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Original Research Article

Use of tamsulosin and dutasteride combination for the management of benign prostatic hyperplasia: a real world practice survey (VELTAM survey)

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ABSTRACT

Background: Benign prostatic hyperplasia has high prevalence ranging from 8-80% affecting male population. Dutasteride and tamsulosin combination has been found to be more effective as compared to individual monotherapy. However, evidence on real world clinical experience on this combination is lacking. Aim and Objective of current study was to gather the evidence on real world clinical experience from the physicians using the combination of tamsulosin and dutasteride for the management of BPH.
Methods: Responses from 1571 physicians who were the current prescribers of tamsulosin with dutasteride combination for the management of BPH were collected in a questioner containing a set of nine questions having multiple choice answers. All the data is expressed as number and percentage.
Results: Majority of the physicians considered tamsulosin with dutasteride combination as the gold standard therapy for the treatment of BPH (88.86%). Most common co-morbidities which physician takes in to consideration was cardiovascular (62.61%) followed by asthma (23.04%). While treating BPH patients with cardiovascular co-morbidities, majority of the physician consider drug-drug interaction as significant criteria to decide the therapy (87.83%).
Conclusions: Physicians considered tamsulosin and dutasteride combination as the gold standard for the management of BPH with cardiovascular co-morbidity. Tamsulosin and dutasteride combination is the first line choice for the management of BPH in real world practice.

Keywords: Benign prostatic hyperplasia, Drug drug interaction, Anti-hypertensive effect, Real word practice data

INTRODUCTION

Non-cancerous enlargement of the prostate is known as benign prostatic hyperplasia (BPH).[1] In BPH bladder wall get thickened due to benign and enlarged prostate that exert a pushing pressure on the urethra. This results in to weakening of the bladder and loss of complete emptying of the bladder, ultimately resulting in urine retention which is known as lower urinary tract symptoms (LUTS).[2]

BPH is a common disease affecting men. Prevalence varies as per the age of the men. It ranges from 8% in men with age between 31-40 years to around 80% in men with age more than 80 years.[3] LUTS due to BPH require therapeutic intervention in order to have sustained improvement in clinical symptoms and quality of life (QoL) of the patients.[4,5] 5-alpha-reductase inhibitors (5-ARIs) and alpha-blockers are the two main pharmacological agents used for the management of BPH/LUTS. Dutasteride is a 5-ARI which reduces the

growth of the cells hence reducing the prostate size by blocking the conversion of testosterone to dihydrotestosterone.[6] On other hand tamsulosin shows its activity by relaxing bladder neck muscles and prostate muscle fibres by being uroselective alpha-blocker. In turn tamsulosin improves urine flow rate.[7]

Combination of both dutasteride and tamsulosin has found to be superior at reducing the relative risk of BPH compared to individual component.[8] Real world clinical experiences at the physician level for this combination is lacking. To best to our knowledge this is the first survey where we tried to evaluate the clinical experience and satisfaction level of the physicians using the combination of dutasteride and tamsulosin for the treatment of BPH/ LUTS. Hence, in present study we tried to gather the evidence on real world clinical experience from the physicians using the combination of tamsulosin and dutasteride for the management of BPH.

METHODS

Current study was a retrospective, multicenter real-world study performed between April 2020 to June 2020 at Berhampore, West Bengal, India. In present survey the response from 1571 physicians who were the current prescribers of tamsulosin with dutasteride combination for the management of BPH were collected. A set of nine questions having multiple choice answers were presented to each physician and the response was collected. As it was a real-world survey, questions were designed and approved by the physicians having expertise in the field being investigated.

Statistical analysis

All the responses of above mentioned nine questions were corrected and a excel sheet was maintained. All the data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution was performed to obtain tables. PRISM was used to prepare the graph. All the data is expressed as number and percentage. No further statistical test was performed.

RESULTS

Out of 1571 participants, majority of them considered tamsulosin with dutasteride as the gold standard therapy for the treatment of BPH; 1396 (88.86%). In present study it was found that most common co-morbidity which physician take into consideration while treatment a patients with BPH was cardiovascular (62.61%) followed by asthma (23.04%). Other co-morbid condition which is being considered are CKD, Cancer and DAB in 2.17%, 5.22% and 2.03% respectively. Majority of the participants (85.65%) responded that cardiovascular co-morbidity is associated with 30-60% of the patients with BPH. While treating BPH patients with CV comorbidities, majority of the physician consider drug-drug interaction as significant criteriato decide the therapy (87.83%).

Table 1: List of questions.

Question number	Question
1	Do you consider Tamsulosin with Dutasteride as the gold standard therapy for the treatment of BPH?
2	According to your clinical experience, what is the satisfaction level of patients taking Tamsulosin+Dutasteride combination therapy?
3	As per your clinical experience, with respect to patients relief, pleases rate combination therapy for BPH (Tamsulosin+Dutasteride).
4	As per your clinical experience, with respect to patients relief please rate combination therapy for BPH (Tamsulosin+Finasteride)
5	As per your clinical experience, with respect to patients relief please rate combination therapy for BPH (Silodosin+Dutasteride)
6	As per your clinical experience, with respect to patients relief please rate combination therapy for BPH (Alfuzosin+Dutasteride)
7	As per your clinical experience, while treating patients for BPH, what are the most important comorbidities clinicians should take into consideration?
8	How many of your BPH patients have cardiovascular co morbidities?
9	While treating your BPH patients with CV co morbidities, do you consider drug-drug interaction as significant criteria?

DISCUSSION

Alpha$_1$-selective adrenergic receptor blockers are considered as first-line medical therapy for BPH. However, combination of both tamsulosin and dutasteride is gaining its importance as the first line treatment for BPH. This has been proved in our survey where we collected the response of 1571 physicians who were using the combination of tamsulosin and dutasteride for the management of BPH. It was revealed that majority of the users considered tamsulosin with dutasteride combination as the gold standard therapy for the treatment of BPH (88.86%).

