

COMPARATIVE ASSESSMENT OF EFFICACY OF TADALAFIL AND TAMSULOSIN ALONE AND IN COMBINATION AMONG MEN WITH BENIGN PROSTATIC HYPERPLASIA

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Article Info: Received 24 October 2021; Accepted 11 December 2021

DOI: <https://doi.org/10.32553/ijmbs.v5i12.2351>

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Conflict of interest: No conflict of interest.

Abstract

Background: Men in 5th and 6th decade of life experience a fall in the quality of life owing to Lower Urinary tract symptoms arising out of benign prostatic hypertrophy. The medical management protocol involves either monotherapy or combination. The present study was done to comparatively evaluate the efficacy of monotherapy as well as combination therapy in treatment of such patients using two drugs, namely Tadalafil and Tamsulosin. **Methodology:** The study comprised of 90 subjects divided equally in three groups. Group A and B were subjected to monotherapy using Tadalafil and Tamsulosin respectively, while Group C was provided a combination. **Observations:** There was statistically significant difference in subjects having Tamsulosin alone or in combination therapy as compared to subjects given Tadalafil alone. **Conclusion:** Tamsulosin alone or in combination therapy has shown a better outcome in the selected study subjects.

Keywords: BPH, LUTS, Tamsulosin, Tadalafil

Introduction

Lower urinary tract symptoms (LUTS) among different group of men with benign prostate hyperplasia BPH often interferes with patients daily activities leading to a reduction in confidence as well as quality of life.¹

Benign prostate hyperplasia is a histological diagnosis which is identified by non-malignant hyperplasia of prostatic tissue due to smooth muscle and epithelial cell proliferation in the prostate transition zone². Benign prostate hyperplasia can result in prostate enlargement which leads to the development of LUTS such as storage, voiding and post-micturition symptoms. An increased smooth muscle tone in the prostate or the vasculature supporting the lower urinary may be a contributing factor also.³

In terms of pharmacological treatment required, the most common drugs are α -blockers and 5-alpha reductase inhibitors (5ARIs). Tadalafil's mechanism as a long-acting phosphodiesterase 5 (PDE5) inhibitor in the treatment of men with BPH-LUTS is associated with increased activity of the nitric oxide/cGMP (Cyclic guanosine monophosphate)/ protein kinase G pathway via PDE5 isoenzymes' inhibition in different lower urinary tract tissues. These results can be detected in smooth muscle relaxation in the bladder, urethra, prostate, and supporting vasculature, increased blood perfusion to the pelvic area, and finally modulation of sensory stimuli from this area^{4,5}

The present study was designed to assess if the present pool of study subjects have a better response to single or combination therapy with tadalafil and tamsulosin as management drugs for LUTS as a result of BPH.

Methodology:

The present study was a randomized, single blind study conducted over a period of 1 year from January 2019 to January 2020 at dept of Urology in Geetanjali Medical College and Hospital, Udaipur, Rajasthan. The study was granted institutional ethical approval prior to commencement of data collection. Written informed consent was taken from all patients for inclusion in the study.

All patients with LUTS, benign prostate hyperplasia and any grade of erectile dysfunction were recruited for this study.

Inclusion criteria was men older than 45 years old, International Prostate Symptom Score (IPSS) ≥ 12 , and having a history of erectile dysfunction.

Patients with previous benign prostate hyperplasia or erectile dysfunction treatment, history of surgical procedure for their prostatic problem, contraindication for tadalafil (i.e. nitrate consumption) or tamsulosin (i.e. allergic reactions), were excluded from the study.

The sample consisted of 90 patients divided equally and randomly in 3 groups. Group A received 5 mg/daily tadalafil; Group B received 0.4 mg/daily tamsulosin; Group C received a combination of 0.4 mg/daily tamsulosin and 5 mg/daily tadalafil.

History and examination details were noted on first OPD visit. Laboratory blood samples were taken to measure blood urea nitrogen, creatinine and prostate specific antigen. Ultrasound of kidneys and bladder including determining residual urine volume and uroflowmetric test were done for each patients.

All patients were asked to fill IPSS and International Index of Erectile Function (IIEF) Questionnaire.

Repeat assessments after three months after the first visit was done along with analysis of resultant data.

Statistical analysis was done using SPSS ver 16 software to determine central tendency and tests of significance.

Observations:

The observations are as depicted in Table 1. Mild, moderate and severe erectile dysfunctions were seen in 18, 30 and 12 participants, respectively. There were no significant differences between prostate volume, prostate specific antigen, post-void residual volume, IPSS score between the three groups ($P > 0.05$).

Table 1: Parameters on First OPD visit

Parameter	Group A	Group B	Group C	P value
Prostate Volume -Mean (ml)	59.2	60.1	60.6	NS
PSA- Mean	2.44	2.47	2.48	NS
PVR Volume-Mean	61.7	60.6	60.1	NS
IPSS Mean	19.9	20.1	20.2	NS

There was no significant difference in prostate specific antigen before and after the treatment in all groups and Post-void residual level was significantly different before and after the treatment, except for group A. Also, this group had no meaningful difference compared to the other groups in this regard ($P > 0.05$). There were significant differences between pre- and post-treatment IPSS in each group ($P < 0.05$).

Table 2: Post Treatment Values of Study Participants

Parameter	Group A	Group B	Group C	P value
Prostate Volume -Mean (ml)	59.2	60.1	60.6	NS
PSA- Mean	2.44	2.47	2.48	NS
PVR Volume-Mean	56.7	41.4	40.5	<0.05
IPSS Mean	16.9	16.1	16.2	<0.05

The common compilations were nausea, myalgia and headaches however no discontinuation was seen in any of the groups.

Discussion:

Both erectile dysfunction and BPH-LUTS are common in men and their prevalence increases with age. Several studies have studied the efficacy of monotherapy with tadalafil and tamsulosin. Also, there are studies on their combination with other drugs or comparing them with each other. However, literature review revealed that no study has evaluated the effect of each of these drugs with their combination in the selected population and geographic area.⁶⁻¹⁰

In other monotherapy studies with these drugs, it was reported that the IPSS results were in line with results of the present study. Double-blind, randomized,

placebo-controlled studies of 5 mg tadalafil once-daily in Japanese men, Japanese, Korean and Taiwanese men and Japanese and Korean men has demonstrated greater improvement in the change from baseline to endpoint in total IPSS for monotherapy with 5 mg tadalafil compared to placebo.¹¹⁻¹³

There are several small sampled clinical trials that have reported tadalafil/ α -blocker combination therapy may have better effect on total IPSS than α -blocker or tadalafil monotherapies in men with BPH-LUTS. This is in concurrence with our results.^{14,15}

The present study investigated the IIEF score and showed that there were significant improvements in each group and between the groups in this regard. These improvements were higher in tamsulosin and combination groups, respectively.

Similarly, Singh and colleagues showed that IIEF score increases significantly in the same three groups (+39.28%, $P < 0.05$; +45.96%, $P < 0.05$; and +60.23%, $P < 0.05$, respectively).¹⁶

In another study Bechara and colleagues showed that the IIEF improved in tamsulosin plus tadalafil group ($P < 0.001$), but not in tamsulosin alone group ($P > 0.05$).¹⁷

Conclusion:

Based on these results, combination therapy with tadalafil and tamsulosin is recommended because of its good outcomes in erectile dysfunction. It is recommended because of its synergistic effects, well toleration and its safety. Due to the limited sample size larger scale studies may be needed to understand the long term effects of this combination therapy.

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