

# COMPARISON OF PHYTOTHERAPY WITH ALPHA ADRENOCEPTERS BLOCKERS IN THE TREATMENT OF SYMPTOMATIC BENIGN PROSTATIC HYPERPLASIA

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## ABSTRACT

**Objective:** To compare the effectiveness of alpha blocker and phytotherapy in relieving the lower urinary tract symptoms (LUTS) in patients with Benign Prostatic Hyperplasia (BPH).

**Methodology:** This randomized controlled trial was conducted in Department of Urology, Institute of Kidney Diseases, Peshawar from June 2017 to December 2018. A total of 308 patients, divided randomly in two groups, with 154 patients in each group, were enrolled using consecutive sampling. Group A received tamsulosin (alpha blocker) while patients in group B were put on Saw Palmetto as Phytotherapy. International Prostate Symptom Score (IPSS) and Uro-flowmetry were recorded before the therapy after 1st, 2nd, 3rd and 6th months respectively. A pre-designed proforma was used to enter the data, which was analyzed on SPSS version 20.0. Descriptive and inferential statistics were calculated where needed.

**Results:** Mean age in group A was  $65.1 \pm 7.09$  years, while group B showed  $64.7 \pm 8.01$  years ( $p=0.442$ ). The mean of IPSS before initiation of treatment in group A was  $15.3 \pm 3.02$  and in group B it was  $16.2 \pm 3.04$  ( $p=0.07$ ), while post treatment IPSS at 6 months, in group A mean was recorded as  $8.5 \pm 7.4$  and in group B it was  $12.07 \pm 2.75$  ( $p=0.01$ ). In Uroflowmetry, group A showed mean pre-treatment maximum flow as  $8.4 \pm 1.3$  and in group B it was  $8.2 \pm 1.1$  ( $p=0.064$ ), while post-treatment maximum flow at 6 months for group A showed mean of  $11.8 \pm 1.5$  and group B had  $8.2 \pm 1.1$  ( $p=0.001$ ).

**Conclusion:** Alpha blockers are more effective than Phytotherapy in management of symptomatic BPH.

**Key Words:** Benign prostatic hyperplasia, Tamsulosin, Saw Palmetto, Phytotherapy

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## INTRODUCTION

Benign Prostatic Hyperplasia (BPH) is the most common benign tumor of men<sup>1</sup>. Based on published data on consequences and complications of the disease, BPH can be considered a progressive disease<sup>1</sup>. The specific risk factors for progression is age, prostate specific antigen (PSA) level and prostate volume and rising post void residual urine. BPH is a histological diagnosis characterized by proliferation of cellular elements of prostate. It involves the stromal and epithelial elements of prostate in peri-urethral and transitional zones of the gland, which results in enlargement of prostate restricting the flow of urine from bladder. A part of ageing process in men, BPH is also considered to be caused by hormonal imbalance, particularly, testosterone and di-hydrotes-

tosterone<sup>2</sup>.

The estimated prevalence is 25% in men aged between 40 to 79 years<sup>1</sup>. About 50% of men exhibit lower urinary tract symptoms (LUTS) by the age of 60 years and the number increases to 90% by the age of 85 years. Clinically the patient may have symptoms of urinary frequency, urgency, nocturia, decreased or intermittent force of stream, incomplete bladder emptying<sup>3</sup>. Regarding the treatment options, the main aim of all the treatments is to improve the quality of life as said by Hippocrates that "Quality of life is more important than life itself". The severity of symptoms is usually assessed by International Prostate Symptom Score (IPSS). Patients with mild to moderate BPH can be treated medically with alpha 1 receptor blockers, phosphate diesterase

inhibitors, 5 alpha reductase inhibitors and phytotherapeutic agents<sup>1-3</sup>.

