



Randomized Study of Medical Line of Treatment and Surgical Line of Treatment in the Management of Benign Prostatic Hyperplasia in A Tertiary Care Centre

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Abstract

Objectives

1. To study BPH, in relation to uroflowmetry after medical line of management and surgical line of management.
2. To study the outcome of both the line of management.

Methods: Between December 2014 to July 2016 we studied 100 men alternatively into medical and surgical categories, age group of above 50 years, who were attending the outpatient department of Surgery at Krishna institute of medical science karad with symptom likely suggestive of LUTS.

Results: In our study group mean increase in the PFR was 46.39 % in medical therapy ($p < 0.05$) and 94.96% improvement in surgical patient ($p < 0.0001$), the difference is highly significant goes in favor of TURP.

Conclusion: We thus conclude the medical treatment should be offered to those patients who are not willing for surgery, are unfit for surgery or having early symptoms of LUTS. In spite of the associated post-operative morbidity in few elderly patients after surgery, of all treatment options, prostate surgery offers the best chance of symptoms improvement with TURP being a gold standard procedure.

Keywords: Benign prostatic enlargement, uroflowmetry, LUTS, TURP, peak flow rates(PFR).

INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most common diseases of the aging men. It is associated with both some lower urinary tract symptoms (LUTS). As the age of the human male advances the prostate gland enlarges¹

Benign Prostatic Hyperplasia (BPH) is a disease suffered almost universally by aging men. With age the prostate gland either atrophies or hypertrophies producing various types of bladder outlet symptoms in a significant number of cases. Based on the clinical definition of BPH as given

by Garraway et al 1991.² which includes an enlargement of prostate (more than 20gm) and either an elevated symptom score (11 or higher on a scale of 0-35) or a reduced peak urinary flow rate (less than 15ml / sec). The prevalence of clinically defined BPH ranged from approximately 14% for men in their forties to 40% for men in their seventies and 80% of the men by the age of 80.

The incidence of the benign prostatic hyperplasia has increased with the proportion to life

expectancy and has become 3rd leading cause of health expenditure in industrialized countries.³

Better understanding of pathophysiology of BPH, which produces symptoms from both, the static (anatomic) and a dynamic (functional) component, has led to the emergence of medical management with promising results.

Caine⁴ in 1986 gave concept of dynamic component which is related to the level of sympathetic stimulation of alpha receptors in the (a) prostatic capsular muscle (b) prostatic adenoma (c) bladder base. This suggested the possibility of treatment with alpha adrenergic antagonists.

The development of BPH, as found by Coffey and Walsh⁵ in 1990 is an Androgen dependent process. Peter and Walsh⁶ in 1987 demonstrated that androgen suppression causes reduction in prostate volume thus decreasing static component of bladder outlet obstruction resulting in BPH. This is the rationale for the use of 5 alpha reductase inhibitors and various anti androgens.

Medical treatment has come to stay because of the limitations of prostate surgery in elderly persons with various co-morbidities or unwilling for surgery. However surgery still remains best treatment of choice, with TURP being the gold standard procedure.

MATERIALS AND METHODS

Between December 2014 to July 2016 we studied 100 men which were alternatively divided into medical and surgical categories, age group of above 50 years, who were attending the outpatient department of Surgery at Krishna institute of medical science karad with symptom likely suggestive of LUTS.

Inclusion Criteria

1. All male patients aged above 50 years with symptoms of LUTS.
2. Patients with positively diagnosed as benign enlargement of prostate by clinical digital rectal examination, investigation like USG is included in this study.

Exclusion Criteria

1. All patients with LUTS not likely due to BPH.
2. Those patients who have undergone open prostatectomy.
3. Patients defiantly requiring surgery.
4. Hard prostate on digital rectal examination.
5. All patients unfit for surgery.
6. Patients with retention of urine with foley's cath in situ.
7. Patients with serum PSA > 4.

