

PROSPECTIVE STUDY OF EFFECT OF FIXED DOSE COMBINATION OF DIFFERENT ALPHA BLOCKERS WITH DUTASTERIDE ON QUALITY OF LIFE IN PATIENTS WITH LOWER URINARY TRACT SYMPTOMS OF BENIGN PROSTATIC HYPERPLASIA BASED ON CHANGES IN DIHYDROTESTOSTERONE LEVELS

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Abstract

Background: The commonest cause for men over the age of 50 years for lower urinary tract symptoms (LUTS) is indeed Benign hypertrophy of prostate (BPH). Benign hypertrophy of prostate (BPH) is characterised by the lower urinary tract symptoms (LUTS), which includes voiding or obstructive symptoms such as retardation of urine and frequency of urine due to incomplete emptying of UB. If untreated it leads to severe urinary tract infection. **Materials and Methods:** 150 patients aged between 50 to 70 were classified into three groups, group-I was treated with FDC Tamsulosin 0.4 mg and Dutasteride 0.5 mg once daily, Group-II Alfuzosin 100mg and Dutasteride 0.5 mg once daily. Group-III Silodosin 4.0 mg and Dutasteride 0.5 mg once daily treated for the period of 6 weeks (follow up by every 4 weeks) in three groups. **Result:** IPSS 8th question score improved significantly by 60.65% 56.62% and 62.2 in group-I, II and III respectively BPH impact score also improved significantly 61.93%, 59.11% and 60.80% in group-I, II and group III respectively, all three treatments found to be more or less similar in improving quantity of life. **Conclusion:** Present pragmatic fixed dosage combination study of alpha blockers with Dutasteride is effective to treat BPH for longer duration and keeps the satisfied quality of life.

INTRODUCTION

The urinary bladder has two main functions storage and voiding (emptying). The commonest cause for men over the age of 50 years for lower urinary tract symptoms (LUTS) is indeed Benign hypertrophy of prostate (BPH).

Benign hypertrophy of prostate (BPH) is characterised by the lower urinary tract symptoms (LUTS), which includes voiding or obstructive symptoms such as hesitancy, poor or intermittent stream, straining, feeling of incomplete bladder emptying, dribbling etc. and storage or irritative symptoms such as frequency, urgency.

There are two medical approaches to the management of BPH, which work through different receptors within the bladder and the prostate.^[1] The alpha blockers block the smooth muscle receptors at the bladder neck in the bladder and within the prostate. There by relaxing the tension that opens the bladder neck allowing for easier, stronger flow

and more complete emptying, which means less frequency, urgency and nocturia. The response is very quick in hours to few days but the long term response is relatively short where most men need an adjustment of dosage or shift to another therapy.^[2] However alpha blockers don't prevent the progression of BPH, which usually culminates in urinary retention and / or need for surgery.^[3]

It is proved that Dutasteride reduces the serum Dihydrotestosterone (DHT) levels by 95% leading to reduction of approximately 94.97 % of DHT levels in prostate.^[4] Thus by mediating prostatic size Dutasteride can regulate the static component of bladder outlet obstruction after 6-12 months of treatment. Hence attempt was made to evaluate the fixed dosage treatment of Dutasteride with different types of alpha blockers in BPH patients.

MATERIALS AND METHODS

150 adults patients aged between 55 to 70 years visited to ACPM Medical College Dhule Maharashtra-424001 were studied.

Inclusive Criteria

Patients more than 45 years of age and diagnosed to have lower Urinary tract symptoms and Benign prostatic Hypertrophy BPH. International prostate symptoms score (IPSS) > 8, prostatic volume > 30 cm³, Total serum prostate antigen (PSA) ≤ 10 ng / ml, two urinary voids at screening with maximum flow rate (Q max) ≥ 5 ml / sec and ≤ 15 ml/sec with a minimum voided volume ≥ 125 ml were selected for study.

Exclusion Criteria

Patients with history or evidence of prostatic cancer, patient's previously undergone prostatic surgery. Patients who were already under the therapy of α -blockers. Patient's intolerance or hyper sensitivity to study drugs were excluded from the study.

Method

The present clinical oriented study was done in accordance with the principles of Good clinical practice (ICH-GCP) and declaration of Helsinki. 150 patients were divided into three groups. Group I was treated with Tamsulosin 0.4 mg and Dutasteride 0.5mg once daily. Fixed dosage combination (FDC) Group-II – FDC of Alfuzosin 10.0 mg and Dutasteride 0.5 mg once daily, Group-III – FDC of Silodosin 4.0 mg and Dutasteride 0.5 mg once daily. Patients were followed up every 4 weeks for a period of 16 weeks. In each group 50 patients were studied.

The quality of life was assessed by IPSS (International prostate symptoms score) 8th question and BPH impact index which are evaluated at base line and end of 16th weeks and modified PPSM questionnaires were evaluated at the end of study. In IPSS 8th question every patient was asked if he had to spend the rest of his life with his urinary condition just the way it is now how would he feel about that and scaled 0 (delighted) to 6 (terrible). BPH impact index is a 4-item patient complicated questionnaire that measures the impact of BPH symptoms on physical symptoms worry about health degree of bother and limitation of daily activities with a higher scores indicating a worse health impact of BPH systems. Possible score can range from 0 (no impact) to 13 (highest negative impact).

