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MEDICAL TREATMENT OF SYMPTOMATIC BENIGN PROSTATIC HYPERPLASIA: A COMPARISON BETWEEN COMBINED DUTASTERIDE AND TAMSULOSIN MONOTHERAPY

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ABSTRACT

Benign prostatic hyperplasia is a common problem in elderly male. The number of symptomatic benign prostatic hyperplasia is also increasing with increased life expectancy. This ultimately results in complications requiring surgical treatment. However there is increasing interest in the use of drug therapy rather than surgical intervention, especially in patients with mild to moderate symptoms and who are unable or unwilling to undergo surgery. The case control study was done on 145 patients with symptomatic benign prostatic hyperplasia to evaluate the efficacy of combination therapy of Dutasteride and Tamsulosin in comparison with Tamsulosin monotherapy in term of relief of symptoms and increase in urinary flow rate. Among them in group-A comprising 46 cases, group-B 47 cases and group-C 45 cases. During study period 2 patients from group-A, 5 patients from group-B and 3 patients from group-C did not attend the follow up schedule. Ultimately 42 cases from each group were compared. Placebo was given to each cases of Group-A, Tamsulosin 0.4 mg to Group-B and combination of Tamsulosin 0.4 mg + Dutasteride 0.5mg to Group-C. a significant improvement of IPSS was found after 12 months of treatment with Tamsulosin (group-B) and combination therapy (Tamsulosin+Finasteride) (group-C). This changes were tested using paired student 't' test. The change was found significant (p= <0.001). Mean change of peak urine flow rate in group-A was 0.29±1.46, in group-B was 5.00±1.25 and in group-C was 5.50±1.70. Hence a significant improvement of peak urine flow rate was found after 12 months treatment with 0.4 mg of Tamsulosin (group-B) and with combination (Tamsulosin + Dutaasteride). Significant decreased of post voidal urine volume and changes of prostate volume was found after 12 months of treatment. From the present study it can be concluded that the best option of treatment for clinically benign prostate hyperplasia with mild to moderate symptoms is combination of 0.4 mg Tamsulosin and 0.5mg Dutasteride once daily. This study inferred that combination therapy is more effective in the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia leading to rapid improvement of symptoms by Tamsulosin and decreased disease progression and sustained improvement by Dutasteride.

KEYWORDS: Dutasteride and Tamsulosin in comparison with Tamsulosin monotherapy.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common condition in aging men, affecting over half of men in their seventh decade and 90% of men in their eighth and ninth decade, with bothersome symptoms reported in nearly 50% of men aged≥50 years in the general population (Paul Siami et al, 2007). The condition is characterized histologically by stromal and epithelial hyperplasia and clinically by lower urinary tract symptoms (LUTS), which are typically divided into irritative (storage) symptoms (i.e. increased frequency, nocturia and urgency etc) and obstructive (voiding) symptoms (i.e. incomplete emptying, weak stream, intermittency and hesitancy etc).

Therapy for symptomatic benign prostatic hyperplasia, whether medical or surgical is primarily geared towards

the relief of bladder outlet obstruction (BOO). Clearly the most direct way to accomplish this is to remove the hyperplastic benign prostatic tissue surgically usually by transuretheral resection or prostate (TURP). However, transurethral resection of prostate requires hospitalization and catheterization and carries a complication rate of around 18% as well as small but significant mortality.[1]

The principal motor control of the prostate is via an action on α1 andreoreceptor which are localized predominantly within the stromal compartment of the prostate (Noradrenalline induces contraction in strip of both normal and hyperplastic prostate and these can be blocked by the additional of selective α1 adenoceptor antagonist).

In Bangladesh, most of the practicing doctors have been prescribing medical therapy for mild to moderate symptoms due to uncomplicated benign prostatic hyperplasia. Some are advocating that only α1 adrenoceptor blocker can relieve symptoms and give better quality of life to a patient suffering from uncomplicated benign prostatic hyperplasia, but other differ to this opinion and add 5α-reductase inhibitors along with α1 blocker. Though very little work have been done in the different part of the world to compare the efficacy of combination therapy with Tamsulosin and Dutasteroid in comparisonb with Tamsulosin monotherapy, but never in our country so far known.

Keeping these views in mind, the present work has been carried out to evaluate the efficacy and safety of medical treatment for symptomatic benign prostatic hyperplasia (BPH) with combined Dutasteride and Tamsulosin in comparison with Tamsulosin monotherapy.[2]

In the present study the additive effect of combination therapy of Dutasteride, a 5α reductase inhibitor and Tamsulosin, a α1 adrenoceptor blocker in comparison with Tamsulosin monotherapy was evaluated.

