# A PROSPECTIVE OBSERVATIONAL STUDY TO EVALUATE THEPRESCRIBING PATTERN AND TO ASSESS THE THERAPEUTIC OUTCOME IN THE MANAGEMENT OF BENIGN PROSTATE HYPERPLASIA USING INTERNATIONAL PROSTATE SYMPTOMSCORE

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***ABSTRACT***

***Background***

*The present study aimed to evaluate the prescribing pattern and to assess the therapeutic outcome in the management of Benign Prostatic hyperplasia using IPSS and to provide a best treatment option for management of BPH.*

***Methodology***

*It is prospective observational study, 80 patients ≥50 years with BPH and treated with alpha-1 blockers and 5-alpha reductase inhibitors were included in our study. The materials we used in our study include Informed consent form, Patient data collection form, and International Prostate Symptom Score.*

***Results***

*In IPSS follow up, we got mean baseline IPSS as 13.18 out of 35 and the mean follow up IPSS as 5.18. It shows that there is significant reduction of symptoms. We got mean difference of monotherapy and combination therapy as 7 and 8. Results with $p<0.05$ were considered as significant.*

***Conclusion***

*The therapeutic outcomes in evaluating treatment benefits in patients with LUTS/BPH were improvement in subjective symptoms and quality of life. Long term adherence to the medications resulted in decrease in bothersome LUTS. Based on mean difference obtained in our results, we conclude that combination therapy is bit more effective than monotherapy.*

## INTRODUCTION:

The prostate is an organ in male reproductive anatomy. This small walnut sized gland sits directly below the bladder and plays a role in producing and fine- tuning semen. Prostate has various functions the most important is producing seminal fluid. It also plays a role in hormone production and helps to regulate urine flow. Prostate problems are common especially in older men. The most common problems include an inflamed prostate, an enlarged prostate and prostate cancer.

Benign prostate hyperplasia (BPH) also known as benign prostatic hypertrophy is a condition affecting middle-aged and older men and is characterized by an enlarged prostate that restricts the normal flow of urine through the urethra. Enlargement of prostate occurs with age leading to bladder outlet obstruction (BOO) which manifests with symptoms of impaired urine voiding and storage referred to as lower urinary tract symptoms (LUTS). Although BPH is not life threatening, its clinical manifestations as LUTS reduces the patients Quality of life (QOL). The prevalence of BPH accounts nearly 8% of men aged between 40-50 years and when men cross 80 years of age the prevalence rate is almost 80%.

The severity of symptoms in people who have prostate gland enlargement varies, but symptoms tend to gradually worsen over time.

Clinical manifestations of BPH include:

- Frequent or urgent need to urinate.
- Increased frequency of urination at night (Nocturia).
- Weak urine stream or a stream that stops and starts.
- Dribbling at the end of urination.
- Inability to completely empty the bladder.

Less common signs and symptoms include:

- Urinary tract infections.
- Inability to urinate.
- Blood in the urine.

The size of the prostate does not necessarily determine the severity of your symptoms. Some men with slightly enlarged prostate can have significant symptoms, while other men with very enlarged prostate can have only minor urinary symptoms. In some men, symptoms eventually stabilize and might even improve over time.

Complications of an enlarged prostate (BPH) can include:

- Sudden inability to urinate (Urinary retention).
- Urinary tract infections (UTIs).
- Bladder stones.
- Bladder damage.
- Kidney damage.

Most men with BPH may not develop these complications. However,acute urinary retention and kidney damage can be serious health threat.

International prostate symptom score (IPSS) questionnaire, Digital rectal examination (DRE), Urinalysis, Prostate specific antigen (PSA) test, Post-void residual volume, Transrectal ultrasound of prostate (TRUP), Transrectalultrasonography guided prostate biopsy will confirm the patients with high PSAare free of prostate cancer.

Treatment guidelines of BPH recommend that men with moderate-to- severe LUTS should offered with an $a_1$-blocker [e.g.: Tamsulosin, Alfuzosin, Terazosin, Doxazosin]; 5a-reductase inhibitors [Dutasteride, Finasteride] in those with a large prostate [>30g[1] or 40ml[4];] and an antimuscarinics [Oxybutynin, Tolteridone, Solifenacin] in those with predominant storage symptoms. Combination therapy is also available that means the combination of $a_1$-blockers and 5a-reductase inhibitors.

