nil) at end of the study in tamsulosin V/S finasteride (p 0.05) group. As shown in figure 3 *Weak Stream Score* significantly improved after second week and become extremely significant (p 0.0001) at end of study in tamsulosin compare to finasteride (p 0.05) as shown in table 4.

In **irritatives symptoms** *Frequency Score* first appear statistically significant (p 0.0009) at 4 weeks and at end of the study frequency was extremely significant (p<0.0001) in tamsulosin compare to finasteride 4 weeks (p 0.24) and12 weeks (p 0.10) respectively as shown in figure 2. *The m*ean changes in *Urgency Score* from baseline to end of study was (p 0.039) in tamsulosin compare to finasteride (p 0.26) as shown in figure 4. *Nocturia Score*: nocturia symptom scores was first appear statistically significant (p 0.01) at 12 weeks with tamsulosin compare to finasteride (p 0.28) in which symptom score was not statistically significant up-to end of study as shown in table 5.

Table 4: Efficacy of Drug on Obstructive symptoms, in between baseline and 12 weeks interval

S. No.	Obstructive symptoms1	Change in total I-PSS from baseline to 12 weeks						P Value baseline to 12 weeks
		Regimen	Baseline	2nd Week	4th Week	8th Week	12th Week	
1	INCOMPLETE EMPTYING SCORE	Tamsulosin(0.4 mg)	2.30 ± 2.40	0.75 ± 1.75	0.40 ± 0.97	0.125 ± 0.35	0.0 ± 0.0	P Nill
		Finasteride (5 mg)	2.22 ±2.27	1.77 ± 2.22	0.88 ± 1.26	0.78 ± 1.30	0.78 ± 1.09	P 0.105
2	INTERMITTENCY SCORES	Tamsulosin(0.4 mg)	2.30 ± 2.41	1.63 ± 1.92	0.6 ± 1.35	0.0 ± 0.0	0.0 ± 0.0	P Nill
		Finasteride (5 mg)	3.22 ± 2.22	2.88 ± 2.52	2.66 ± 1.94	1.66 ± 1.58	1.11 ± 2.20	P 0.05, Not quit significant
3	WEAK STREAM SCORE	Tamsulosin(0.4 mg)	3.67 ± 1.73	2.37 ± 2.39	0.7 ± 1.25	0.12 ± 0.35	0.3 ± 0.67	P 0.0001, Significant
		Finasteride (5 mg)	3.66 ± 2.17	3.44 ± 1.87	3.0 ± 2.10	3.12 ± 1.83	1.77 ± 1.71	P 0.05, Not quit Significant

Table 5: Efficacy of Drug on Obstructive symptoms, in between baseline and 12 weeks interval

S. No.	Irritative symptoms1	Change in total I-PSS from baseline to 12 weeks						p Value baseline to 12 weeks
		Regimen	Baseline	2nd Week	4th Week	8th Week	12th Week	
1	FREQUENCY SCORE,	Tamsulosin(0.4 mg)	3.70 ± 1.57	2.63 ± 1.69	1.40 ± 0.97	0.62 ± 0.51	0.20 ± 0.63	P 0.0001, Significant
		Finasteride (5 mg)	3.0 ± 1.93	2.44 ± 1.87	2.0 ± 1.58	1.88 ± 1.61	1.66 ± 1.22	P 0.10, Not significant
2	URGENCY SCORE	Tamsulosin(0.4 mg)	1.80 ± 2.39	0.87 ± 1.81	0.20 ± 0.42	0.87 ± 1.80	0.1 ± 0.31	P 0.039, Significant
		Finasteride (5 mg)	1.11 ± 2.20	1.11 ± 2.20	1.00 ± 2.00	0.33 ± 1.00	0.22 ± 0.66	P 0.26, Not significant
3	NOCTURIA SCORE	Tamsulosin(0.4 mg)	4.0 ± 1.56	4.12 ± 0.99	3.80 ± 1.23	3.25 ± 1.38	2.8 ± 0.79	P 0.01, Significant
		Finasteride (5 mg)	3.77 ± 1.64	3.44 ±1.59	3.22 ± 1.78	3.22 ± 1.48	2.88 ± 1.76	P 0.28, Not significant

Notable adverse reaction of tamsulosin was similar to finasteride shown in table 3. 14.28% of finasteride and 10.86% of tamsulosin patients experienced treatment emergent adverse events. In tamsulosin group 2(4.34%) cases showed dizziness, 1(2.1%) headache, 1(2.1%) distended abdomen, and 1(2.1%) decreased libido. In finasteride group only 2 patients report ADR**,** 1 (7.14%) show distended abdomen and other 1(7.14%) showed dizziness as shown in table 6.

