



## PROSTATIC HYPERPLASIA;

### COMPARISON BETWEEN TAMSULOSIN AND TERAZOSIN FOR EFFICACY IN MEDICAL MANAGEMENT OF LOWER URINARY TRACT SYMPTOMS SECONDARY TO PROSTATIC HYPERPLASIA

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**ABSTRACT:** Lower Urinary Tract Symptoms. Alpha-1 adrenoceptor antagonists are most frequently prescribed medical management for LUTS and among these tamsulosin and terazosin are the most common. **Objectives:** To access comparison of efficacy of tamsulosin and terazosin for management of LUTS due to prostatic hyperplasia in terms of International Prostate Symptom Score (IPSS). **Place and duration:** Study being conducted at Department of Urology and Kidney Transplantation, Allied Hospital, Faisalabad for period of 24 months from 01-07-2014 to 30-06-2016. **Methodology:** 659 male patients enrolled in study and randomly assigned to Group A (Patients being administered with tamsulosin) and Group B (Patients being administered with terazosin) and improvement in IPSS monitored over period of two weeks. **Results:** 659 patients enrolled with mean age+sd as 61.9+10.2 years. Group A includes 330 patients while Group B include 329 patients. Among Group A, 250 patients showed significant improvement in IPSS while in Group B, 215 patients showed significant response to medical management in terms of IPSS and both groups showed statistically comparative response. Statistical response of management also determined in terms of variables of IPSS severity, prostatic size and age of patient and found that efficacy of the two groups were statistically comparable for patients with mild IPSS while in patients with moderate IPSS has response to treatment with tamsulosin but no statistical association of efficacy for treatment with terazosin. No statistical response was found for improvement in symptoms in cases with severe IPSS in either groups. When response monitored in terms of prostate size in both groups, it was found that both groups have statistical response when prostate size is less than 35 grams, between 35-55 grams but in case when prostate size was more than 55 grams, no statistical response was found with group B patients. When response was measured in terms of variable of age, results were consistent with the fact that statistically significant response of efficacy was found in either groups for age group 45-55 years and 56-65 years but no statistical response was found for Group B when considered for age group more than 65 years. **Conclusion:** Based on results it is concluded that both tamsulosin and terazosin has got comparative results in overall response. However, tamsulosin has superiority in treatment when IPSS is moderate, prostate size is more than 55 grams and age of patient is more than 65 years.

**Key words:** Lower Urinary Tract Symptoms (LUTS), Prostatic Hyperplasia, Alpha-1 Adrenoceptor Antagonists, Tamsulosin, Terazosin.

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## INTRODUCTION

LUTS due to benign prostatic hyperplasia is disease of aging male and it is estimated that 25 % of men over 40 years age suffer from LUTS<sup>1</sup> and histological appearance of benign prostatic hyperplasia in autopsies is found as 20 % in men between age 41 years to 50 years, 50 % in men between 51 years to 60 years and above 90 % in

the men with age 80 years and above.<sup>2</sup> Patients with prostatic hyperplasia usually presents with LUTS resulting from irritative symptoms like urinary frequency, urgency, nocturia and urge<sup>3</sup> and obstructive symptoms like poor stream, difficulty in initiating urination, sensation of incomplete bladder emptying and dribbling of urine.<sup>4</sup> Various tools have been designed to assess severity

of LUTS and quantification of improvement/deterioration of patients symptoms. Such tools include IPSS and AUA symptom index score but IPSS is the most commonly used assessment tool.<sup>5</sup> Treatment modalities for LUTS include life style modification of patient, watchful observation, medical therapy and surgery.<sup>6</sup> As newer drugs are being introduced, trend for treatment of LUTS has changed from surgery towards medical treatment which has showed promising results.<sup>7</sup> Among pharmacological agents, alpha-1 adrenoceptor antagonists (tamsulosin, terazosin, doxazosin and alfuzosin)<sup>8</sup> and 5 alpha-reductaseinhibitor (finasteride)<sup>9</sup> are recommended for medical treatment of benign prostatic hyperplasia. Among these tamsulosin and terazosin are widely used agents because of their efficacy, cost effectiveness and availability across the globe. Terazosin has equal affinity for both alpha-1A and alpha-1B<sup>10</sup> so is titrated in dose from low to high so is associated with delayed response<sup>11</sup>, whereas tamsulosin achieves rapid effect without any dose titration<sup>12</sup> and tamsulosin is recognized as more effective agent in treatment of LUTS secondary to benign prostatic hyperplasia.<sup>13</sup> Both tamsulosin and terazosin impart their effect by blocking alpha receptors present in prostatic urethra, prostatic capsule and bladder trigone area, especially tamsulosin being uro-selective alpha blockers is associated with lesser systemic side effects. Both drugs targets the dynamic portion of obstruction caused by prostate, relaxes the outflow stream out of bladder neck and thus reduces symptoms of LUTS. A study being conducted with objective to assess comparison for efficacy in improvement of LUTS secondary to benign prostatic hyperplasia, between tamsulosin and terazosin and to access statistical association between efficacy of two said agents and variables like IPSS, prostate size and age of patient.