The efficacy of the phytotherapy in relieving the LUTS has been documented in literature<sup>4</sup> but all those studies were lacking the comparison of efficacy with commercially available alpha blockers. The attraction of phytotherapeutic agents appears to be related to the perception of therapeutic healing powers of natural herbs, their ready availability, and lack of adverse effects. Phytotherapy used in LUTS secondary to BPH are extracted from barks, roots and seeds of plants containing phytosterols, fatty acids, lectins, flavanoids, plant oils and polysaccharides<sup>4</sup>. The exact mechanism of action for herbal products is not known but it is postulated that it acts by possessing anti-androgenic, pro-apoptotic, and anti-inflammatory<sup>5</sup> effects. Phytotherapeutic agents are considered as an emerging therapy by the American Urology Association (AUA) guidelines but not yet recommended in the treatment of BPH due to lack of evidence. Fagelman in his meta analysis on Saw Palmetto as Phytotherapy reported that it was most widely used over the counter medication for symptomatic BPH in United States of America (USA) and Europe<sup>5</sup>. Some, however, believe that the overall effectiveness is still questionable on the basis of suboptimal studies<sup>5-7</sup>.

The rationale of the study is based upon the research question that does phytotherapy possess equal effectiveness in relieving bothersome symptoms of BPH. It is important because the mushroom growth and promotion of phytotherapy in market has to be addressed scientifically in the era of evidence based medicine. The objective of the study was to compare the effectiveness of tamsulosin as alpha blocker and phytotherapy in relieving the LUTS in patients with benign prostatic hyperplasia.

## METHODOLOGY

This randomized controlled trial was conducted at Department of Urology, Institute of Kidney Diseases, Peshawar, from June 2017 to December 2018. A total of 308 patients, enrolled in this study, were divided into 2 groups by lottery method with 154 in each group. All the patients between age group of 50 to 90 years with LUTS and moderate IPSS score were included in the study. Patients who had LUTS due to causes other than BPH like neurogenic bladder, hematuria and urethral stricture, patients who were using drugs other than alpha blockers or phytotherapy e.g. 5 alpha reductase inhibitors, and all those patients who had surgery for prostate, were excluded from study.

Permission from ethics committee of the hospital was taken All patients who fulfilled the above mentioned criteria and gave informed consent were included in the study. Group A were given tamsulosin (alpha

blocker) 0.4 mg once daily, while group B were given phytotherapy, Saw palmetto 320 mg daily. LUTS were recorded with IPSS score and Uroflowmetry before the therapy and after 1st, 2nd, 3rd and 6th months respectively. A pre-designed proforma was used to enter the data and was analyzed on SPSS version 20. Independent sample t-test was applied to test difference of means between the two groups.

## RESULTS

The mean age in group A was recorded to be  $65.1 \pm 7.09$  years, while in group B it was  $64.7 \pm 8.01$  years ( $p=0.442$ ). The age distribution in both of the groups is shown in table 1. Alpha blocker in group A showed rapid decline in symptoms at 4 week as compared to phytotherapy group, the details are displayed in figure 1. In terms of means of IPSS, group A had significant decline in IPSS (6.8 points). The details of mean IPSS before the initiation of treatment and at follow up of 6 months in both groups are shown in table 2.

Objective clinical improvement was recorded in maximum flow and average flow rates measured by Uroflowmetry in group A, details are shown in table 3.