There are several surgical procedures used in the treatment of BPH. The most approached surgical therapy of BPH is transurethral resection of the prostate [TURP]. The procedure involves cutting away a section of the prostate by using a resectoscope inserted through the urethra under spinal or general anaesthesia.

The prescription patterns explain the extent and profile of drug use, trends, quality of drugs and compliance with regional, state or national guidelines like standard treatment

guidelines, usage of drugs from essential medicine list and use of generic drugs

A validated questionnarie can be used to evaluate men with suspected BPH to quantity symptom severity. The validated questionnarie IPSS used to monitor symptoms and guide decisions about how to manage the disease. The IPSS is made up of 7 questions related to LUTS including urine frequency, urgency, intermittence, incomplete emptying, weak urinary stream, straining and nocturia. A score of 0 to 7 indicates mild symptoms, 8 to 19 indicates moderate symptoms and 20 to 35 indicates severe symptoms. As this is a prospective observational study IPSS follow-ups are much needed to be performed before and after the medication therapy through telephone in order to evaluate the decrease in symptoms and also to know the improvement in therapeutic outcome

In order to assess the rationality of therapy we need to study the pattern of prescription and evaluate the drug related problems like ADRs, Medication errors and drug-drug interactions. This study aims to evaluate the prescribing pattern as well as to assess the therapeutic outcome in the management of BPH using IPSS. IPSS follow-ups are needed to be performed periodically in order to evaluate the significant decrease in bothersome LUTS and improvement in therapeutic outcome.

## METHODOLOGY:

Department of Urology, Sri Venkateswara Institute of Medical Sciences, SPMC(W) – Tirupati, was selected as the field of work. The sample size of our study was determined using an anticipated effect size of 0.5 (cohen's d) and using online calculator we got n=80 as minimum size. Therefore we carried out the study with 80 patients.The study proposal was prepared and the approval was obtained from the Head of the Institution and the Institutional ethical Committee. A detailed data collection form with a bilingual patient Informed Consent was prepared. Data collection was done according to inclusion and exclusion criteria. The detailed purpose of the study and benefits are explained in local language to the individual patients and care takers before obtaining the informed consent without any force or compulsion.

All the patients diagnosed with BPH and suggested with a-blockers and 5a-reductase inhibitors therapy with a valid prescription attending urology department were enrolled for the study. All the patients were examined and the demographic details, clinical features were documented and tabulated. The patients were evaluated with IPSS before and after the therapy. The patients were followed up to 6 months after the suggestion of therapy and collected the IPSS again. The details of the scores was tabulated and were categorized accordingly and then used a criteria to describe the effectiveness of the drugs (a-blockers and 5a-reductase inhibitors) were taken in the study.

# RESULTS

### Frequency Of Age Distribution

In this study, 80 male patients are included. Among them 38 (47.5%) patients were under the age group of 50-60, 25 (31.25%) patients were under the age group of 61-70, 16 (20%) patients were under the age group of 71-80, 1 (1.25%) patients were under the age group of 81- 90.

**Table 5.1:** Frequency of age distribution of patient

| Age(yr) | Frequency | Percent age (%) |
|---|---|---|
| 50-60 | 38 | 47.5 |
| 61-70 | 25 | 31.25 |
| 71-80 | 16 | 20 |
| 81-90 | 1 | 1.25 |

