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Medical Management of Benign Prostate Hyperplasia and its Outcome

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Abstract

Introduction: Benign prostatic hyperplasia, one of the most common diseases among ageing men. BPH prevalence increases from approximately 50% at 60 years to 90% in men older than 85 years. Lower urinary tract system significant impact on the overall quality of life.The treatment options include: **1.** Watchful waiting: if the symptoms are mild and not causing any change. **2.** Medical treatment - Alfa-receptor antagonists, 5 alfa-reductase antagonists, antimuscarinics, phosphodiesterase 5 inhibitors and their combinations. **3.** Surgical management is preferred in patients with an IPSS score more than 19-traditional monopolar Transurethral resection of the prostate (TURP), Prostatic Urethral Lift.

Aims and Objectives

Aim of the study: To study the outcomes of medical management of BPH based on the IPSS. Objectives of the study: *Primary Objective:* To study the outcomes of medical management of BPH in terms of reduction of IPSS, change in prostate size, post-void residual volume as assessed by USG with medical management. *Secondary Objectives:* 1. To study the age distribution in BPH 2. To study the symptomatology of BPH.

This prospective observational study was carried out. A total of 55 patients presenting with lower urinary tract symptoms secondary to BPH were enrolled for the study. International Prostate Symptom Score was assessed on presentation and patient was started on either monotherapy or combination therapy depending on the prostate volume and then reassessed at 3 and 6 months after starting drug therapy.

Conclusion: Medical treatment for LUTS/BPH aims to produce rapid, sustained, and safety improvements in the lower urinary tract symptoms associated with benign prostatic hyperplasia that affect the quality of life in the majority of men over the age of 45. Combined therapy of an α1-adrenergic receptor antagonist (tamsulosin) plus a 5-alpha reductase inhibitor (dutasteride) is a good approach

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for meeting these objectives.

Keywords: Benign prostate hyperplasia, Medical management, Tamsulosin, Duterastide, Lower urinary tract symptoms, Acute retention of urine, Prostate volume, Postvoid residual volume.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is the non-malignant enlargement of the prostate gland. It refers to stromal and glandular epithelial hyperplasia that occurs in the periurethral transition zone of the prostate that surrounds the urethra resulting in compression of the urethral canal to cause partial, or sometimes virtually complete, obstruction of the urethra, interfering with the normal flow of urine and leads to the symptoms of urinary obstruction and irritation, collectively referred to as lower urinary tract symptoms (LUTS).[1,2]

Male LUTS can be classified into three categories, voiding (hesitancy, slow stream, intermittency, incomplete emptying), storage (frequency, urgency, nocturia, urge urinary incontinence) and postmicturition (Postvoid dribbling).[1,2]

Medical therapy for BPH attempts to shrink or stop the growth of the prostate or open the urethral channel within the prostate, without using surgery. The FDA has currently approved multiple drugs to relieve the symptoms associated with an enlarged prostate. Medications in the class known as 5-alpha-reductase inhibitors (5-ARIs) result in decreased production of the hormone dihydrotestosterone (DHT), which is responsible for the growth of the acinar glands of the prostate. These include Finasteride, FDA-approved in 1992, and dutasteride, FDAapproved in 2001. The 5-ARIs may either prevent the progression of growth of the prostate or shrink the prostate in some men. Another class of drugs used for treating BPH is the alpha-1-adrenergic receptor blockers (alpha-blockers), which act by relaxing the smooth muscle of the prostate and bladder neck to improve urine flow and reduce bladder outlet obstruction. This class includes terazosin, doxazosin, tamsulosin, and alfuzosin. Terazosin and doxazosin were developed as blood pressure pills, but tamsulosin and alfuzosin were developed specifically to treat BPH. There is excellent clinicaltrial data that shows that combination therapy with a 5-ARI and an alpha-blocker (finasteride and doxazosin) together is more effective than using either drug alone to relieve symptoms and prevent BPH 56 progression. The dual-drug regimen reduced the risk of BPH progression by 67 percent, compared with 39 percent for doxazosin alone and 34 percent for finasteride alone.[2,3]

The major goals in the treatment of BHP include improvement in symptom scores, quality of life, patient satisfaction and lowering the risk of disease progression and the need for further surgical interventions.[3,4]

The American Urologists Association have given Symptom Index (AUASI) and International Prostate Symptom Score (IPSS) which are now 2 considered the gold standard measurement tools for the assessment of BPH symptoms and response to treatment in clinical practice.[4]

Medical treatment is offered to men who have bothersome LUTS using Alfa-receptor antagonists, 5 alfa-reductase antagonists, antimuscarinics, phosphodiesterase 5 inhibitors and their combinations.[5,6]

The purpose of our study was to see the outcome of medical management in benign prostatic hyperplasia in the department of general surgery at the tertiary care centre.