## DISCUSSION

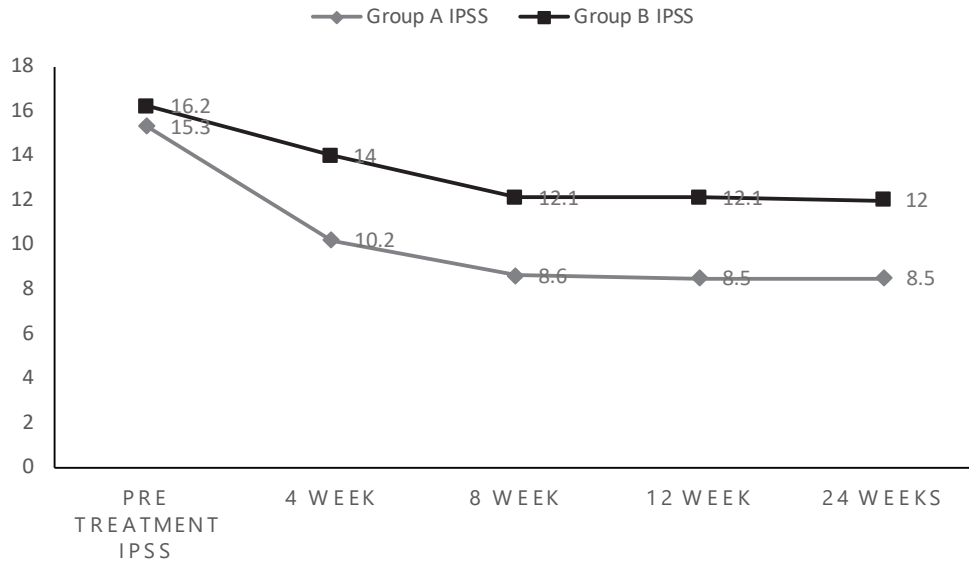
BPH is the most common benign tumor of aging male. The median age of the clinical presentation of BPH in west is 53 years<sup>1,8,9</sup>, but owing to lack of health education in countries like Pakistan, the mean age of presentation of patients with BPH recorded in this study was above 60 years. Alpha blockers are considered as first line medication for the management of symptomatic BPH. The phytotherapy has been introduced widely in the market with claims of equal effectiveness as alpha blockers in management of BPH. Our study indicated that tamsulosin was superior to Saw Palmetto. IPSS value at the end of 6 months for tamsulosin was 8.5 from pretreatment IPSS value of 15.3, while the IPSS mean for phytotherapy was 12.07 after six months as compared to pretreatment mean of 16.2. So, the mean decrease in IPSS score in group A was 6.8 versus 4.2 in group B. This means that the clinical improvement in LUTS was more marked in patients who used tamsulosin as compared to those on phytotherapy.

Alpha blockers are considered as first line medication for the management of moderately symptomatic BPH<sup>10-12</sup>. The multiple herbal products are currently used over the counter in management of BPH<sup>13-15</sup>. There has been conflicting reports on over all efficacy of Saw Palmetto as herbal effect<sup>5,16</sup>. Nadeem, et al. in a comparative study of Phytotherapy versus Terazosin reported higher efficacy for Phytotherapy. However, they didn't disclose the type of phytotherapy as they mentioned only "Anti BPH Capsule"<sup>17,18</sup>. The sample size of their study was only 50 which was very low as compared to

**Table 1: Age distribution of patients (n=308)**

Age	GROUP A (Alpha Blocker)	Group B (Phytotherapy)
50-60 years	85 (55%)	82 (52%)
61-70 years	55 (35.7%)	57 (37%)
71-80 years	14 (9%)	15 (9.7%)
Total	154 (100%)	154 (100%)
Mean and SD	62 year ± 10.34	60 year ± 8.98

**Figure 1: Graph showing decrease in decline of IPSS in both Groups (p=0.001)**



**Table 2: Mean pre treatment IPSS and post treatment IPSS at 6 months**

International Prostate Symptom Score (IPSS) Mean±SD	Group A (Alpha Blocker)	Group A (Alpha Blocker) Group B (Phytotherapy)	P value
Pre-Treatment IPSS	15.3 ± 3.02	16.2 ± 3.04	0.07
Post-Treatment IPSS at 6 months	8.5 ± 7.4	12.07 ± 2.75	0.01

**Table 3: Mean pre treatment and post treatment urinary flow rates**

Uroflowmetry Mean (SD) (ml/sec)	Group A (Alpha Blocker)	Group B (Phytotherapy)	P value
Pre-Treatment Maximum flow	8.4 ± 1.3	8.2 ± 1.1	0.064
Post-Treatment Maximum flow at 6 months	11.8 ± 1.5	8.2 ± 1.1	0.001
Pre treatment Average flow	6.2 ± 1.4	5.99 ± 1.3	0.53
Post-Treatment Average Flow at 6 month	8.3 ± 1.7	7.1 ± 2.1	0.67

our study. However, Kwon Y, et al. supported our stance in his study of larger sample size<sup>19</sup>.

