

## **Prazolin as a treatment for benign prostatic hypertrophy: a study in a tertiary care centre**

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**Received:** 10 April 2016

**Accepted:** 18 April 2016

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### **ABSTRACT**

**Background:** Benign prostatic hypertrophy (BPH) is one of the most common disorders effecting elderly men resulting in lower urinary tract symptoms (LUTS), including urinary frequency, retention, nocturia, intermittent force of the urinary stream, sensation of incomplete bladder emptying etc. The medical treatment preferred of late is with alpha-1 blockers or 5-alpha-reductase inhibitors or anti androgens. Prazosin, an older alpha-1 adrenergic blocker is considered a very useful drug in the treatment of PBH.

**Methods:** 97 patients, above 45 years of age and diagnosed with mild to moderate benign prostatic hyperplasia with lower urinary tract symptoms were included into the study. All patients were given prazosin 0.5 mg orally twice daily for a week. After 1 week, the night dose was increased to 1mg form 0.5 mg while the morning dose remained as 0.5 mg. All the patients were asked to record their symptoms for three days before each visit to the hospital. The parameters to record were nocturia, frequency, urgency, straining, force of urine and decreased force of urine, intermittency, and sensation of the urine residue. All these parameters were recorded on a scale of 0-5, where 0 is the total absence of symptoms and 5 is the most severe symptom.

**Results:** There was an improvement in the systolic and the diastolic blood pressure after 4 weeks of treatment. There was marked improvement in the urine output in the patients after 4 weeks of treatment. There was reduction in the nocturia and the frequency of urine by the patient. There was significant reduction in the urgency and the hesitancy of the urine. About 71 (80%) patients showed improvement in the sense of residual urine by the patients, while 66(74%) showed improvement in the terminal dribbling of urine. 65 (73%) of the patients showed relief from prolonged micturation, while nocturia and day time frequency showed improvement in over 60% of the cases.

**Conclusions:** We therefore conclude that prazosin is also a very effective drug for the treatment of BPH, in terms of the urine outflow and decreased frequency and nocturia.

**Keywords:** Prazosin, Benign prostate hypertrophy, Lower urinary tract symptoms

### **INTRODUCTION**

Benign prostatic hypertrophy (BPH) is one of the most common disorders effecting elderly men. BPH is the 4<sup>th</sup> most commonly diagnosed disease among men above 50 years of age, after coronary disease and hyperlipidemia, hypertension, and type 2 diabetes.<sup>1</sup> It is estimated that a man above 50 years of age has 10-20% chance of requiring treatments for BPH.<sup>2</sup> It is one of the most common benign human neoplasms.<sup>3</sup>

BPH is mainly caused because of the rapid and nonmalignant division of the stromal and epithelial cells in the prostate gland. It causes bladder outflow obstruction both via static factor due to the mechanical compression due to the increase in the volume of the prostate and by the fluctuating dynamic influence resulting from alterations in the neural control of prostate muscle.<sup>4</sup>

Many a times, BPH is many types of lower urinary tract symptoms (LUTS), including urinary frequency, retention, nocturia, intermittent force of the urinary

stream, sensation of incomplete bladder emptying etc. Not all men with PBH have an enlarged prostate.

Most of the times, if the symptoms are mild, the best way would be just to watch and wait until the pharmacological treatment is required. Surgical intervention is the treatment of choice in severe cases.<sup>5</sup> But this type of treatment is associated with a great deal of morbidity.<sup>6</sup> The reoperation rate is about 2.8-8% at 5 years and upto 12-15% at 8 years following Trans-Urethral Resection Prostate (TURP).<sup>6-8</sup> The morbidity and sometimes associated mortality along with the slow clinical progression of the benign prostatic obstruction and recent public awareness has resulted in the advent of alternate treatment for this condition.<sup>9</sup>

The medical treatment preferred of late is with alpha-1 blockers or 5-alpha-reductase inhibitors or anti androgens. The utility of alpha adrenergic blockers is based on their ability to inhibit bladder outlet obstruction that is related to alpha-1 adrenergic mediated contraction of prostatic smooth muscle<sup>5</sup>. Prazosin, an older alpha-1 adrenergic blocker is considered a very useful drug in the treatment of PBH.<sup>10</sup>

There have been few studies in the affectivity of Prazosin on BPH in our area. Hence we performed this study.

## METHODS

This study was conducted by the Department of pharmacology on 97 patients diagnosed with benign prostatic hyperplasia who attended the Urology outpatient department at NRI Medical College with a history of dysuria.

After getting the clearance from the institutional ethical committee, Informed consent was obtained from all the patients involved in the study. The patients (all male) were above 45 years of age and diagnosed with mild to moderate benign prostatic hyperplasia with lower urinary tract symptoms. All these patients did not have any indication for prostatectomy.

A detailed medical history was taken from all the patients including demographic details. Patients with diabetes mellitus, history of cardiovascular disease or cerebrovascular disease or other severe associated disease, patients with earlier prostatectomy were excluded from the study. Patients were not allowed to take drugs which could influence the outcome of the study such as alpha and beta adrenoceptor agonists and antagonists, anticholinergics, antiandrogens.