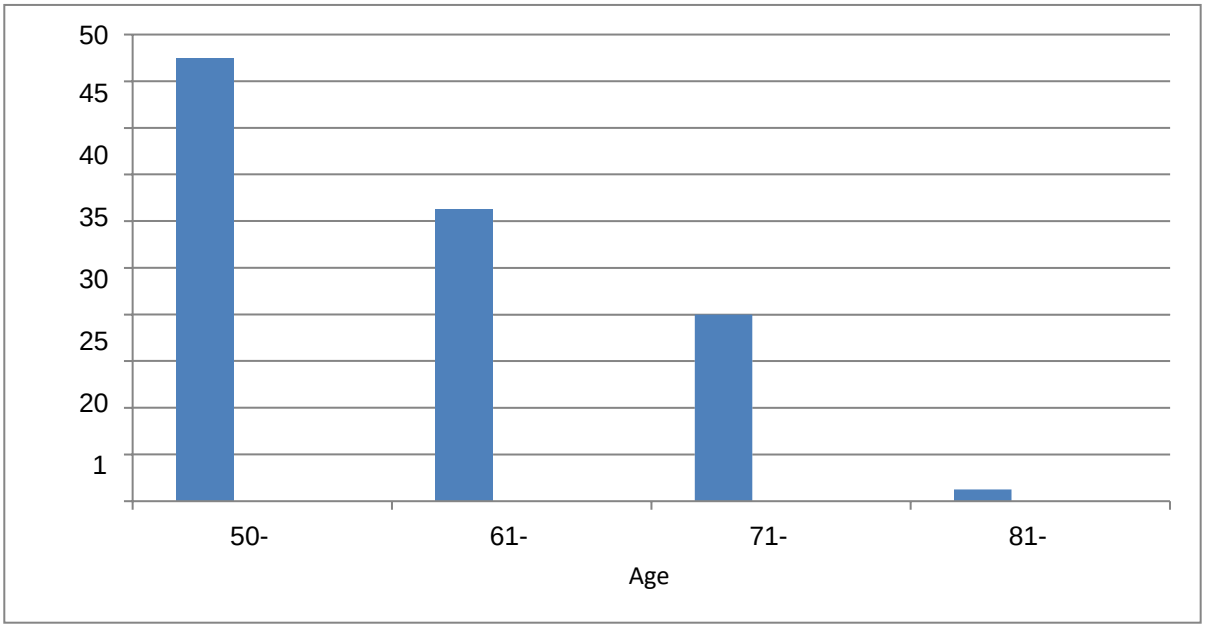


**Figure 5.1:** Frequency of age distribution of patients

## According To Symptoms:

Total number of patients with irritative LUTS were 16 (20%), total number of patients with obstructive LUTS were 12(15%), and total number of patients with both irritative and obstructive LUTS symptoms were 52(65%).

**Table 5.2** Frequency distribution of patients according to symptoms

| Symptoms | Frequency | Percentage (%) |
|---|---|---|
| Irritative | 16 | 20 |
| Obstructive | 12 | 15 |
| Irritative + Obstructive | 52 | 65 |