Study Design

- The ethical committee of Krishna institute of medical sciences and deemed university karad approved this Randomized comparative prospective study and men included in this study gave written informed consent.
- Out of 100 patients, 50 were chosen for surgery in the form of TURP and rest 50 men were considered for medical treatment (Tamsulosin + Dutasteride).
- Patients were selected randomly in OPD and who were not willing for surgery.
- Apart from the above criteria patients chosen for medical treatment had early symptoms of LUTS and had lower grades of prostatic enlargement n mild to moderate IPSS scoring. Men considered for surgery had moderate to severe IPSS scoring, had higher grades of prostatic enlargement.

TREATMENT PROTOCOL

Surgical Treatment

Trans Urethral Resection of Prostate (TURP)

All the patients in the surgical treatment group underwent Transurethral resection of prostate (TURP). Over the years, TURP as a treatment modality for BPH has gained popularity throughout the world. It is now considered the gold standard for the surgical management of BPH.

Medical Treatment

Tamsulosin 0.4 mg and dutasteride 0.5 mg is prescribed as single dose at bed time.

RESULTS

BASE LINE CHARACTERS

A total of 100 male patients were enrolled in the study, 50 patients were offered medical treatment and 50 were offered surgical treatment alternatively. Patients assigned to both the groups were similar in terms of age and associated illness. The baseline IPSS scores in the medical management group were in majority moderate range for all patients while those in surgical group

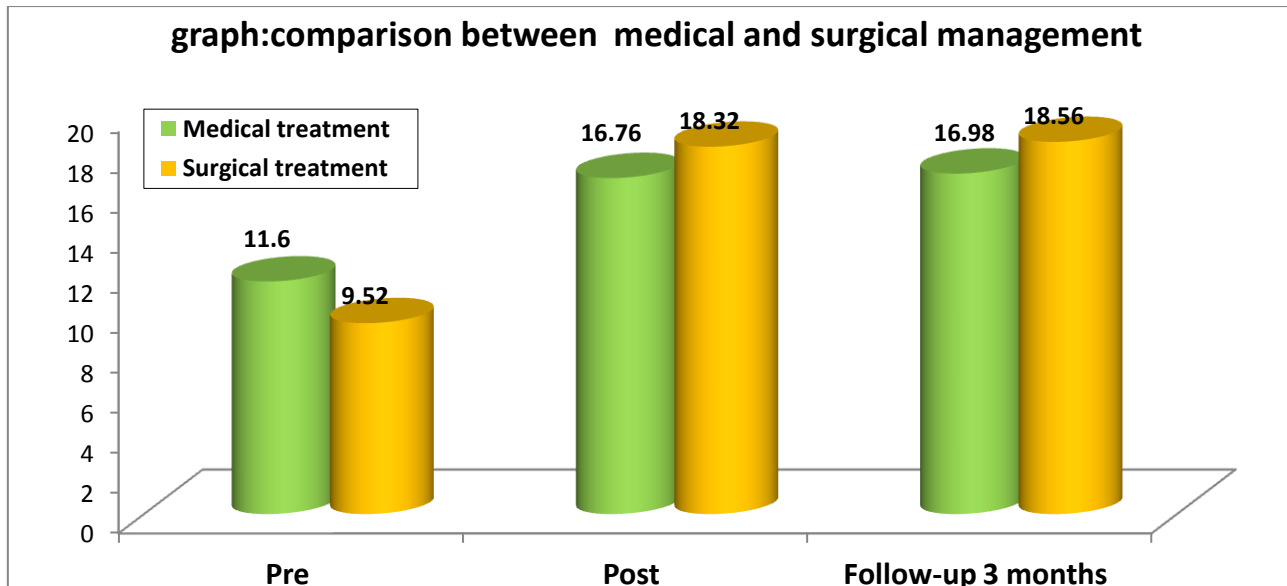
were both in moderate and severe range both the groups were below 15ml/sec.