AIMS AND OBJECTIVES

Aim of the study: To study the outcomes of medical management of Benign prostate hyperplasia based on the International Prostate Symptom Score.

Objectives of the study

Primary Objective: To study the outcomes of medical management of BPH in terms of reduction of IPSS, change in prostate size, post-void residual volume asassessed by USG with medical management.

Secondary Objectives: 1. To study the age distribution in BPH, 2. To study the symptomatology of BPH.

MATERIALS AND METHODS

This prospective observational study was carried out at a Tertiary care centre in a government set up over two years from September 2019 to September 2021 after approval by the Institutional Ethical committee.

A total of 55 patients presenting with lower urinary tract symptoms secondary to BPH were enrolled for the study. Due to the Covid-19 Pandemic, there was reduced patient input in both Outpatient and In-patient departments in this period of time. The effort was taken to contact patients using a mobile survey and during follow up the patient was examined by taking Pandemic precautions. A detailed clinical history was taken from all patients followed by thorough clinical examination, urine routine examination, ultrasonography and PSA. The drug was given based on International Prostate Symptom Score (IPSS) and prostate volume. Based on IPSS and prostate volume; monotherapy in the form of Tamsulosin 0.4mg was given to 35 patients with Moderate to Severe IPSS and Prostate Volume less than 40cc while a combination of tamsulosin with dutasteride was given to patients with moderate to severe IPSS and prostate volume more than 40 cc. Patients were also informed about the possible Side-effects. Patients were asked to follow up after 3 months and 6 months and their IPSS, prostate volume and pre and Postvoid volume were measured. Data was analysed and the efficacy of the medical management was studied.

Study design: Prospective observational study

Inclusion criteria: 1. Age more than 45 years; **2.** All patients with IPSS more than 8; **3.** Patients with a post-void volume less than 100ml; **4.** Patients with LUTS persistent secondary to BPH after treatment of Urinary tract infections.

Exclusion criteria: 1. Non-ambulatory patients; **2.** Age less than 45 years; **3.** All patients with IPSS less than 8 ;4. Postvoid volume of more than 100ml; 5. Supine BP less than 90/60; **6.** Patient with previous surgery intervention for BPH; **7.** Patients with Neurogenic bladder, Prostate Carcinoma, stricture urethra, Vesical calculi, recent gross hematuria, acute urine retention, history of prostate surgery were excluded from this study; **8.** LUTS secondary to urinary tract infection which resolved after a course of antibiotics and no abnormality in Urine routine and Urine Culture and Sensitivity.

RESULTS

The most common age group in the present study was 51-80 years of age (84.9%).

Sensation of incomplete bladder emptying was the most common voiding symptom seen in 50 of the patients (90.9%).

Frequency of micturition was the commonest storage symptom in all of the patients (100%).

Moderate IPSS score was found in 34 patients (61.8%) and 21 patients (38.2%) had severe IPSS scores before starting drug therapy. After 3 months IPSS decreased from 18±3.17 to 13.9±3.1. At 6 months follow up IPSS decreased to 6.27±3.4.

Grade 1 Prostate volume (20-40cc) was seen in 47.3% which did not show significant change after 6 months of treatment.

There was a significant decrease in the post-void residual volume at the end of treatment. The baseline PVR was 36ml decreased to 8ml after 6 months of treatment.

Improvement in IPSS ≥ 25% was observed in 39.6% of cases and ≥ 3 points improvement was seen in 81.8% of cases.

Of 55 patients 45 patients were responders.[10] were non-responders. Tamsulosin responders were 74.3% (26 patients out of 35). The combination of Tamsulosin and Dutasteride responders was 95% (19 out of 20 patients).

The total incidence of individuals experiencing adverse effects in our study was 12.6% (7/55).