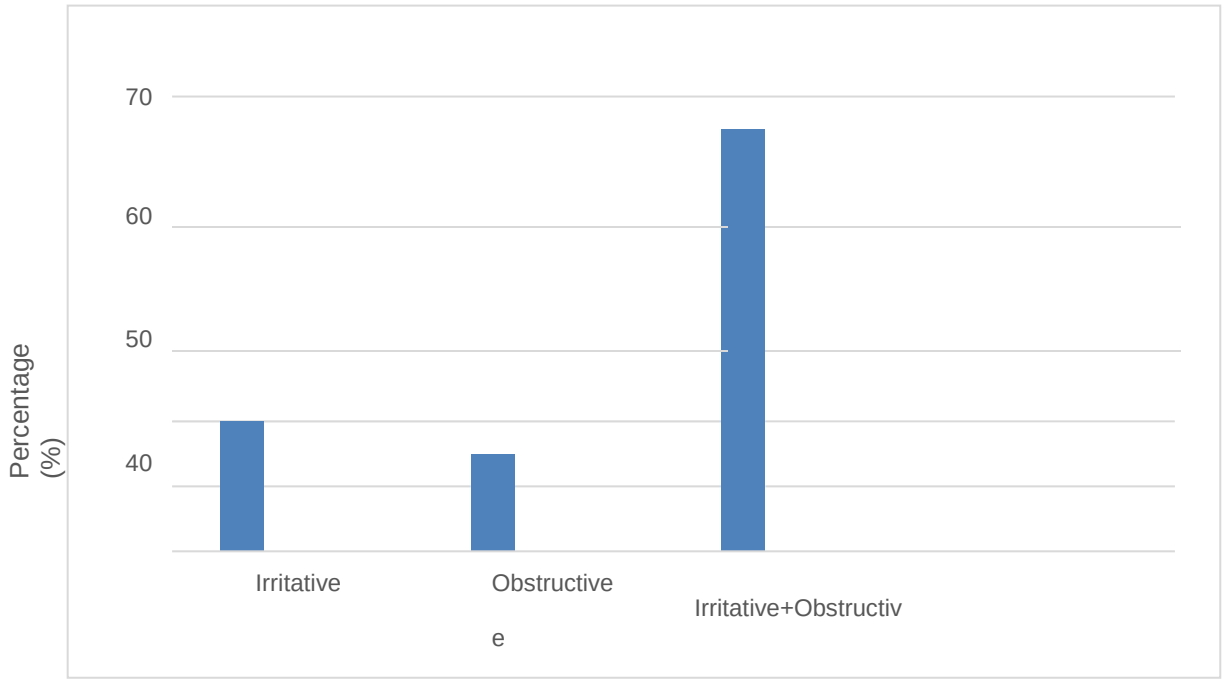


**Figure 5.2** Frequency distribution of patients according to symptoms.

In our study, out of 7 symptoms of LUTS, Nocturia and Frequency were highly reported with 73.75% and 72.5%. Second most highly reported symptoms were urgency with 65%. Third most highly reported symptoms were weak stream, intermittency and incomplete emptying with 56.2%, 52.5% and52.5%. And least reported symptom was straining with only 35%.

## LUTS Distribution

**Table 5.3** Frequency distribution of LUTS

| Symptoms | Frequency | Percentage (%) |
|---|---|---|
| Incomplete emptying | 42 | 52.5 |
| Frequency | 58 | 72.5 |
| Intermittency | 42 | 52.5 |
| Urgency | 52 | 65 |
| Weak stream | 45 | 56.25 |
| Straining | 28 | 35 |
| Nocturia | 59 | 73.75 |

## According To Treatment:

In our study out of 80 patients, 16 (20%) patients were receiving monotherapy and 64 (80%) patients were receiving combination therapy.

**Table 5.4:** Frequency distribution according to treatment.

| Category | Frequency | Percentage (%) |
|---|---|---|
| Monotherapy | 16 | 20 |
| Combination therapy | 64 | 80 |