Grades of prostatic enlargement were assessed by Digital Rectal Examination (DRE) and pre medication and post medication peak flow rates (PFR) were measured, pre-operative and post-operative peak flow rates (PFR) were measured.

When compared between the two studies groups showed that grade 2 enlargement was common in surgical treatment group while majority of men in medical treatment group had grade 1 prostatic enlargement. As grade 1 and 2 can be offered both medical and surgical mode of treatments.

Table: comparison between medical and surgical management:

URO flow	Medical treatment	Surgical treatment
	Mean ± SD	Mean ± SD
Pre	11.60 ± 1.62	9.52 ± 1.51
Post	16.76 ± 1.53	18.32 ± 2.54
Follow-up 3 months	16.98 ± 1.52	18.56 ± 2.33
Student's Paired 't' test value	11.24	23.54
'p' value and significance	p=0.0142, significant	p=0.0001, highly significant



By applying Student's Paired 't' test there is a significant increase in mean values of uroflowmetry peak flow rate(PFR) from pre medication to post medication and from follow-up 3 months (p<0.05). Thus there is a 46.39% increase in mean values of PFR from pre to post medication and pre medication to follow-up at 3 month in medical treatment group. By applying Student's Paired 't'

test there is a highly significant increase in mean values of PFR from pre-operative to post-operative and from pre-operative to follow-up 3 at month (p<0.0001). Thus there is a 94.96% increase in mean values of (PFR) from pre to post operative and at follow-up 3 month in surgical treatment group.

DISCUSSION

This study was designed to compare the efficacy and safety of medical management and surgical management in men with symptomatic benign prostatic hyperplasia. Patients completed three month of follow up, during which the medical treatment group continued to receive the drug. 100 patients were selected on the basis of inclusion and exclusion criteria mentioned above. 50 patients were included in the medical treatment group. Specifically, males with absolute indications for surgery were excluded from the medical treatment group. These criteria were designed to exclude individual with underlying medical conditions such as primary neurologic syndromes, which may masquerade as bladder outlet obstruction.

A. MEDICAL TREATMENT GROUP

- a) alpha 1 antagonist: Tamsulosin
- b) 5 alpha reductase inhibitors: Dutasteride

The combination of an alpha-blocker and 5-ARIs (combination therapy) is an appropriate and effective treatment for patients with LUTS associated with demonstrable prostatic enlargement based on volume measurement, post voided volume, peak flow rates and/or enlargement on DRE. These two drugs combination increase peak flow rates and reducing the risk of acute urinary retention and prostatic surgery.

PFR increment was significantly greater in men with more prostate volume. After treatment increased in peak flow rate (Qmax) was seen after 1 month of treatment and increase in PFR seen in 3 months.

B. SURGICAL TREATMENT GROUP

This group patient underwent Transurethral Resection of Prostate (TURP).

The recent development of pharmacological treatment of BPH has been accepted by many patients with early symptoms of LUTS, patients who are high-risk cases for surgery, or those who are unwilling for surgery. However, surgical

management still remains the best treatment option with TURP being the gold standard.

Patient Population

The two groups in our study were of comparable size and age composition.

Age Incidence

Average age group in our study was 70 years. There was no patient below the age of 50 years. Youngest patient in our study group was 50 years and oldest was 80 years. These above findings confirm those of the Schwartz study who has shown that symptomatic BPH is rare before the age of 40 years³.

Lepor H et al⁷ in 1989, reported in their study on the efficacy & safety of medical management in the treatment of BPH that the mean age of patients was 63.9 ± 1.0 . A similar study by Lepor H, Ridaud G,⁸ in 1991) on efficacy of TURP in men with BPH, reported that the mean age of patients was 66.6 ± 1.2 . In our study the mean age of patients in medical treatment group was 68.30 ± 20.58 , and the mean age in surgical treatment group was 66.80 ± 22.06 .