## METHODOLOGY

### Study design

Randomized open label study.

### Setting

Department of Urology and Kidney Transplantation, Allied Hospital, Faisalabad.

### Duration

The study was conducted for 24 months from 01-07-2014 to 30-06-2016.

### Sample size

659 male patients were enrolled in the study.

### Sampling technique

Non probable consecutive sampling.

### Inclusion criteria

Male patients with active lower urinary tract symptoms due to prostatic enlargement seeking consultation in out-door services.

### Exclusion criteria

Patients with active lower urinary tract infection, refractory retention, clinical history and examination suggestive of prostatic malignancy i.e. hematuria, bone pains, hard enlarged prostate on digital rectal examination and serum PSA level exceeding 4 ng/ml, patients with enlarged prostate with complications like bladder stone, bladder diverticulum, obstructive uropathy and uremia, patients with previous history of catheterization, patients with neurogenic bladder and patients with any history surgery for prostate disease.

### Procedure

All patients divided into two groups randomly i.e. Group A patients who were administered with oral tamsulosin preparation with dose of 0.4 mg OD at night and Group B patients administered with oral terazosin 2 mg OD at night and given for period of 2 weeks consecutively and assessed with International Prostatic Symptom Score (IPSS) pre and post medication circumstances and improvement by three numbers in IPSS was taken as clinically significant improvement.

Severity of IPSS as;

Score	Severity
0-7	Mildly symptomatic
8-19	Moderately symptomatic
20-35	Severely symptomatic

In the Past Month:	Not at All	Less than 1 in 5 Times	Less than Half the Time	About Half the Time	More than Half the Time	Almost Always	Your Score
1. <b>Incomplete Emptying</b> How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. <b>Frequency</b> How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. <b>Intermittency</b> How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. <b>Urgency</b> How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. <b>Weak Stream</b> How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. <b>Straining</b> How often have you had to strain to start urination?	0	1	2	3	4	5	
	<b>None</b>	<b>1 Time</b>	<b>2 Times</b>	<b>3 Times</b>	<b>4 Times</b>	<b>5 Times</b>	
7. <b>Nocturia</b> How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
<b>Total I-PSS Score</b>							

**Statistical tool**

Obtained data observed in terms of improvement in IPSS for either groups and association of variables of IPSS severity, prostate size and age of patients with IPSS improvement in two groups. Obtained data analyzed using SPSS 21 and chi square test applied as statistical tool for assessment and level < 0.05 taken as significant.

years age) with mean age+sd as 61.9+10.2 years. Group A patients who were administered with Tamsulosin includes 330 patients among whom 250 patients showed significant improvement in IPSS while in Group B who were administered with terazosin includes 329 patients among whom 215 patients showed significant response to medical management in terms of IPSS and both groups showed statistically comparative response. Patients were stratified according to variables (Table-I).

**RESULTS**

659 patients were enrolled in study and included patient from age 45 years and more (upper limit 80

Group	IPSS Severity			Prostate Size			Age		
	Mild	Moderate	Severe	<35 G	35-55 G	>55 G	45-55 Years	56-65 Years	>65 Years
Group A	100	164	66	87	110	133	83	155	92
Group B	102	157	70	98	108	123	80	162	87
Total	202	321	136	185	218	256	163	317	179

**Table-I. Patient stratification with variables**

Statistical response of management also determined in terms of variables of IPSS severity (Table-II), prostatic size (Table-III) and age of patient (Table-IV) and found that efficacy of the two groups were statistically comparable for patients with mild IPSS while in patients with moderate IPSS has response to treatment with tamsulosin but no statistical association of efficacy for treatment with terazosin. No statistical response was found for improvement in symptoms in cases with severe IPSS in either groups. When response monitored in terms of prostate size in both groups, it was

found that both groups have statistical response when prostate size is less than 35 grams, between 35-55 grams but in case when prostate size was more than 55 grams, no statistical response was found with group B patients. When response was measured in terms of variable of age, results were consistent with the fact that statistically significant response of efficacy was found in either groups for age group 45-55 years and 56-65 years but no statistical response was found for Group B when considered for age group more than 65 years.