MATERIALS AND METHOD

The present study was a prospective purposive case control study conducted in the department of Urology, Dhaka Medical College Hospital, Dhaka from July 2012 to June 2014. Study population included the patients who attended the outpatient department of Urology complaining lower urinary tract symptoms due to benign prostatic hyperplasia.

Total 145 cases were selected purposively according to selection criteria from the patients attending urology out patient department of Dhaka Medical College Hospital with lower urinary tract symptoms due to benign prostatic hyperplasia. Among them 19 cases were not reported at different time of the study period.

Patients were sequentially placed in 3 groups. 1st case was put in Group-A, 2nd case in Group-B, 3rd case in Group-C and again 4th case in Group-A and so on. This sequence was followed among patients of this study groups. Total 138 cases were selected for this study. Among them in group-A comprising 46 cases, group-B 47 cases and group-C 45 cases. During study period 2 patients from group-A, 5 patients from group-B and 3 patients from group-C did not attend the follow up schedule. Ultimately 42 cases from each group were compared.

Placebo was given to each cases of Group-A, Tamsulosin 0.4 mg to Group-B and combination of Tamsulosin 0.4 mg + Dutasteride 0.5mg to Group-C.

Before starting the treatment, each patient was evaluated by history, physical examination, digital rectal examination (DRE), International Prostate Symptoms Scoring (IPSS), urinalysis, Ultrasonogram, uroflowmetry and serum specific antigen. By ultrasonogram volume of the prostate and post voidal residual was determined.

After starting the dose of placebo, Tamsulosin 0.4mg and combination of Dutasteride and Tamsulosin, each patient was then observed and followed up at 3rd month (1st visit), 6th month (2nd visit), 9th month (3rd visit) and 12th month (4th visit) treatment. On each follow up visit, each patient was evaluated by history to find out improvement of stream, IPSS, uroflowmetry to see peak urinary flow rate, ultrasonogram to see post voidal residual urine volume and prostate volume. During follow up it was observed for any adverse event. The result of follow up of patients of all three groups were then compared.

RESULTS

Changes in IPSS

In group-A, mean IPSS was 16.64±1.19 at baseline, which become 15.95±1.71 at end point and therefore mean changes of IPSS was 0.69±1.35. In group-B, mean IPSS was 16.67±1.37 at base line, which became 10.83±0.91 at end point and therefore mean changes of IPSS, was 5.83±1.59.

In group-C, mean IPSS was 16.69±1.12 at baseline, which became 0.902±1.05 at end point and therefore changes of IPSS was 7.67±1.69. Mean changes of IPSS in group-A was 0.69±1.35, in group-B was 5.83±1.59 and in group-C was 7.67±1.69.

Hence a significant improvement of IPSS was found after 12 months of treatment with Tamsulosin (group-B) and combination therapy (Tamsulosin+Finasteride) (group-C). This changes were tested using paired student 't' test. The change was found significant (p= <0.001). But non significant changes in the patient of group A. Again significant changes was found in group-C over group-A and group-B. This tested by using unpaired student 't' test and the change was found significant (p= <0.001).

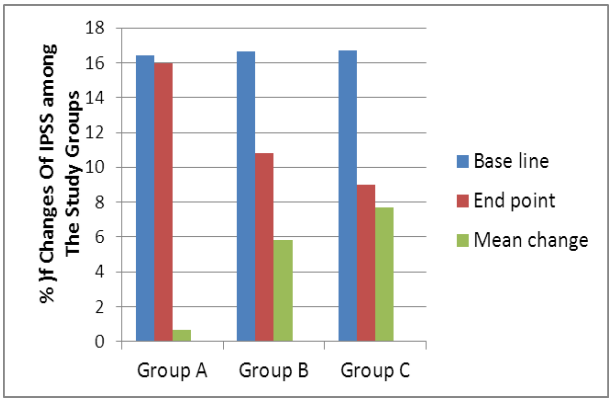

Figure 1: Bar diagram is showing changes in IPSS from baseline to end point among the study groups.

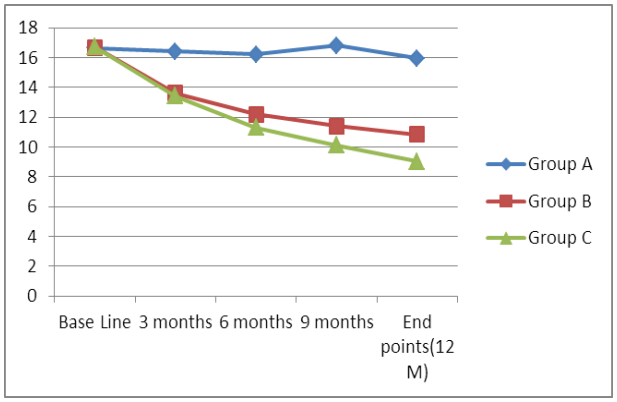

Figure 2: Line diagram is showing the changes in IPSS from baseline during the follow up visit.