Associated illness

Mebust and colleagues in 1989 noted that only 23% of the patients did not have a significant medical problem prior to surgery. In surgical treatment group, 9% of patients had hypertension, 5% of patients had diabetes mellitus, 7% had cardiac problems, 5% had pulmonary complications and 2% had inguinal hernia. In our study in the medical management group, 10% of patients had hypertension, 3% of them had diabetes mellitus, 6% had cardiac problem and 20% had anemia.

Volume of Prostate

The average volume of the prostate gland as obtained by trans abdominal USG was 56 grams. The smallest prostate gland has a weight of 30 grams and the largest was of 60 grams. Estimation of the weight of the prostate is very important

because most urologists prefer to perform transurethral resection and other minimally invasive surgeries for the prostate volume of less than 60 gms while open, suprapubic and retropubic surgery is done for glands above 60 gms. The ultrasound of the prostate by suprapubic route (Trans abdominal) did not correlate with weight of gland as assessed by transrectal route. Transrectal is considered as more accurate. The transrectal ultrasound provides urologist with an accurate estimation of transition zone and median lobe prostate. In our study the average volume of the prostate for age group 50-60 years was 56 cc. while it was 60cc for the age group 61-70 years. The volume for 71-80 years was 58 cc. This suggests that there was no correlation between age and prostate volume. These findings coincide with those of Mukendo Kojima et al.⁹ who demonstrated that there was no significant linear correlation between age and prostate volume.

A.U.A score: (IPSS)

In our study group out of 100 cases 34 patient (34%) presented with severe grade of (that is between 19-35), 66 patients (66%) presented with moderate score (8-19). It indicates that there is no correlation between the age of the patient and A.U.A symptom score.

Complications of BPH

In the American Urological Association Cooperative Study in 1989¹⁰, 70% of patients had more than one indication for surgery. 27% of patients had acute urinary retention, 12.3% had recurrent urinary tract infection, and 3% had bladder stones. Mc Connell et al¹⁰ in 1994 reported that 20 to 30 % of men undergoing prostate surgery have urinary retention, and 1 to 2% of them have concomitant bladder stones. In our study, 7(14%) cases had reported with acute retention of urine, 4 (8%) cases had UTI.

SURGERY COMPLICATIONS

1) Transurethral resection syndrome or dilutional hyponatremia

None of our case developed this complication. In AUA cooperative study (Mebust et al 1989), TUR syndrome occurred in 2% of patient TUR syndrome is an alteration in homeostasis produced by extravasation due to the perforation of capsule and intravasation due to the sucking in of irrigation fluid in the venous sinuses.

2) Clot retention

Only one case of TURP had clot retention this was within 8 hrs of surgery. Clot retention is caused by a clot sufficiently large to obstruct catheter leading to obstruction and bladder distension. It was managed by as follows:

- Post operative warm normal saline irrigation at faster rate.
- Bladder wash
- Replacing Foleys catheter if it was blocking the catheter.
- Cystoscopic removal of large clot

Rarely it requires suprapubic approach to remove the clot if it is large enough. In our study, 1 patient had clot retention was managed first by fast normal saline irrigation, and Foleys was changed but it was not responded. So cystoscopy was done and whole clot was removed.

In co-operative study done by American Urological Association incidence of clot retention after TURP was 3.9%¹¹. In our study it was 2%.

3) Incontinence of Urine

Incontinence after operation on prostate arises after varying degree of trauma to external sphincter. In our study group permanent incontinence has not occurred to any of the patient. Two of our i.e 4 % patient developed incontinence temporary for 5-6 days after removal of catheter. The patient become continent after 3-4 days. The co-operative study conducted by A.U.A permanent incontinence after TURP is 0.5% of patient¹¹.