The diagnosis of benign prostatic hyperplasia was based on the medical history, physical examination like digital rectal examination of the prostate, transabdominal ultrasonography, urinary flow rates using uriflowmetry. Absence of diabetes, urinary tract infection and any other renal diseases was also considered.

All patients were given prazosin 0.5 mg orally twice daily for a week. Prazosin causes an acute symptom complex which is characterized by dizziness and fainting spells with severe hypotension. After the first dose, the patients are observed for 4-6 hours in the hospital for any side effects. After observing that there was no postural hypotension, they were discharged. After 1 week, the night dose was increased to 1mg from 0.5 mg while the morning dose remained as 0.5 mg. The patients were asked to return for check up every week and in case of any adverse side effects. At the time of the check-up, blood pressures were recorded, analysis of cardiovascular parameters were measured. The patients were followed up for a total of weeks and clinical parameters and any side effects were noted.

All the patients were asked to record their symptoms for three days before each visit to the hospital. The parameters to record were nocturia, frequency, urgency, straining and force of urine and decreased force of urine, intermittency, and sensation of the urine residue. All these parameters were recorded on a scale of 0-5, where 0 is the total absence of symptoms and 5 is the most severe symptom, based in the International Prostatic symptom Score (IPSS). Mean of the 3 days were calculated.

At the end of the study, all the clinical parameter and the lab tests were repeated to observe any adverse results.

The statistical analysis was done by t test and Wilcoxon Sign Rank test.

## RESULTS

Out of the 97 patients, 8 were excluded from the study. 3 of them had adverse side effects and 5 of them failed to turn up for the follow up.

The final results were noted after the 4 week observation and compared with the base line values.

There was no significant difference in the weight or BMI of the patient, though there was an improvement in the systolic and the diastolic blood pressure. There was no difference on the prostate volume either.

There was marked improvement in the urine output in the patients after 4 weeks of treatment. There was reduction in the nocturia and the frequency of urine by the patient. There was significant reduction in the urgency and the hesitancy of the urine (Table 1).

About 71 (80%) patients showed improvement in the sense of residual urine by the patients, while 66 (74%) showed improvement in the terminal dribbling of urine. 65 (73%) of the patients showed relief from prolonged micturition, while nocturia and day time frequency showed improvement in over 60% of the cases (Table 2).

**Table 1: Comparison of the details between before and after treatment with prazosin.**

Parameters	Before treatment	After treatment
Age	64.7 ± 4.1	
Prostate volume (gms)	43.1 ± 5.1	
Nocturia	2.14 ± 0.17	1.82 ± 0.24
Day time frequency	2.72 ± 0.13	1.83 ± 0.41
Urgency	1.91 ± 0.18	0.67 ± 0.08
Hesitancy	1.85 ± 0.04	0.73 ± 0.07
Terminal dribbling	0.29 ± 0.14	0.07 ± 0.01
Straining	1.43 ± 0.06	0.79 ± 0.04
Sense of residual urine	1.59 ± 0.19	0.92 ± 0.09
Prolonged micturation	2.14 ± 1.10	1.02 ± 0.76
Micturation force	2.67 ± 1.02	1.46 ± 0.23
Intermittency	1.95 ± 0.99	1.11 ± 0.47
Peak flow (ml/sec)	8.01 ± 0.84	11.13 ± 2.04
Average flow (ml/sec)	3.26 ± 0.43	6.02 ± 0.33
Blood pressure		
Systolic	140 ± 11	135.4 ± 3.05
Diastolic	86.2 ± 3.1	81.3 ± 4.5

**Table 2: Number of patients showing improvement in the urine output.**

Variables	Number of patients showing improvement
Nocturia	57 (64.1%)
Day time frequency	59 (66.3%)
Urgency	48 (53.9%)
Hesitancy	61 (68.5%)
Terminal dribbling	66 (74.2%)
Straining	58 (65.2%)
Sense of residual urine	71 (79.8%)
Prolonged micturation	65 (73%)
Micturation force	59 (66.3%)
Intermittency	44 (49.4%)

## DISCUSSION

For a long time the most effective treatment for PBH was surgery.<sup>11</sup> Although this was the gold standard, 0.2% incidence of perioperative mortality was observed apart from side effects such as retrograde ejaculation.<sup>12</sup>

It was in 1981 when Caine, et al reported that phenoxybenzamine was an efficient treatment for BPH. Since then, there have been a few advances in treatment namely,  $\alpha$ -adrenoceptor antagonists to treat this condition.<sup>13</sup> These are the first-generation, non-selective  $\alpha/\alpha 2$  antagonist (e.g. phenoxybenzamine), the selective  $\alpha$ -antagonists (e.g. the short acting agents prazosin and alfuzosin, as well as the long acting drugs such as terazosin and doxazosin). Tamsulosin is a  $\alpha 1A$ -adrenoceptor antagonist.<sup>14</sup>

As there were a number of adverse reactions for the non-selective first generation adrenoceptor, the selective  $\alpha$ -antagonists have been preferred.<sup>15</sup>

