



PROSTATIC HYPERPLASIA (BPH); TAMSULOSIN WITH AND WITHOUT TOLTERODINE IN PATIENTS HAVING BENIGN PROSTATIC HYPERPLASIA (BPH) WITH IRRITATIVE (OVERACTIVE BLADDER) SYMPTOMS.

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is the progression of prostatic cells and urinary tract obstruction leads to lower urinary tract symptoms (LUTS) and also leads to severe complications if left untreated.¹⁻³ The treatment response assessed by an international prostatic symptom scoring (IPSS) which is a good tool for rationalize the individuals and evaluate the response of conventional treatment.^{4,5} The available options for treatment include surgical and medical; however, the frequency of medical therapy has recently increased.⁶ Alfa adrenergic receptors blockers (tamsulosin) are often priority medical treatment for patients with LUTS due to their good efficacy & rapid onset of action. Its usage improves IPSS more than 4 points within few weeks while the tolterodine significantly improves urgency urge in continence, 24-hour or day time frequency & urgency related voiding along with improvement in nocturia. Conventionally these patients treated with alpha- receptor antagonists

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ABSTRACT... Objectives: To determine the efficacy of tamsulosin with and without tolterodine in patients having benign prostatic hyperplasia (BPH) with irritative (overactive bladder) symptoms. **Study Design:** Randomized clinical trial. **Setting:** Department of Urology and Kidney Transplantation, Sheikh Zayed Hospital Lahore. **Period:** Six months from July to Dec 2017. **Patients and Methods:** Sixty patients of BPH had irritative (overactive bladder) & obstructive presentation were recruited. Patients were categorized in two groups and were compared for efficacy according to international prostatic symptom scoring while the data analyzed in SPSS 16. **Results:** Patients with BPH having irritative (overactive bladder) symptoms, after receiving Tamsulosin with Tolterodine, 76.60% (23/30) of patients reported symptomatic improvement whereas only 40.00 % (12/30) of subjects improved with tamsulosine only. Rate of improvement was observed to be higher in individuals with tamsulosine with tolterodine (Group B) than group A (includes tamsulosin only) with statistical significance) chi-square = 8.297; p=0.004). **Conclusion:** Efficacy of tamsulosin with tolterodine is higher than tamsulosin alone in subjects with BPH had irritative (overactive bladder) & obstructive symptoms.

Key words: Benign prostatic hyperplasia (BPH), Tamsulosin, Tolterodine, Overactive Bladder

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only and the antimuscranic agents not used due to potential risk of acute urinary retention.⁷⁻⁹ It has been observed that individuals with BPH having irritative (overactive bladder) & obstructive symptoms, after receiving doxazosin with tolterodine reported IPSS improvement in 73% cases whereas only 35% of patients improve with doxazosine only.¹⁰⁻¹² Our study is designed to see frequency of improvement in IPSS in patients with BPH in our population after the use of tamsulosin with or without tolterodine. If the improvement in IPSS is >3 points in significant numbers of patients in the group who receive tamsulosin with tolterodine then we will recommend it a better treatment modality for these patients. We are expecting more favorable results in our population with the use of tamsulosin with tolterodine because of differences in life style, dietary habits and environmental factors as compare to the west. Unfortunately very little local data and literature are available on this subject. Rationale of this study is to see the similar effect in our

population so that superior of the two treatment modalities could be used and advocated in future in such cases.

PATIENTS AND METHODS

This six months randomized controlled trial was conducted in the Department of Urology & Kidney Transplantation Sheikh Zayed Post graduate medical institute Lahore. 60 cases (30 cases in each group) are calculated by using 5% level of significance 80% power of test with an expected improvement in Tamsulosin 35% and 73% Tamsulosin plus Tolterodine. The inclusion criteria were all men ≥ 50 years, with Benign prostatic hyperplasia (diagnosed on Ultrasound prostate) having obstructive and irritative (overactive bladder) symptoms and total international prostate symptom score (IPSS) between 9-35 for ≥ 3 months while the exclusion criteria were subjects with bladder outlet obstruction due to causes other than BPH and any disorders in which antimuscranic medications are contraindicated.