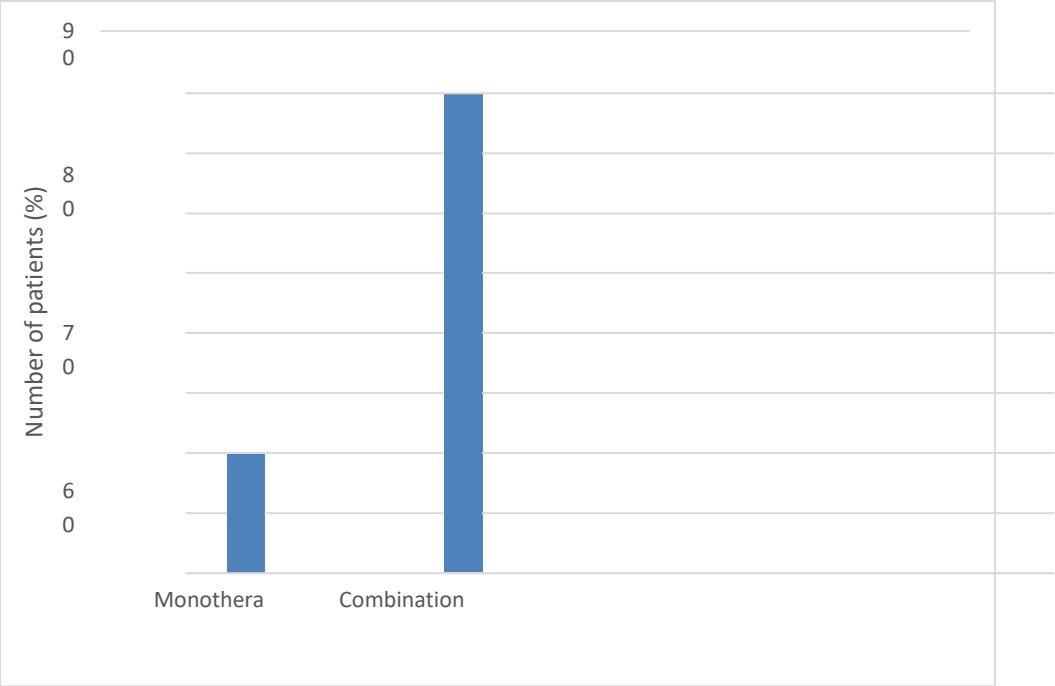


**Figure 5.4:** Frequency distribution according to treatment.

In our study, out of 80 patients, 16(20%) patients were receiving monotherapy of a- blockers, none of them were receiving monotherapy of 5a-reductase inhibitors and 64 (80%) patients were receiving combination therapy of a-blockers and 5a- reductase inhibitors.

**Table 5.5:** Frequency distribution of drugs according to therapy.

| Category | Drugs | Frequency | Percentage (%) |
|---|---|---|---|
| Monotherapy | a-blockers | 16 | 20 |
| | 5a-reductase inhibitors | 0 | 0 |
| Combination therapy | 5a-reductase inhibitors | 64 | 80 |

In our study, out of 80 patients 09 (11.25%) patients were prescribed with Silodosin, 06 (7.5%) patients were prescribed with Tamsulosin, 01 (1.25%) patient were prescribed with Alfuzosin, 44 (55%) patients were prescribed with combination of Silodosin + Dutasteride and 20 (25%) patients were prescribed with Tamsulosin + Dutasteride.

**Table 5.6:** Frequency of drugs according to prescription.

| Category | Drugs | Frequency | Percentage (%) |
|---|---|---|---|
| Monotherapy | Silodosin | 09 | 11.25 |
| | Tamsulosin | 06 | 7.5 |
| Combination therapy | Alfuzosin | 01 | 1.25 |
| | Silodosin+ Dutasteride | 44 | 55 |
| | Tamsulosin+ Dutasteride | 20 | 25 |