Table 6: Commonly observed adverse effects during therapy.

S. No.	Adverse effects	Tamsulosin (0.4 mg) (n=46)	Finasteride (5 mg) (n=14)
1	Dizziness	2 (4.34%)	1 (7.14 %)
2	Headache	1 (2.1%)	00
3	Abdominal distension	1 (2.1%)	1 (7.14 %)
4	Decreased Libido	1 (2.1%)	00
5	Ejaculation Disorder	00	00
6	Others (Hypersomnia)	00	00

DISCUSSION

Benign prostatic hyperplasia is the most common conditions associated with ageing in men, effecting 90% of those older than 80 years of age[10]. Symptoms such as urgency, dribbling and a weak urinary stream were present in the majority of men over 60 years of age[11]. In our study it was observed that maximum no. of cases belong to 60-69 year age groups, the maximum sufferers (46.87%) were government servant like[12] Platz *et al, (*1998) in which physical activity was inversely related with total benign prostatic hyperplasia. Our study showed that tamsulosin 0.4 mg significantly improved total and individual symptom scores; Improvements in total I-PSS was 82.6% in tamsulosin as compare to finasteride (45.51%). This improvement in total I-PSS was similar to the previously reported study[11] in which the improvement in total I-PSS score was 34% with tamsulosin. Previously 2 open-labels, observational study[11] showed following results. In study 1, the change in total I-PSS score from baseline to 3rd visits (after 4 weeks treatment) was 8.5 point or 68% and in study 2, it was more than 10 point or 87% a from baseline to 4th visits (12 weeks) in tamsulosin group. In the present study total symptom score first appear significant after 4 weeks similar to European study[13] *in which* obstructive and irritative symptom scores were improved significantly first after 4 weeks and improvement was continued up to end point. In our study; finasteride decreases total symptom scores at several points from 2nd weeks and continue up to 3 months. The changes in total I-PSS scores first appear significant after 2 month (8 weeks) with finasteride, and maximum decrease in the scores was 9 points, occurs at 3rd months. This is similar to a *European* study[14] in which total symptom scores was significantly decreases from 2 weeks through 12 months, ($p<0.02$ at months 10 and $p<0.001$ at months 12). In that study the maximum decrease in score at 12 months was 2.7 points. Similar to present study *Connell et al, (1998)*[15] *showed* mean decrease in total symptom scores were 3.3 points ($p<0.001$) after 3 years and first appear significant at 4 months after treatment In present study, obstructive (voiding) symptom was not statistically significant from baseline to end point. Intermittency and weak stream scores were reaches near the significant level at 12 weeks (P 0.05). In our study maximally effective obstructive symptoms was weak stream and intermittency, and least effective was straining symptom. *A PROSPECT* study[16] was demonstrated that the obstructive symptom score change from baseline was 1.0 point at 4 months (not significant) and it appear significant after 12 months. The changes in the obstructive symptom scores were similar to changes in the total symptom scores reported by 12 months double-blind study[14]. While *PROWESS study*[17] showed that significant changes in obstructive symptom scores were apparent from 4- months (p 0.05) and through months 24 ($p<0.01$) of therapy. In our study Irritative symptoms were not significantly improved with finasteride during 3-months of therapy. Data from *Gormley et al, (1992)*[14] suggested that non obstructive symptom scores were decreased significantly at 10 (p 0.05) and 12 months ($p<0.01$) of finasteride therapy. Tamsulosin and finasteride was well tolerated during the 12 weeks of treatment; the incidence of adverse events in total population was 6 (13.1%) in tamsulosin and 2 (14.28%) in finasteride.

CONCLUSION

Both tamsulosin and finasteride reduced the total and individual I-PSS scores, while tamsulosin was highly efficacious compare to finasteride and in tolerability both are equal in patients with lower urinary tract symptoms during short-term therapy. Improvement in lower urinary tract symptoms with tamsulosin was 82.67% as compare to finasteride (45.50%). The overall incidence of side effects was not significantly different between groups. Adverse events of tamsulosin; other than ejaculatory disorder were similar to finasteride. 13.0 % ADR occurred in patients treated with tamsulosin, more than half of which had occurred within the 1-4 weeks of treatment however; in finasteride group 14.28% ADR is reported during therapy.

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