Efficacy

Reduction in international prostatic symptom scoring of more than three points from the baseline at 12 wks would be termed as efficacious.

Irritative / Overactive Bladder Symptoms

These include Patient having anyone or more of the following symptoms i:e daytime frequency (>8 micturation/day), urgency, urge incontinence, and nocturia (2 or >2 /night).

Obstructive Symptoms

Any one of the following symptoms i-e straining at micturation, sense of incomplete emptying of bladder, poor urinary stream and intermittency.

IPSS

Is a self-administered questionnaire. All patients presenting in Urology outpatient department (OPD) of Sheikh Zayed Post graduate medical institute Lahore, which fulfill inclusion criteria will be included in my study after the approval of ethical review committee. Group A (Tamsulosin 0.4 mg HS) and Group B (Tamsulosin 0.4 mg HS + Tolterodine 2mg BD). Total 60 patients will be included in my study

with 30 patients in each group. Baseline IPSS will be recorded in each patient. Patients will be followed up at 1, 3, 6, 9, and 12 weeks and final outcome interms of IPSS improvement will be measured at the end of 12 weeks. Efficacy will be interpreted in terms of IPSS improvement related to baseline IPSS. All data will be recorded in predesigned performa attached here. Frequency and percentage will be computed for efficacy. Chi-square test will be used to compare between groups for efficacy in SPSS version 16. $P \leq 0.05$ will be considered significant result. Stratification will be done to control effect modifier like age to observe an effect of efficacy.

RESULTS

Thirty patients were treated with tamsulosin 0.4mg HS (Group A) and other thirty patients in Group B, were treated with tamsulosin 0.4 mg HS + Tolterodine 2mg BD. Most of the patients were between 61 to 70 years of age. The average age of the patients was 63.90 ± 8.27 years (95%CI: 61.81 to 65.99) similarly average total international prostate symptom score was 17.93 ± 4.617 (95%CI: 16.76 to 19.10). Comparison of efficacy between groups is presented in table 3. Rate of overall efficacy was 58.3%. Patients with BPH having irritative (overactive bladder) symptoms after receiving tamsulosin with tolterodine, 76.6% (23/30) of patients reported symptomatic improvement whereas only 40.0% (12/30) of individuals improved with tamsulosin only. The improvement was observed to be higher in group B than group A (Chi-square =8.297; $p=0.004$). For the age 51 to 60 and 61 to 70 years of age, insignificant difference was observed and Group B was also reported symptomatic improvement higher as compare to Group A. The results are presented in Figure-1 and Table-I to V.

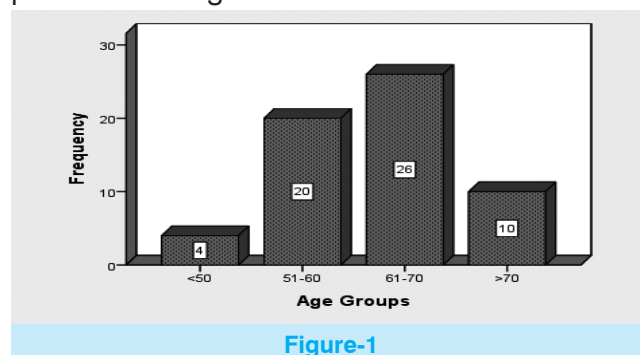


Figure-1

Efficacy	Group A n=30	Group B n=30	Total
Yes	12(20.00%)	23(38.30%)	35(58.30%)
No	18(30.00%)	07(11.70%)	25(41.70%)

Table-I. Comparison of efficacy of tamsulosin with or without tolterodine
Chi-Square = 8.297 p= 0.004