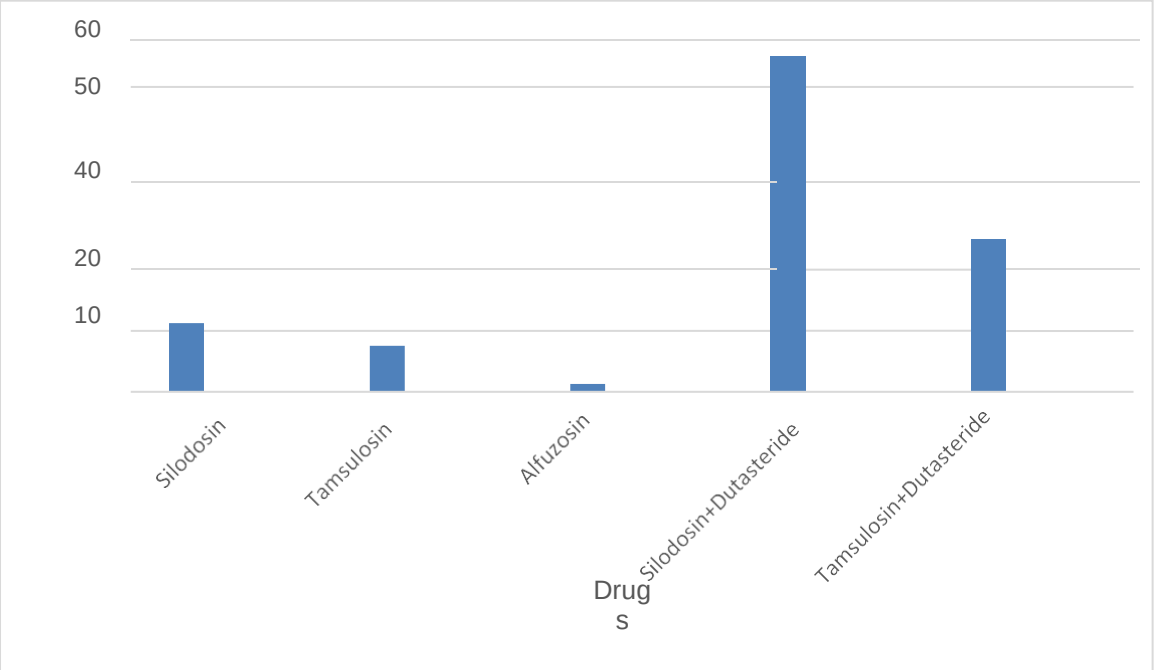


**Figure 5.6:** Frequency of drugs according toprescription.

## ACCORDING TO IPSS:

In our study, the mean baseline IPSS score of 80 patients was 13.8 out of 35, and the mean follow up IPSS score was 5.18 out of 35. The baseline IPSS score was taken before starting of the therapy and the follow up IPSS was taken after the use of therapy up to 6 months.

**Table 5.7** Average of IPSS

| Category | Baseline | Follow-up |
|---|---|---|
| Average IPSS | 13.18 | 5.18 |

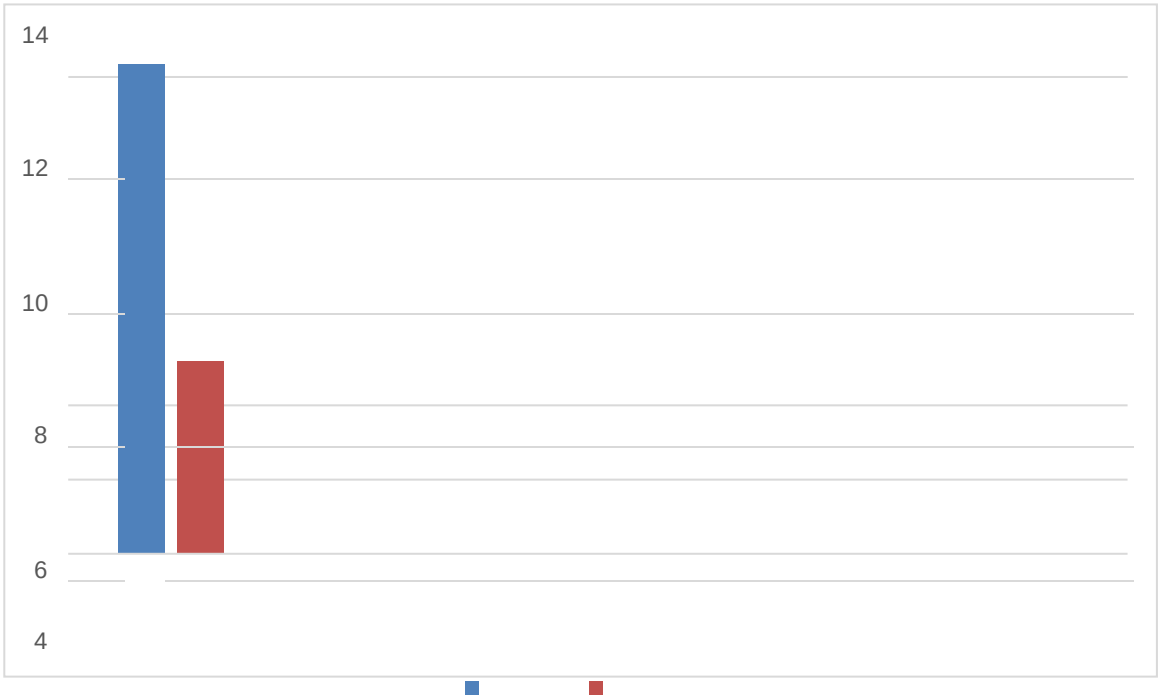


**Figure 5.7** Average of IPSS.

In our study of 80 patients, The mean of baseline (before therapy). IPSS score and mean of follow up (after therapy) IPSS score of monotherapy was 11 and

The mean of follow up IPSS score of combination therapy (a-blockers and 5a-reductase inhibitors) was 13 and 5. The mean difference of monotherapy is 7 and for combination therapy is 8.