In another study conducted by Ibishev, et al. in 2019<sup>20</sup>, superior efficacy of Saw Palmetto was reported in combination with other herbal products in patients with BPH associated with prostatitis. So the probable benefit of herbal product seems to be more in inflammatory process<sup>20</sup>. Ibishev, et al. in their article did not compare the efficiency of phytotherapy with alpha blockers. Similar results were observed in another study conducted by Bent S, et al. in which symptomatic improvement in patients with BPH was recorded in patients using Saw palmetto, in terms of IPSS after one year and this was found superior to placebo<sup>21</sup>. Kion Y and Dogra PN have reported that alpha blockers and Phytotherapy were equally effective in the symptomatic management of BPH<sup>19,22</sup>, however, the limitation of their studies was non randomization and small sample size.

In this study, alpha blockers were superior in both subjective component of decreasing the IPSS and objective component in improving max flow and average flow on uroflowmetry supported by another study in literature<sup>20</sup>. Yuan JQ, et al. mentioned great improvement in relieving symptoms and Uroflowmetry with alpha blocker as compared with Phytotherapy<sup>8</sup>. In Another study conducted by Alcaraz A, et al. the alpha blockers were most effective in reduction of 6.3 IPSS points versus phytotherapy which only decreased 2.1 points with significant improvement of 68% for alpha blockers<sup>9</sup>. These findings are in accordance with present study, as we also reported 45% improvement in symptomatic improvement of patients with BPH. In a meta-analysis published in 2012, regarding the role of phytotherapy in BPH, it was concluded that phytotherapy failed to significantly decrease the IPSS and increase the voided volume in comparison with alpha blockers<sup>23</sup>. The findings of Cochrane Review are in accordance with present study<sup>24</sup>.

The strength of the study is that it was a randomized controlled trial of larger sample size; had good follow up of 6 months and without any conflict of interest. The weakness of the study is that due to some constraints, we could not do blinding of the study.

The Urologists, family physicians and general practitioners can draw useful inference from the results of present study. As our study design was centered towards the effectiveness of alpha blockers and Phytotherapy. Nevertheless the adverse effects of alpha blockers are widely known in literature which is almost nil for the phytotherapy. So, further studies are desired especially for ascertaining the safety profile of phytotherapy.

## CONCLUSION

The Alpha blockers are more effective than Phytotherapy in management of symptomatic Benign Prostatic Hyperplasia (BPH).

## REFERENCES

1. Ali L, Orakzai N, Ali M. Transvesical Prostatectomy in elderly patients: an experience at Saidu Teaching hospital Swat. *Ann Pak Inst Med Sci* 2008; 4:148-51.
2. Lepor H, Williford WO, Barry MJ, Brawer MK, Dixon CM, Gormley G et al. The efficacy of terazosin, finasteride, or both in Benign Prostatic Hyperplasia. Veterans Affairs Cooperative Studies Benign Prostatic Hyperplasia study group. *N Engl J Med* 1996; 335:533-40.
3. Macdonald R, Tacklind JW, Rutks I, Wilt TJ. Serena repens, monotherapy for Benign Prostatic Hyperplasia (BPH): an updated cochrane systematic review. *Br J Urol Int* 2012; 109:1756-61.
4. Bent S, Kane C, Shinohara K, Neuhaus J, Hudes ES, Goldberg H et al. Saw palmetto for benign prostatic hyperplasia. *N Engl J Med* 2006; 354:557-66.
5. Fagelman E, Lowe FC. Saw Palmetto Berry as a Treatment for BPH. *Rev Urol* 2001; 3:134-8.
6. Gerber GS. Saw palmetto for the treatment of men with lower urinary tract symptoms. *J Urol* 2000; 163:1408-12.
7. Wilt TJ, Ishani A, Stark G, MacDonald R, Lau J, Mulrow C. Saw palmetto extracts for treatment of benign prostatic hyperplasia. A systematic review. *J Am Med Assoc* 1998; 280:1604-9.
8. Yuan JQ, Mao C, Wong SYS, Yang ZY, Fu XH, Dai XY et al. Comparative effectiveness and safety of monodrug therapies for lower urinary tract symptoms in patients with BPH. *Medicine (Baltimore)* 2015; 94:e974.
9. Alcaraz A, Rodriguez JC, Urzaiz MU, Lopez RM, Cerda JLR, Rubio FR et al. Quality of life in patients with lower urinary tract symptoms associated with BPH: Change over time in real-life practice according to treatment – the qualiprost study. *Int Urol Nephrol* 2016; 48:645-56.
10. Russo A, Capogrosso P, Croce GL, Ventimiglia E, Boeri L, Briganti A et al. Sereonarepens, selenium and lycopene to manage lower urinary tract symptoms suggestive for benign prostatic hyperplasia. *Expert Opin Drug saf* 2016; 15:1661-70.
11. Kim SW. Phytotherapy: Emerging therapeutic option in urologic disease. *Transl Androl Urol* 2012; 1:181-91.
12. Keehn A, Taylor J, Lowe FC. Phytotherapy for benign prostatic hyperplasia. *Curr Urol Rep* 2016; 17:53.
13. Nickel JC, Mendez-Probst CE, Whelan TF, Paterson RF, Razvi H. 2010 update: Guidelines for management of Benign Prostatic Hyperplasia. *Can Urol Assoc J* 2010; 4:310-6.