PPSM was evaluated by a modified and validated method.

Duration of study was January-2020 to March-2021.

Statistical Analysis

Base line characteristic and PPSM questions were studied with t test and compared with ANOVA test. The statistical analysis was carried out in SPSS software.

RESULTS

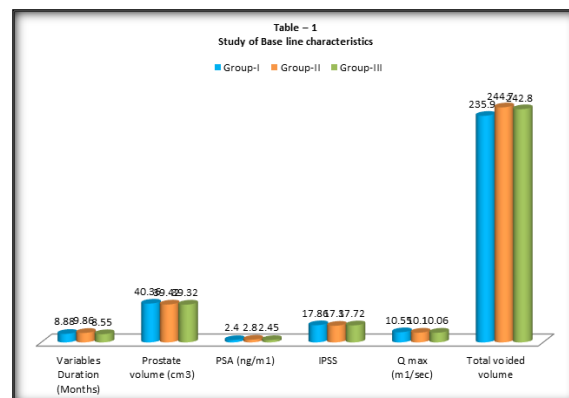


Figure 1: Study of Base line characteristics

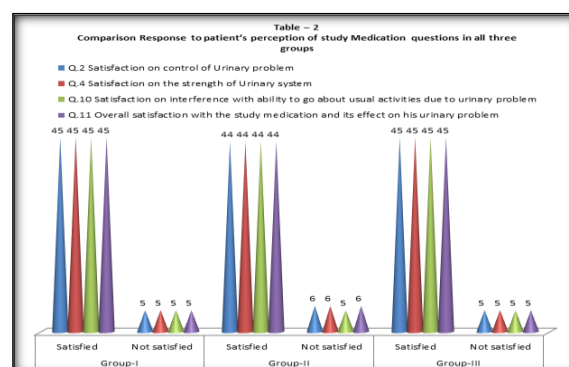


Figure 2: Comparison Response to patient's perception of study Medication questions in all three groups

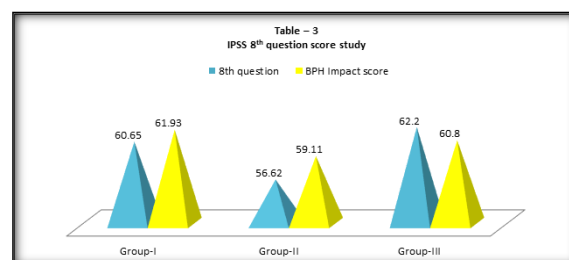


Figure 3: IPSS 8th question score study

Table 1: Study of Base line characteristics in BPH patients

Variables	Duration (Months)	Group-I Mean \pm SD (50)	Group-II Mean \pm SD (50)	Group-III Mean \pm SD (50)
		8.88 (\pm 1.30)	8.86 (\pm 1.20)	8.55 (\pm 0.75)
Prostate volume (cm ³)		40.36 (\pm 1.15)	39.42 (\pm 10.00)	39.32 (\pm 1.00)
PSA (ng/ml)		2.4 (\pm 0.14)	2.80 (\pm 0.14)	2.45 (\pm 0.12)
IPSS		17.86 (\pm 0.52)	17.3 (\pm 0.44)	17.72 (\pm 0.51)

Q max (ml/sec)	10.55 (±0.45)	10.10 (±0.42)	10.06 (±0.33)
Total voided volume	235.90 (±10.02)	244.7 (±9.2)	242.80 (±9.3)

- Duration (months) – 8.88 (±1.30) in group-I, 9.86 (± 1.20) in group-II, 8.55 (± 0.75) in group-III.
- Volume of prostate – 40.36 (±1.15) (cm)³ in group-I, 39.42 (± 1.00) in group-II, 39.32 (± 1.00) in group-III.
- PSA (prostatic specific Antigen) – 2.4 (±0.14) in group-I, 2.80 (± 0.14) in group-II, 82.45 (± 0.12) in group-III.
- IPSS – 17.86 (±0.52) in group-I, 17.37 (± 0.44) in group-II, 17.72 (± 0.51) in group-III.
- Q max (maximum Unitary flow rate ml/sec) – 10.55 (±0.45) in group-I, 10.10 (± 0.42) in group-II, 10.06 (± 0.33) in group-III.
- Total Voided volume – 235.90 (±10.2) in group-I, 244.7 (± 9.2) in group-II, 242.80 (± 9.3) in group-III

Table 2: Comparison Response to patient's perception of study Medication questions in all three groups

PPSM Question	Group-I		Group-II		Group-III	
	Satisfied	Not satisfied	Satisfied	Not satisfied	Satisfied	Not satisfied
Q.2 Satisfaction on control of Urinary problem	45	5	44	6	45	5
Q.4 Satisfaction on the strength of Urinary system	45	5	44	6	45	5
Q.10 Satisfaction on interference with ability to go about usual activities due to urinary problem	45	5	44	5	45	5
Q.11 Overall satisfaction with the study medication and its effect on his urinary problem	45	5	44	6	45	5