**Table 5.7** Mean difference of monotherapy and combination therapy

| Category | Follow-up | Mean of IPSS | Mean Difference |
|---|---|---|---|
| Monotherapy | Before | 11 | 07 |
| | After | 4 | |
| Combination therapy | Before | 13 | 08 |
| | After | 5 | |

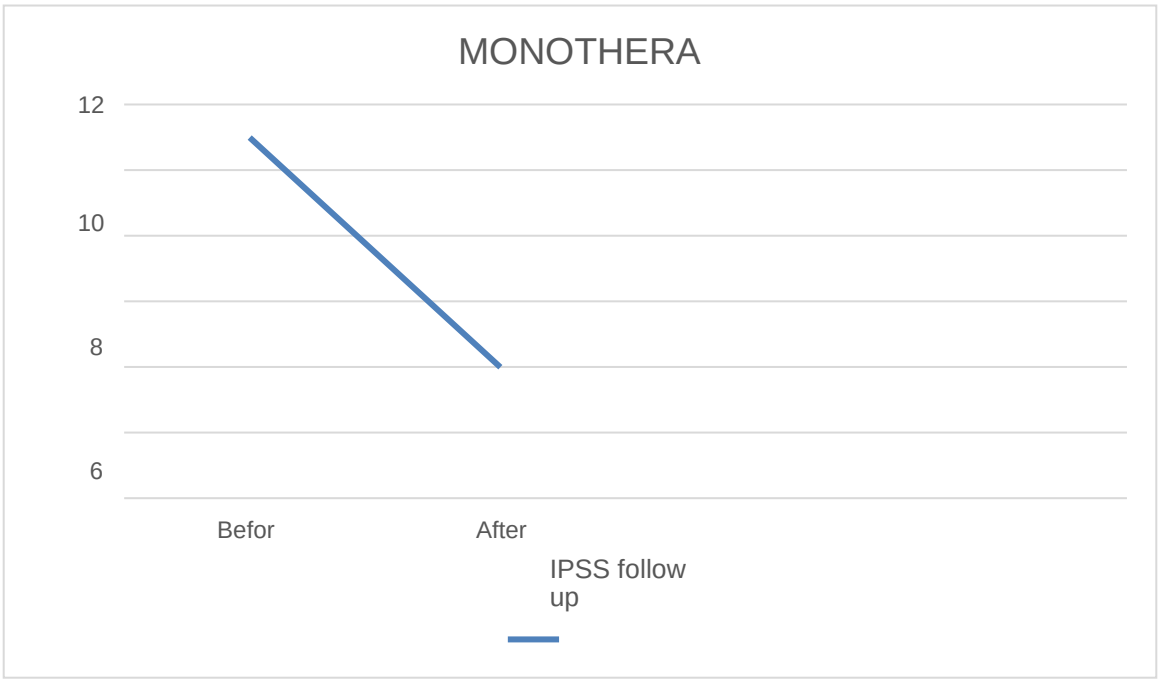


**Figure 5.8:** Mean difference of Monotherapy

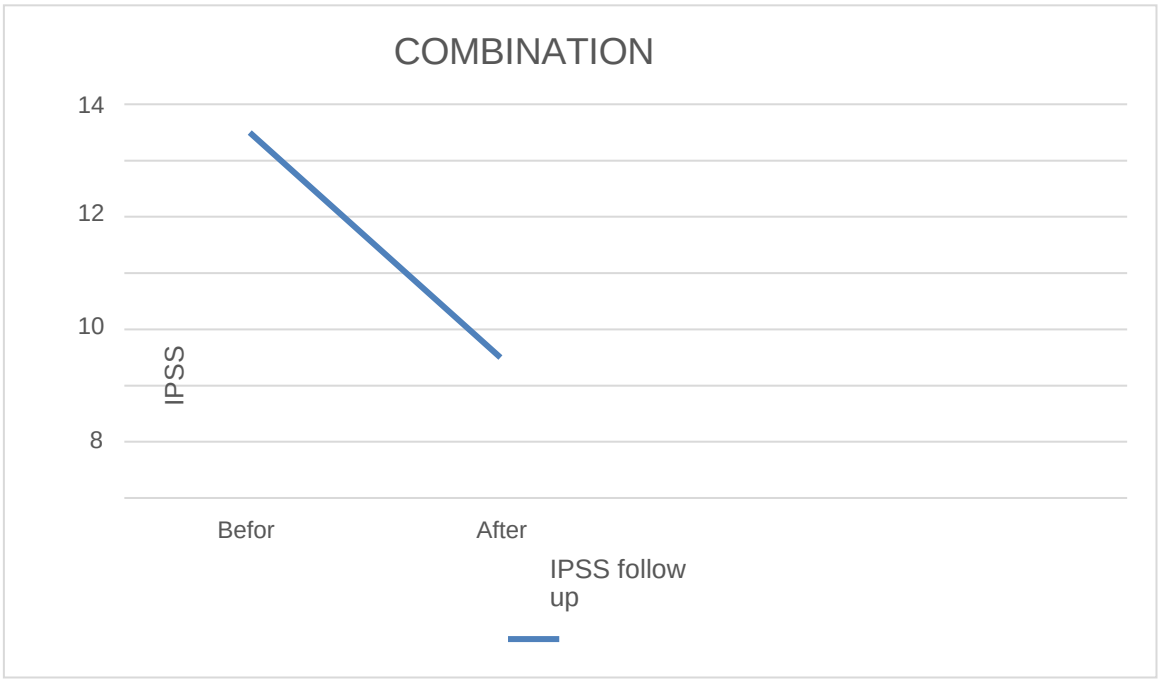


**Figure 5.9:** Mean difference of Combination therapy.

## DISCUSSION

The present study was carried out with 80 patients, who are presented with LUTS/BPH in department of Urology of SVIMS hospital, Tirupati. It was a prospective observational study to evaluate the prescribing pattern and to assess the therapeutic outcomes in management of BPH. The main outcomes in evaluating treatment benefits in patients with LUTS/BPH are the improvement of subjective symptoms and the impact on the quality of life and on the bother of the LUTS/BPH.

This study provides an overview of treatment patterns for men aged ≥50 years with LUTS/BPH. A variety of Alpha-1 blockers and 5-alpha reductase inhibitors were prescribed during follow up. Out of 80 patients 16 were prescribed monotherapy of alpha-1 blockers and 64 were prescribed combination therapy of alpha-1 blockers + 5-alpha reductase inhibitors.

In monotherapy, silodosin is the most prescribed drug with 11.25%, followed by tamsulosin with 7.5% and least prescribed alfuzosin with 1.25%. In combination therapy silodosin+dutasteride is most prescribed with 55%, followed by tamsulosin+dutasteride with 25%.