14. Boggs W. Increased Risk of severe hypotension in men treated with tamsulosin. Medscape Medical News. [Accessed December 7, 2013]. Available at <http://www.medscape.com/viewarticle/815216>.
15. Bird ST, Delaney JAC, Brophy JM, Etminan M, Skeldon SC, Hartzema AG. Tamsulosin treatment for benign prostatic hyperplasia and risk of severe hypotension in men aged 40-85 years in the United States: risk window analyses using between and within patient methodology. *Br Med J* 2013; 347:f6320.
16. Guelce D, Thomas D, Elterman D, Chughtai B. Recent advances in managing benign prostatic hyperplasia: The Rezūm System. *F1000Res* 2018; 7:F1000 Faculty Rev-1916.
17. Nadeem HMR, Mohiuddin E, UdDin S, Daniyal M, Us-manghani K. Comparison of anti BPH capsule (herbal) and terazosin HCl in the treatment of benign prostate hyperplasia. *Pak J Pharm Sci* 2017; 30:289-93.
18. Langan RC. benign prostatic hyperplasia. *Prim Care* 2019; 46:223-32.
19. Kwon Y. Use of saw palmetto (*Serenoa repens*) extract for benign prostatic hyperplasia. *Food Sci Biotechnol* 2019; 28:1599-606.
20. Ibishev KS, Krainy PA, Mitusov VV, Sizyakin DV, Magomedov GA. A comparative analysis of the effectiveness of *Serenoa repens* and *Serenoa repens* in combination with *Urtica dioica* for lower urinary symptoms suggestive of benign prostatic hyperplasia associated with chronic inflammation in prostate tissue. *Urologia* 2019; 1:40-6.
21. Bent S, Kane C, Shinohara K, Neuhaus J, Hudes ES, Goldberg H et al. Saw palmetto for benign prostatic hyperplasia. *N Engl J Med* 2006; 354:557-66.
22. Dogra PN, Biswas NR, Ravi AK, Mani K, Kumar V. Comparative evaluation of Prostina and terazosin in the treatment of benign prostatic hyperplasia. *J Indian Med Assoc* 2005; 103:108-10.
23. Tacklind J, Macdonald R, Rutks I, Stanke JU, Wilt TJ. *Serenoa repens* for benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2012; 12:CD001423.
24. Cambio AJ, Evans CP. Outcomes and quality of life issues in the pharmacological management of benign prostatic hyperplasia (BPH). *Ther Clin Risk Manag* 2007; 3:181-96.

### CONTRIBUTORS

LA conceived the idea, planned the study and drafted initial manuscript. FH, SO helped acquisition and analysis of data and critically revised the manuscript. S, Q and KT helped in critical revision, statistical analysis and finalization of the manuscript after reviewers' suggestions. All authors contributed significantly to the submitted manuscript.