DISCUSSION

A total of 55 patients presenting with lower urinary tract symptoms secondary to BPH were screened and enrolled for observational study in our government set up Tertiary care centre from 1st September 2019 to 31st September 2021.

Age Distribution: studies conducted by Singh *et al.*, Pande *et al.*, Casabe *et al.* it was observed that the mean age of patients with BPH causing LUTS was 68.4±11.8 years, 61±7.88 years, 63.7 years and 66.42±9.84 years respectively.[5-7]

The most common age group in the present study was 51-80 years of age and the youngest patient was 45 years while the eldest patient was 85 years. The mean age of patients was 64.38 years which is similar to the abovementioned studies.

Voiding Symptoms: The sensation of incomplete bladder emptying was the most common voiding symptom seen in 50 of the patients (90.9%) while straining to urinate was the least voiding symptom seen in 4 patients (7.3%).

Storage Symptoms: Frequency of micturition was the commonest Storage symptom in all of the patients N=55 (100%) while 38 patients (69.1%) had urgency.

International Prostate Symptom Score: In the present study baseline, IPSS is 18.58±3.17, of which Moderate IPSS score was found in 34 patients (61.8%) and 21 patients (38.2%) had severe IPSS score before starting drug therapy. After 3 months IPSS decreased from 18±3.17 to 13.9±3.1. At 6 months follow up IPSS decreased to 6.27±3.4.

Prostate Volume: In the present study, Grade 1 Prostate volume was seen in 47.3% which did not show significant change after 3 months of therapy. Pande *et al.*, in 2014, reported that there was no significant reduction in prostate volume after 12-week of therapy in either group of silodosin or tamsulosin while Singh *et al.* 2014 also observed no significant change in the prostate volume after 12 weeks. Other studies like those by Djavan *et al.* in 2011 and Drake *et al.* in 2015 showed no change in prostate volume even after 2 and 1 year of drug therapy respectively.[5,6,8,9]

Postvoid Residual Volume: In the present study, there was a significant decrease in the post-void residual volume at the end of treatment compared to baseline and improvement was seen by the three months after starting medical therapy. The median baseline PVR was 36ml decreased to 8ml at the end of the treatment at the end of 6 months. Studies like Garg *et al.* (Baseline PVR of 76.98±17.10 ml reduced to 45.12±8 ml by the end of 6 months), showed a significant decrease in Postvoid volume similar to the present study.[10] However, studies by Pande *et al.*, and Manohar *et al.* showed no significant decrease in Postvoid residue.[6,11]

Responders based on IPSS Change In the present study, we observed that out of 55 patients the improvement in IPSS ≥ 25% was observed in 39.6% of cases (42.8% on Tamsulosin and 35% on Tamsulosin and Dutasteride) and ≥ 3 points improvement was seen in 81.8% of cases (74.3% of cases on Tamsulosin alone and 95% of cases on combination therapy) at the end of 3 months. A similar study by Roehrborn *et al.* 2008 in their CombAT study, which was a multicentre (446 investigators in 35 countries), randomized, double-blind, parallel-group study of 4844 subjects over 2 years, and recognized responders based on IPSS change.(12) They were 72% on Combination therapy, 65% on Dutasteride, 62% on Tamsulosin. This study showed a greater improvement in IPSS after drug therapy, more with combination therapy than monotherapy. Another similar study Garg *et al.* in 2017 studied 110 subjects, who received a once-daily dose of the combination of silodosin 8 mg and dutasteride 0.5 mg for a period 62 of six months there was improvement of IPSS is seen by 27.75% compared to baseline.[10] Yu *et al.* in 2011 conducted a study whereof 170 (81.3%) patients who completed the study, 86.2% in the silodosin group and 81.9% in the tamsulosin group achieved a ≥25% decrease in IPSS (P = 0.53). This study goes in contrast to our study.[13] This variation of results from our study could be probably because of having a smaller number of patients, shorter follow up period and inclusion of patients of older age group in our study and IPSS is a subjective score.