In this case, the most highly reported symptoms are storage symptoms (irritative LUTS) which includes frequency, urgency, and nocturia. This storage symptoms effects on patients quality of life. So, the chances of non-adherence is very low. If patients have voiding symptoms (obstructive LUTS), it doesn't effect patients much and their quality of life. So, they may neglect and chances of discontinuation of therapy will be high. Long term adherence and treatment duration are the key to a successful therapy.

In this study, to assess the therapeutic outcome in the management of BPH, we have used IPSS. The baseline IPSS score was collected from the patients before start of the medication therapy and follow up IPSS was collected after certain period of time. The mean of baseline IPSS is 13.18% and for follow up IPSS it is 5.18%. This shows there is great improvement in the symptom reduction and patients quality of life.

Both monotherapy (alpha-1 blockers) and combination therapy (alpha-1 blockers+5-alpha reductase inhibitors) were shown reduction in the symptom and improvement in the quality of life. As we see, the mean difference of monotherapy is 7 and for combination therapy it is 8. So, based on this we can say combination therapy is bit more effect than monotherapy. Our study results are consistent with several recently published studies.

## CONCLUSION

After studying the prescribing pattern in BPH management and assessing therapeutic outcomes in BPH patients based on IPSS follow up. It is observed that, the therapeutic outcomes, treatment benefits in patients with LUTS/BPH were improved with evidences in subjective symptoms and quality of life. Long term adherence to the medication resulted in decrease in the bothersome Lower Urinary Tract Symptoms (LUTS). Based on mean difference obtained in our results, we conclude that combination therapy is bit more effective than monotherapy.

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