Since Caine, et al reported the therapeutic efficacy of phenoxybenzamine in BPH,  $\alpha$ -adrenoceptor antagonists of three different types have been used to treat this condition.<sup>6</sup> These are the first-generation, nonselective  $\alpha 1/\alpha 2$ -antagonists (e.g. phenoxybenzamine), the selective  $\alpha$ -antagonists (e.g. the short-acting agents prazosin and alfuzosin and the long-acting drugs, terazosin and doxazosin) and the prostate-specific  $\alpha 1A$  -adrenoceptor antagonists, e.g. tamsulosin.<sup>13</sup>

There have been very few studies on Prazosin in the management of BPH as compared to the other selective alpha adrenergic blockers, especially after Americal Urology Association blushed its BPH guidelines.<sup>10</sup>

The AUA guidelines states that 4 alpha-adrenergic blockers that can be considered for the treatment of BPH and for patients with lower urinary tract syndrome, secondary to BPH are alfuzosin, doxazosin, tamsulosin, and terazosin.<sup>10</sup> These guidelines also state that the data to support prazosin as an effective agent for treatment of the disease is insufficient. Hence, this study was conducted.

In the present study, prazosin was effective in lowering the blood pressure in the hypertensive patients. This was observed in another study by Tsujii, et al wherein he compared the efficacy of Prazosin, Terazosin, and Tamsulosin for the treatment of BPH and found that there was significant lowering of blood pressure after the treatment of Prazosin and Terazosin.<sup>16</sup>

There was significant improvement of urine flow among the patients with a marked increase in the peak and average flow. This resulted in an improvement in the nocturia and daytime frequency. There was a significant decrease in the hesitance and urgency as well, with minimal terminal dribbling and straining. More than 60% of the patients showed marked improvement in all these categories. After 2 weeks of treatment, although there was a slight improvement in the urine outflow, the difference was not significant. This was seen in other studies also where a minimum of 4 weeks treatment was essential to observe a difference.<sup>13-15</sup>

Similar results were observed by Basalingappa, et al who also observed an improvement of more than 60% in most of the parameters.<sup>17</sup>

The mechanisms of the  $\alpha$ -1 blockers to improve the irritative symptoms of the BPH are still unclear. It is estimated to be related to the obstruction-induced changes in the bladder function that lead to detrusor instability or decreased compliance. Therefore, this alpha 1- blockers has a direct effect on the bladder to increase the bladder capacity and provide relief to the patient.<sup>18</sup>

There is an improvement of 52.6% in the urine flow rate with the treatment of alpha 1 blocker, which is, considerably less than would be expected after surgery, illustrating the differences in the goals of both therapies.<sup>17</sup>

Treatment through medication is a preferred mode of treatment of BPH nowadays and as a result several new drugs are now available. Alpha-1-adrenoceptor antagonists and 5 $\alpha$  reductase-blockers are preferred for the treatment. 5 $\alpha$  reductase-blockers are known to reduce the static component of benign prostatic obstruction by decreasing the size of the prostate, while  $\alpha$  1-adrenoceptor antagonists can relieve LUTS from BPH by reducing the dynamic component of obstruction, thus making these drugs preferable for treating [patients with smaller prostates.<sup>19</sup> Therefore suitable doses of these drugs should be given for effective treatment.

't' is apparent that medication is becoming the preferred option for managing BPH and several new drugs, e.g.  $\alpha$ 1-adrenoceptor antagonists and 5 $\alpha$ -reductase blockers, are now available to treat this condition. 5 $\alpha$ -reductase inhibitors reportedly reduce the static component of benign prostatic obstruction by decreasing the size of the prostate. Alternatively,  $\alpha$ 1-adrenoceptor antagonists can relieve LUTS from BPH by reducing the dynamic component of obstruction, making these agents preferable for treating patients with smaller prostates.<sup>24</sup> Suitable doses of these drugs vary according to race, constitution and the socio-economic condition of the country. Careful comparative studies of these drugs are necessary to establish the ideal therapeutic strategy for symptomatic Since Caine et al. reported the therapeutic efficacy of phenoxybenzamine in BPH,  $\alpha$ -adrenoceptor antagonists of three different types have been used to treat this condition.<sup>6</sup> These are the first-generation, nonselective  $\alpha$ 1/ $\alpha$ 2-antagonists (e.g. phenoxybenzamine), the selective  $\alpha$ -antagonists (e.g. the short-acting agents prazosin and alfuzosin and the long-acting drugs, terazosin and doxazosin) and the prostate-specific  $\alpha$ 1A -adrenoceptor antagonists, e.g. tamsulosin.<sup>13</sup>

## CONCLUSION

We therefore conclude that Prazosin is also a very effective drug for the treatment of BPH, in terms of the urine outflow and decreased frequency and nocturia. The results are mostly observed after 4 weeks of treatment.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Kumar DP, Ravishankar K. Prazolin as a treatment for benign prostatic hypertrophy: a study in a tertiary care centre. *Int J Basic Clin Pharmacol* 2016;5:639-42.