Changes in peak urine flow rate (Q_{max})

Mean change of peak urine flow rate in group-A was 0.29±1.46, in group-B was 5.00±1.25 and in group-C was 5.50±1.70. Hence a significant improvement of peak urine flow rate was found after 12 months treatment with 0.4 mg of Tamsulosin (group-B) and with combination (Tamsulosin + Dutaasteride) (group-C). This changes was tested using paired student't' test and the change was statistically significant (p= <0.001). Minimum changes was seen in group-A. Again improvement of peak urine flow rate is more significant in group-C than group-A, but non significant changes was found than group-B.

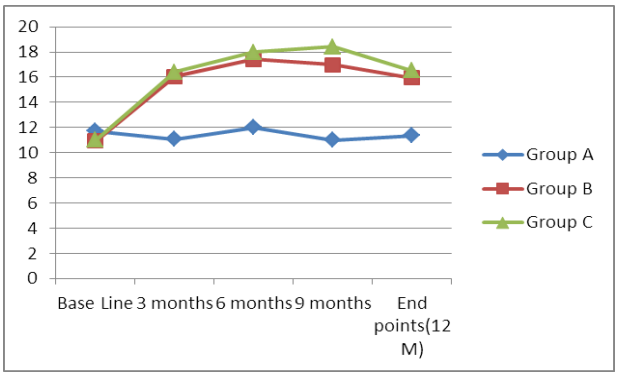

Figure 3: Line diagram is showing the changes in peak urine flow rate (Q_{max}) from baseline during the follow up visit.

Change In Post void Residual Urine Volume

significant decreased of post voidal urine volume was found after 12 months of treatment with 0.4 mg of Tamsulosin (Group-B) and with combination therapy (Tamsulosin 0.4 mg + Dutasteride 0.5 mg, group-C). This changes was tested using paired student't' test and change was found significant (p=<0.001). Non significant changes was found in group-A. Again the change of post-voidal residual urine volume is more significant in group-C than group-B. This changes was test by unpaired student 't' test and change was found significant (p= <0.001).

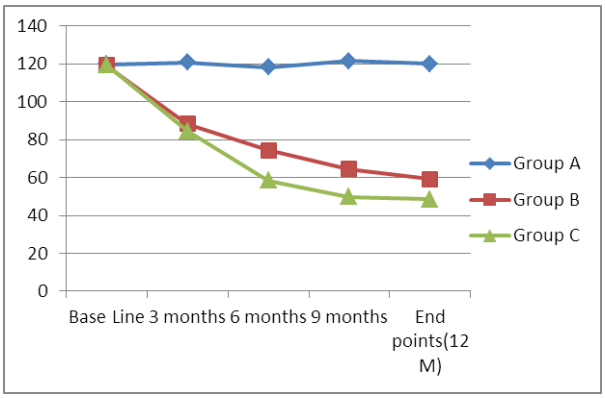

Figure 4: Line diagram is showing the changes in post voided residual urine volume from baseline during the follow up visit.

Changes of prostate volume in different groups

The volume of the prostate of each patient was measured by ultrasonography and compared.

In group-A, mean prostate volume was 45.88±1.50 at base line, which became 46.71±1.73 at end point and therefore changes of mean prostate volume was 0.83±1.74. In group-B, mean prostate volume was 44.93±1.69 at base line, which became 44.21±2.54 at end point and therefore change of mean prostate volume was 0.71±1.70. In group-C, mean prostate volume was 46.81±1.53 at base line, which became 38.50±1.66 at end point and therefore of mean prostate volume was 8.31±1.57. Mean changes of prostate volume in group-A was 0.83±1.74, in group-B was 0.71±1.70 and in group-C was 8.31±1.57.

DISCUSSION

There are few studies to compare the efficacy and safety of monotherapy versus combination drugs therapy for the treatment of benign prostatic hyperplasia in the world suggested that combination therapy is more effective at reducing symptoms score in men with enlarged prostate at 1 year. The additive benefit of Dutasteride provide in reducing symptoms, risk of acute retention of urine and invasive surgery was observed within the 1st year of treatment.