The combination of avodart and tamsulosin (CombAT) study included 4844 men ≥50 years of age with a clinical diagnosis of BPH who were given a combination of tamsulosin and dutasteride found that combination therapy provided significantly greater symptom benefit

than either monotherapy and was found to be safe and well tolerable.[8]In present study 67.97% of the physicians using the combination were satisfied with the results and 28.55% of them were extremely satisfied with the combination therapy (Table 1, Figure 1).

Table 2: Responses of the participants based on their clinical experience (n=690).

Question	Extremely satisfied	Satisfied	Neither satisfied nor dissatisfied	Dissatisfied	Extremely dissatisfied
Satisfaction level of patients taking tamsulosin+dutasteride combination therapy	197 (28.55)	469 (67.97)	16 (2.32)	7 (1.01)	1 (0.14)
Patients relief with tamsulosin+dutasteride combination	171 (24.78)	482 (69.86)	27 (3.91)	9 (1.30)	1 (0.14)
patients relief with tamsulosin+finasteride combination	24 (3.48)	360 (51.17)	229 (33.19)	74 (10.72)	3 (0.43)
patients relief with silodosin+dutasteride combination	189 (27.39)	341 (49.42)	108 (15.65)	51 (7.39)	1 (0.14)
patients relief with alfuzosin+dutasteride combination	102 (14.78)	304 (44.06)	196 (28.41)	82 (11.88)	6 (0.87)

Table 3: Distribution according to co-morbidity which physician take into consideration while treatment a patient with BPH.

Co-morbidity	Percentage
Cardiovascular	62.61
Asthma	23.04
CKD	2.17
Cancer	5.22
DAB	2.03

Finding of current survey is the confirmation for CombAT trial in real world practice for the management of BPH. Further strengthening the findings of present survey, a previous study by Djavan et al evaluating the improvement in symptom and impact of tamsulosin and dutasteride combination on quality of life of patients and reported that combination therapy not only provides better symptom improvement and improved urinary flow rate but is also associated with a more favorable impact on quality of life and patient satisfaction with treatment than monotherapy.[9] Montorsi et al have also found significantly better symptom improvement based on the BPH impact index and International prostate symptom score (IPSS) question 8 with tamsulosin and dutasteride combination than monotherapy.[10] Though BPH is not considered as the life-threatening condition, however, it's impact on the quality of life (QOL) is significant and should be considered while choosing intervention. BPH often occurs along with the age-related comorbidities. Among those most common are cardiovascular disease, hypertension, and erectile dysfunction.[11] In our survey, majority of the physician (85.65%) found that cardiovascular co-morbidity is associated with 30-60% of the patients with BPH. Presence of co-morbid condition along with BPH is a factor determining the choice of the treatment. In present study most common co-morbid condition which physician takes into consideration while treating patients with BPH was cardiovascular diseases followed by asthma (Table 2). Tamsulosin is more selective for the $alfa_{1A}$-and $alfa_{1D}$-AR subtypes and has less affinity for the $alfa_{1B}$ subtype, which regulates blood pressure via vascular smooth muscle contraction.[12-14] Hence tamsulosin can safely be used among the patients with cardiovascular diseases as it does not have any impact on the predisposing factor such as blood pressure. Previous studies have shown that inappropriate drug selection can lead to most frequently associated drug-related problems (DRPs) such as adverse reactions, drug choice problems, dosing problems, and drug interactions in the management of BPH. Zaman et al reported 24.9% durg-durg interaction related issue among all the DRPs in the management of BPH.[15] In present survey majority of the users responded that while treating BPH patients with CV comorbidities, majority of them consider drug-drug interaction as significant criteria to decide the therapy (87.83%). Previous drug drug interaction studies have shown that tamsulosin has limited drug drug interaction as compared to other alpha blockers. Roehrborn et al found that tamsulosin and dutasteride combination therapy has similar withdrawal rate due to drug-related adverse events as compared to monotherapy. [8]Hence, it seems that this combination has less drug drug interaction in the presence of cardiovascular co-morbidities in the management of BPH. Being a real-world study and lack of control group and randomization; present study

findings cannot be applied to whole population. There is a need of a large randomized clinical trial to provide strength to present study findings.

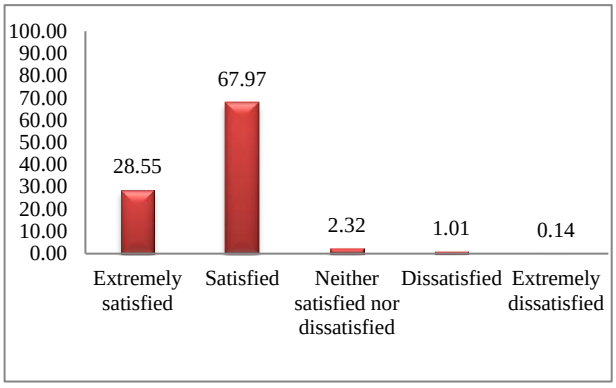

Figure 1: Satisfaction level of tamsulosin+dutasteride combination.

CONCLUSION

Present survey has found that physicians consider tamsulosin and dutasteride combination as the gold standard for the management of BPH as satisfaction level of patients using this combination was high. This combination also provides benefits in patients with cardiovascular co-morbidity due to the antihypertensive effect of tamsulosin. Majority of the physician consider drug-drug interaction as significant criteria to decide the therapy which can be resolved by using tamsulosin in the combination. To conclude tamsulosin and dutasteride combination is the first line choice for the management of BPH.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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