Group	IPSS Severity								
	Mild			Moderate			Severe		
	Total	Response	P Value	Total	Response	P Value	Total	Response	P Value
Group A	100	71	.000	164	141	.000	66	38	.218
Group B	102	91	.000	157	83	.473	70	41	.151

Table-II. Statistics response for IPSS severity

Group	Prostate Size								
	<35 G			35-55 G			>55 G		
	Total	Response	P Value	Total	Response	P Value	Total	Response	P Value
Group A	87	57	.004	110	98	.000	133	95	.000
Group B	98	79	.000	108	69	.004	123	67	.321

Table-III. Statistics response for prostate size

Group	Age								
	45-55 Years			56-65 Years			>65 Years		
	Total	Response	P Value	Total	Response	P Value	Total	Response	P Value
Group A	83	59	.000	155	122	.000	92	69	.000
Group B	80	58	.000	162	117	.000	87	40	.453

Table-IV. Statistics response for patient age

**DISCUSSION**

Benign prostatic hyperplasia is one of the most common diagnosis for the men seeking medical advice in Urology clinics and the disease prevalence is age dependent, with presenting age for initial symptoms is mostly more than 50 years<sup>14</sup> evident by the figures as that the disease occurs in approximately 8% of men with age between 31 to 40 years, 42% of men in age group between 51 to 60 years, 71% of men with age 61 to 70 years, and about 88% of the men having lower urinary tract symptoms for age 81 years and above.<sup>2</sup> Clinically benign prostatic hyperplasia manifest itself with lower urinary tract symptoms which range in symptoms from frequency of urination, poor urinary stream, nocturia, hesitancy, urgency and forceful voiding.<sup>15</sup> The initial presentation for

the symptoms is mostly delayed and progression is slow.<sup>16</sup>

Patients are managed with watchful waiting<sup>17</sup>, life style modification, medical treatment and surgery (Open/minimally invasive) depending upon severity of the disease, complications associated with the prostatic enlargement and patient co-morbid factors.<sup>18</sup> Medical management of patients include administration of alpha blocker and 5-alpha reductase inhibitors. The α-adrenergic blockers include doxazosin, tamsulosin, silodosin, alfuzosin, and terazosin.<sup>19</sup> Mechanism for action of these agents is by their role to reduce smooth muscle tone in the prostate and the urinary bladder neck which helps in decreasing lower urinary tract symptoms (LUTS) which are

secondary to benign prostatic enlargement.<sup>18,19,20</sup> The 5- $\alpha$  reductase inhibitors for the treatment of LUTS include dutasteride and finasteride, which exert their role by acting as blocking agent for the conversion of testosterone to dihydrotestosterone which in response suppresses the growth of the prostate and thus results in improvement of LUTS.<sup>9</sup>

Work has been done in past to compare tamsulosin and terazosin for the efficacy results during medical management of LUTS secondary to BPH. A study conducted with fixed dose of 0.2 mg tamsulosin was compared with the step-up dosing pattern of 1–5 mg terazosin in a direct, single-blind, parallel-group comparison for duration of 4 and 8 weeks of treatment and the study concluded as 74% and 79% were considered International Prostate Symptom Score (IPSS) responders (> 20% decrease), 51% and 45% of the patients managed with tamsulosin and terazosin were considered  $Q_{max}$  responders (> 20% improvement) and 72% and 67% of the patients were found to have moderately improved symptoms with tamsulosin and terazosin, respectively.<sup>10</sup> Another study showed comparable results for tamsulosin and terazosin for improvements in symptoms and  $Q_{max}$ .<sup>21</sup> Although data is deficient for any effect of variables like prostate size, patient age and IPSS severity in terms of response of the two drugs, tamsulosin and terazosin, when compared. This study was conducted in order to access efficacy comparison of tamsulosin and terazosin for management of LUTS secondary to benign prostatic hyperplasia and assessment of response when compared in terms of variables of prostate size, patient age and IPSS severity.

## CONCLUSION

Based on results it is concluded that both tamsulosin and terazosin has got comparative results in overall response. However, tamsulosin has superiority in treatment when IPSS is moderate, prostate size is more than 55 grams and age of patient is more than 65 years.

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*“The greatest achievement is to outperform yourself.”*

**Denis Waitley**

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