4) Post operative Urinary Tract Infection

UTI occurs after TURP due to prolonged catheterization. In our study group 1 patient (2%) had post op urinary tract infection. In a co-operative study, conducted by AUA incidence of UTI after TURP was 25%. A positive correlation between incidence of urinary tract infection and post operative catheterization was established by Jackman Chisholm and G.D¹².

5) Urethral catheterization

Urethral catheterization is must after surgery for BPH. Prolonged catheterization leads to increased morbidity of patient. In our study most of the patient required catheterization for 3-5 days. In Rob and Smith's operative, it has been stated that, urethral catheterization after TURP can be safely removed after 2-3 days if urine is clear¹³.

6) Period Of hospitalization

This is one of the criterion which increases morbidity of BPH. After TURP patient were discharged after 6-7 day.

7) Mortality

The mortality rate has decreased significantly following TURP over the past three decades

In our study there was no mortality. In most series the early mortality rate for TURP is 0.02%

Medical Treatment

Combination therapy: tamsulosin 0.4mg and dutasteride 0.5 mg is used

Combination therapy has advantage of, it reduces IPSS score, prostate volume, increases the urinary flow rate, decreases the rate of acute retention of urine and prostatic surgery. Two-year data from the multicenter Comb AT study shows that combination therapy with dutasteride and tamsulosin results in significantly greater decreases in IPSS and significant increases in peak urinary flow rates versus monotherapy with either dutasteride or tamsulosin. Additionally, a significantly greater reduction in total prostate and transition zone volume was achieved in the

combination group as compared to monotherapy with tamsulosin. Adverse drug events are more common with combination therapy but study withdraw rates are similar among the treatment groups and are less than 5%. In our study group, there was significant improvement in the PFR in the medical group i.e 46.39 %. In our study group mean increase in the PFR was 46.39 % in medical therapy and 94.96% improvement in surgical patient. The complications in our study group was, Loss of libido 2%, post-operative UTI 2%, UTI 2% in combination therapy, retention of clot 2%.

CONCLUSION

The treatment of clinical BPH is targeted to improve symptoms of LUTS, relieve obstruction, improve bladder emptying, and prevent urinary tract infection and renal function deterioration. The treatment option of BPH has drastically changed over the last decade owing to the availability of several treatment options and an altered perception of the natural history and pathophysiology of the disease process. Prostatectomy resects the obstructing tissue. Medical therapies are targeted to relieve obstruction by relaxing smooth muscle (alpha-blockers) or promoting regression of the disease process (androgen ablation). In this study 100 patients were selected, out of which 50 were offered medical treatment and rest 50 were taken up for surgical treatment in the form of TURP alternatively. The peak flow rate (PFR) was the main parameters which were compared between the two study groups. Though there was clinically significant % improvement in the PFR scores 46.39% in the medical treatment group, when compared to TURP % improvement in PFR was 94.96% in surgical group, the difference was highly significant ($p < 0.0001$) and was in favor of TURP. As regards of cost of the treatment, patients who opt for medical therapy should have symptoms bothersome enough to make a lifetime commitment to medical therapy and its expenditure on drugs, while TURP is large one time procedure. It is also a well-known fact that

prostatic cancer often co-exists with BPH, hence one disadvantage of medical therapy is lack of tissue for histopathological examination, whereas in TURP we are obtaining tissue which is routinely sent for histopathological studies so that incidental cases of prostatic cancer can be detected. The ultimate role of the emerging alternative strategies of BPH management namely hormonal, pharmacologic, thermal and device remain to be fully defined. TURP remains the standard against which all new therapies must be measured. We thus conclude the medical treatment should be offered to those patients who are not willing for surgery, having early symptoms of LUTS. In spite of the associated post-operative morbidity in few elderly patients after surgery, of all treatment options, prostate surgery offers the best chance of symptoms improvement with TURP being a gold standard procedure. Surgical excision has been the cornerstone in the management of BPH for nearly a century. In the last 50 years TURP has become established as the procedure of choice in most patients with Benign Prostatic Hyperplasia.

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