Adverse Events: The total incidence of individuals experiencing adverse effects in our study was 12.6% (7/55). Four patients had giddiness, two had features of decreased libido. Ejaculation disorder was seen in one each while none complained of impotence, liver or renal dysfunction before or after treatment. Reassurance was given to those with giddiness and as the elderly patients had decreased libido and ejaculation disorder they were also counselled and reassured. Yu *et al.* reported that 1 % of patients receivingtamsulosin complained of abnormal ejaculation.[13] Pande *et al.* 2014 found dizziness or postural hypotension in 3 subjects out of 27 in the tamsulosin group.[6] Drake *et al.* observed that of 1066 patients receiving treatment in NEPTUNE II 499 patients (46%) experienced treatment adverse events.[9] Most common were dry mouth (12.4%), constipation (5.2%), dyspepsia (2.7%), urinary retention (1.1%), Erectile dysfunction (1%). Manohar *et al.* observed adverse effects in 54 out of 269 patients (20.07%).[11] Dizziness was the most common side effect in all of the 3 groups.

CONCLUSION

The primary objectives of the medical treatment for LUTS/BPH are to produce rapid, sustained, and safety improvements in the lower urinary tract symptoms associated with benign prostatic hyperplasia that affect the quality of life in the majority of men over the age of 45. Although this study is short term and limited in the number of patients, it provides evidence that the combined

therapy of an α1-adrenergic receptor antagonist (tamsulosin) plus a 5-alpha reductase inhibitor (dutasteride) is a good approach for meeting these objectives. Additional studies on a greater number of patients for a longer period are needed to substantiate the preliminary evidence of this study.

Limitation: 1. Sample size was less due to Covid-19 Pandemic. **2.** PSA was not done in patients aged >75 years as there was no family history of prostate carcinoma and Digital Rectal Examination was not evident of malignant signs. **3.** Lack of long term follow up owing to a limited study period of 2 years.

Table 1: Age Distribution

Age (years)	Number of patients	%	Responders	%
45-50	5	9.1	5	100
51-60	15	27.3	12	80
61-70	17	30.9	16	94.1
71-80	15	27.3	10	66.6
>80	3	5.5	2	66.6

Table 2: Voiding Symptoms

Voiding symptoms	Patients	Percentage
Hesitancy	23	41.8
Decreased force and calibre of stream	23	41.8
The sensation of incomplete bladder emptying	50	90.9
Straining to Urinate	4	7.3
Postvoid dribbling	13	23.6

Table 3: Storage Symptoms

Storage symptoms	Pre drug	Percentage
Frequency	55	100
Urgency	38	69.1
Nocuria	50	90.9

Table 4: International Prostate Symptom Score

IPSS	Pre drug	After 3 months of drug therapy	After 6 months of drug therapy
<7	0%	0%	49.1
8-19	34(61.8%)	94.4%	50.9
20-35	21(38.2%)	5.6%	0
Mean±SD	18.58±3.17	13.9±3.1	6.27±3.4

Table 5: comparison of pre and post drug therapy Prostate Volume

Prostate volume (cc)	Pre drug	After 3 months	After 6 months
Normal: < 20 cc	7 (12.6%)	11 (19.8%)	9 (16.4%)
Grade 1: 20-40 cc	29 (52.7%)	26 (47.3%)	26 (47.3%)
Grade 2: 40-60 cc	18 (32.7%)	17 (30.9%)	19 (34.5%)
Grade 3: 60-80 cc	0 (0%)	0 (0%)	0 (0%)
Grade 4: > 80cc	1 (1.8%)	1 (1.8%)	1 (1.8%)

Table 6: comparison of pre and post drug therapy Postvoid residual volume

Postvoid residual volume (ml)	Pre drug	After 3 months	After 6 months
< 10	2 (3.6%)	13 (23.6%)	72.7%
11-25	16 (29.1%)	21 (38.2%)	12 (21.8%)
26-50	19(34.5%)	14 (25.4%)	0 (0%)
51-75	6 (10.9%)	5 (9.1%)	1 (1.8%)
76-100	12 (21.9%)	1 (1.8%)	1 (1.8%)
Mean	38.9±25.2	20.6±16.9	8.3±12.7

Table 7: Responders based on IPSS Change

IPSS change	Tamsulosin Responders	(Tamsulosin + Dutasteride) responders	Total Responders
>25% reduction after 3 months	15(42.8%)	7(35%)	22(39.6%)
>3 points reduction after 3 months	26(74.3%)	19(95%)	45(81.8%)

Table 8: Side effects

Side effects	No. of patients
Decreased Libido	2
Giddiness	4
Ejaculation disorder	1
Impotence	0

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