Comparison of response to patient's perception of study medication question in all three groups

PPSM Question – satisfaction on control of urinary problem 45 satisfied and 5 not satisfied in group-I, 44 satisfied and 6 not satisfied in group-II, 45 satisfied and 5 not satisfied in group-III

- Question 4 – Satisfaction on the strength of urinary system – 45 satisfied and 5 unsatisfied in group-I, 44 satisfied and 6 were unsatisfied in group-II, 45 satisfied and 5 were unsatisfied in group-III.
- Question 10 – Satisfaction on interference with ability to go to usual activities 45 satisfied, 5 unsatisfied in group-I, 44 satisfied, 6 unsatisfied in group-II, 45 satisfied, 5 unsatisfied in group-III.
- Question 11 – overall satisfaction and effect on his urinary problem 45 satisfied, 5 unsatisfied in group-I, 44 satisfied, 6 unsatisfied in group-II, 45 satisfied, 5 unsatisfied in group-III

Table 3: IPSS 8th question score study

IPSS	Group-I	Group-II	Group-III
8 th question	60.65%	56.62%	62.2%
BPH Impact score	61.93%	59.11%	60.80%

IPSS 8th question score improved significantly by 60.65 / in group-I, 56.62% in group-II and 62.2% in group-III and BPH impact score 61.93% in group-I, 59.11% in group-II and 60.80% in group-III.

DISCUSSION

Present prospective study of effect of fixed dosage combination of different alpha blockers with Dutasteride on quality of life in patient of LUTS of BPH in Maharashtra population. In the base line characters Duration of treatment (months) 8.88 (±1.30) in group-I, 9.86 (± 1.20) in group-II, 8.55 (±0.75) in group-III, Volume of prostate (cm³) 40.36 (±1.15) in group-I, 39.42 (±1.0) in group-II, 39.32 (±1.00) in group-III, PSA (ng/ml) 2.4 (±0.14) in group-I, 2.80 (±0.14) in group-II, 2.45 (±0.12) in group-III. IPSS 17.86 (±0.52) in group-I, 17.37 (±0.44) in group-II, 17.72 (±0.51) in group-III, Q Max (ml/sec) 10.55 (±0.45) in group-I, 10.10 (±0.42) in group-II, 10.06 (±0.33) in group-III, Total voided volume 235.9 (±10.2) in group-I, 244.7 (±9.2) in group-II, 242.80 (±9.3) in group-III [Table-1]. In comparative study of satisfaction in group-I and II was 45 and dissatisfaction was 5, but in group 44 patients were satisfied [Table-2]. IPSS

8th question score was 60.65% in group-I, 56.62% in group-II, 62.21% in group-III, BPH impact score was 61.93% in group-I, 59.11 in group-II, and 60.80% in group-III (Table-3). These findings are more or less in agreement with previous studies.^[5,6,7] Comb AT combinations of Avodart and Tamsulosin study generated some very useful and valuable information on the efficacy of combination Therapy using in moderate to severe LUTS, secondary to BPH. The launch of combination therapy 5 ARI (The 5 alpha reductase inhibitors) was in 1990, because they work through different mechanism they prevent conversion of testosterone to dihydrotestosterone (DHT). It is the DHT when bound to RNA in the cells of the prostate, that stimulates growth of the cells in glands within the prostate. After 3-6 months of therapy the cells and glands of the prostate have been deprived of DHT will shrink. There are two 5 ARI iso-enzymes, type-I, type-II. Finasteride will inhibit only the type-2 receptors where as Dutasteride will inhibit both type-

I and type-II. This extra inhibition results greater reduction of DHT of almost 95% versus 71%^[8]. The question number 8 (eight) is the motivational Index. The higher the bothersome Index. Patients will accept risk / benefit ratio discussion about the benefits of present study balanced against the potential side effects of the medication.^[9] Moreover the present FDC is cost effective treatment hence it is beneficial to lower middle class patients also and avoid the patients to undergo surgical treatment. The patients who are dissatisfied by fixed dosage combination therapy the standard surgical treatments option has been trans urethral resection of prostate (TURP) for a long time.^[10] but prior to surgical approach one has to try for fixed dosage combination therapy which satisfied majority of patients for longer time and last resort will be the surgical approach (TURP).

CONCLUSION

Fixed dose combination of Dutasteride, 5 ARI with three alpha-adrenergic antagonists, Tamsulosin, Alfuzosin and Silodosin, caused a significant and comparable improvement in quality of life in LUTS and BPH patients. All the three FDC were equally effective with respect to satisfaction with the study medications. The results indicate that any of the FDC can be used with respect to quality of life and medication and satisfaction.

Limitation of Study

Owing to tertiary location of research centre and small number of patients and lack of latest techniques we have limited findings and results

- This research paper is approved by Ethical committee of ACPM Medical College hospital Dhule, Maharashtra-424001.
- No Conflict of Interest
- Self-funding.

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