The α1-blockers and 5α-reductase inhibitors have gained widespread acceptance for the treatment of symptomatic

clinically benign prostatic hyperplasia. The primary objective of the medial therapy for benign prostatic hyperplasia is to improve the quality of life by relieving lower urinary tract symptoms and prevent complications. IPSS score, peak urine flow rate and prostate volume are used to determine the effectiveness of the medical treatment for benign prostatic hyperplasia in different part of the world. In this study IPSS score, peak urine flow rate, post voidal residual urine volume and prostate volume are used to assess the effectiveness of the treatment.

Improvement of IPSS was found after 12 months of treatment with Tamsulosin and combination of Tamsulosin 0.4mg + Dutasteride 0.5mg therapy (p=<0.001). But a negligible changes of IPSS were observed in group-A. Again it was observed that better improvement of symptom score in group-C than in group-B (p=<0.001). Similar improvement was observed in a separate study that IPSS was decreased significantly after 24 months of treatment with combination of Dutasteride & Tamsulosin.[3] The author found that mean changes of IPSS was -8.5.

Efficacy of combination (Tamsulosin + Dutasteride) therapy were determined in a separate study and observed peak urine flow rate improved 2.4ml/sec (± 0.12) after 24 months of treatment and Tamsulosin (0.4mg per day) improved peak urine flow rate 3.6ml/sec.[4] In a separate study the mean peak urine flow rate significantly improve from 7.8±3.5ml/sec to 11.1±3.5ml/sec after 4 weeks treatment with 0.4 mg of Tamsulosin.[5] Hence prostate volume was reduced significantly in group-C after 12 months of treatment, but in group-B a negligible changes of prostate volume were observed. In group-A volume of prostate were observed to became little increase. It has been shown in a several study that volume of the prostate become reduces after 12 months of treatment with a-blocker and 5a-reductase inhibitors.

It was reported in a study that, mean changes of prostate volume was -26.9%(± 0.62%) after 24 months treatment in combination of Tamsulosin and Dutasteride and 0.0%(±0.84%) with Tamsulosin alone[3]. In another study, it was shown that a-blocker did not reduce the prostate volume significantly.[6]

In a study most common adverse events reported after Tamsulosin were asthenia, dizziness and headache which is comparable with the present study.[7] In another study, Dutasteride produced sex related adverse effects and they observed that ejaculatory disorder were developed in 2.7% cases, decreased libido 3.4% and impotence 1.7% cases.[3]

From the present study it can be concluded that the best option of treatment for clinically benign prostate hyperplasia with mild to moderate symptoms is combination of 0.4 mg Tamsulosin and 0.5mg Dutasteride once daily. This study inferred that combination therapy is more effective in the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia leading to rapid improvement of symptoms by Tamsulosin and decreased disease progression and sustained improvement by Dutasteride. Combination therapy not only ameliorates symptoms of benign prostatic hyperplasia but may also decrease the risk for complications and prostate related surgery.

REFERENCES

1. Coffey DS, Walsh PC, Clinical and experimental studies of benign prostatic hyperplasia, Uro Clin North Am, 1990; 17: 461-475.
2. Abrams P. Speakman M, Stott M. et al. A dose-ranging study of the efficacy and safety of tamsulosin, the first prostate-selective a1A-adrenoceptor antagonist, in patients with benign prostatic obstruction (symptomatic benign prostatic hyperplas). Br. J Urol, 1997; 80: 587-596.
3. Claus G. Roehrborn, Jack Barkin, Paul Siami et al. Clinical outcomes after combined therapy with dutasteride plus tamsulosin or either monotherapy in men with benign prostatic hyperplasia (BPH) by baseline characteristics: 4-year results from the randomized, double-blind Combination of Avodart and Tamsulosin (CombAT) trial. BJU International, 2011; 107: 946–954.
4. J Miller TH Tarter, Combination therapy with dutasteride and tamsulosin fothe treatment of symptomatic enlarged prostate Clinical Interventions in Aging, 2009; 4: 251-258.
5. Horiuchi K, Tsuboi N, Hatrori T, et al. The short term effect of tamsulosin in Japanese men with benign prostatic hyperplasia. J Nippon Med Sch, 1999; 66(6): 382-386.
6. Clark RV, Hermann DJ, Cunningham GR, et al. Marked suppression of dihydrotestosterone in men with benign prostatic hyperplasia by dutasteride, a dual 5alpha-reductase inhibitor. J Clin Endocrinol Metab, 2004; 89(5): 2179–84.
7. Kevin T. McVary,* Claus G. Roehrborn, Andrew L. Avins et al. Update on AUA Guideline on the Management of Benign Prostatic Hyperplasia. The Journal of Urology, 2011; 185: 1793-1803.