Efficacy	Group A n=1	Group B n=3	Total n=4
Yes	00(00.00%)	03(75.00%)	3(75.00%)
No	01(25.00%)	00(00.00%)	01(25.00%)

Table-II. Comparison of efficacy of tamsulosin with or without tolterodine for the age group ≤50 years
Chi-Square = 4.00 p= 0.250 Fisher Exact test applied

Efficacy	Group A n=09	Group B n=11	Total n=20
Yes	03(15.00%)	08(40.00%)	11(55.00%)
No	06(30.00%)	03(15.00%)	09(45.00%)

Table-III. Comparison of efficacy of tamsulosin with or without tolterodine for the age group 51 to 60 years
Chi-Square = 3.11 p= 0.175 Fisher Exact test applied

Efficacy	Group A n=16	Group B n=10	Total n=26
Yes	08(30.80%)	08(30.80%)	16(61.50%)
No	08(30.80%)	02(07.70%)	10(38.50%)

Table-IV. Comparison of efficacy of tamsulosin with or without tolterodine for the age group 61 to 70 years
Chi-Square = 2.34 p= 0.218 Fisher Exact test applied

Efficacy	Group A n=4	Group B n=6	Total n=10
Yes	01(10.00%)	04(40.00%)	05(50.00%)
No	03(30.00%)	02(20.00%)	05(50.00%)

Table-V. Comparison of efficacy of tamsulosin with or without tolterodine for the age group >70 years
Chi-Square = 1.67 p= 0.524 Fisher Exact test applied

DISCUSSION

Using anticholinergic agent inpatients is still a concern of many physicians. The study by Lee KS, et al compared doxazosin with and without tolterodine, out of 144 subjects 76 (53%) were diagnosed as having bladder outlet obstruction and 68(47%) bladder outlet obstruction (BOO) + overactive bladder (OAB). After 3 month, 60(79%) with bladder outlet obstruction and 24 (35%) with bladder outlet obstruction and overactive bladder reported revealed improvement (IPSS reduced by more than three points). In non improved 6 of 16 with BOO and 32 of 44 with BOO + OAB

had improvement on adding tolterodine.¹³ The common side effect of tolterodine was dry mouth observed in 27% patients. In present study, it demonstrates that in patients with symptomatic BPH along with OAB, combination therapy of Tamsulosin (0.4mg HS) plus tolterodine (2mg BD) improves IPSS and hence quality of life (QoL). Mean age was slightly different in both groups. Most of the patients were between 61 to 70 years of age. The average age of the patients was 63.90 ± 8.268 years (95%CI: 61.81 to 65.99) similarly average total international prostate symptom score was 17.93±4.62 (95%CI: 16.76 to 19.10). Rate of overall efficacy was 58.33%. The results of the study are found to be consistent with those previously reported with other α₁-blockers along with 2 mg tolterodine twice daily in patients with BOO + OAB.^{14,15} This shows that tamsulosin along with tolterodine, in particularly, improves the IPSS, although other uro-selective alpha-blockers and anticholinergic, have also been shown to improve the IPSS. In our study, it is apparent that subjects treated with tamsulosin with tolterodine had significant improvement than those treated with tamsulosin alone and it is statistically significant and comparable to international and national studies as well.¹⁶⁻¹⁸

CONCLUSION

In conclusion, this randomized control study clearly demonstrates that anticholinergic drugs, along with alpha-blockers, are quite effective and safe in patients of BPH having irritative (OAB) and obstructive symptoms.

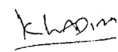


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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Khadim Hussain Awan	Contributions of conception and design, acquisition of data, analysis and interpretation of data.	
2	Riaz Hussain Awan	Drafting the article and shares its expert research opinion and experience in finalizing the manuscript.	
3	Seema Nayab	Contributed in conception and interpretation of data and give his expert view for manuscript designing.	
4	Faqir Muhammad Awan	Collection and acquisition of data, analysis and interpretation of data and make it suitable for final revision and a corresponding author.	