

COMPARISON OF EFFICACY OF PDE5 INHIBITORS (SILDENAFIL) VERSUS ALPHA-BLOCKERS (TAMSULOSIN) IN TREATMENT OF LOWER URINARY TRACT SYMPTOMS (LUTS) SECONDARY TO BENIGN PROSTATIC HYPERPLASIA

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Abstract: Benign prostatic hyperplasia (BPH) is a prevalent condition leading to lower urinary tract symptoms (LUTS) in men, affecting their quality of life. Various medications, including phosphodiesterase five inhibitors (PDE5-Is) and alpha-blockers (ABs), are used for treatment, but direct comparison studies between these drugs are limited. This study aimed to compare the efficacy of sildenafil (PDE5 inhibitor) versus tamsulosin (alpha-blocker) in patients with LUTS secondary to BPH. A randomized controlled trial was conducted at the Department of Urology, KEMU/Affiliated Hospital, Lahore. A sample size of 100 patients (50 in each group) was calculated using the WHO calculator based on expected efficacy rates. Patients aged 40-70 years with BPH and LUTS were included. Exclusion criteria included high PSA levels, history of prostatic surgery, acute urinary retention, or active urinary tract infection. Patients were randomly assigned to receive sildenafil 25mg OD or tamsulosin 0.4mg HS for three months. Efficacy was assessed by changes in the International Prostate Symptom Score (IPSS) after treatment. The demographic characteristics of the study population showed a mean age of 60 years with a similar distribution of comorbidities between the groups. After three months of treatment, 80.9% of patients in the sildenafil group showed a significant improvement in IPSS compared to 55.5% in the tamsulosin group. The chi-square test indicated a significant difference in efficacy between the two groups ($p < 0.05$). Sildenafil demonstrated superior efficacy compared to tamsulosin in reducing LUTS secondary to BPH. These findings suggest that sildenafil may be considered as a first-line treatment option for patients with BPH and LUTS.

Keywords: Benign Prostatic Hyperplasia, Lower Urinary Tract Symptoms, Sildenafil, Tamsulosin

Introduction

Benign prostatic hyperplasia (BPH) is a prevalent condition characterized by the enlargement of the prostate gland, leading to lower urinary tract symptoms (LUTS) in men, particularly in middle-aged and elderly individuals (Russo et al., 2018). The global burden of BPH has been increasing steadily, affecting men's quality of life and posing significant healthcare challenges (Park et al., 2020). LUTS associated with BPH includes obstructive, irritative, and post-micturition symptoms, which significantly impact patients' daily activities and psychological well-being (Iheanacho et al., 2022).

Various treatment options are available for managing BPH/LUTS, including alpha-blockers (ABs), muscarinic receptor antagonists (MRAs), phosphodiesterase five inhibitors (PDE5-Is), and beta3-adrenoceptor agonists (B3As) (De Nunzio et al., 2020). Among these, alpha-blockers have been widely used as a first-line treatment due to their efficacy in relieving symptoms by relaxing smooth muscle in the prostate and bladder neck (Romics, 2007). However, recent studies have suggested a potential role for PDE5 inhibitors in the management of BPH/LUTS, particularly in patients with concomitant erectile dysfunction (Calogero et al., 2018).

While several studies have demonstrated the efficacy of sildenafil (a PDE5 inhibitor) and tamsulosin (an alpha-blocker) in improving LUTS in patients with BPH, direct

comparison studies are limited, and the optimal management strategy remains controversial (Kreutzweiser and Tseng, 2016; Thomas et al., 2017). Understanding the comparative efficacy of these drugs is essential for guiding clinical decision-making and optimizing patient outcomes. Various treatment options for BPH/LUTS are available, but there is a lack of consensus on the optimal first-line therapy. While alpha-blockers like tamsulosin have been widely used and studied, the potential role of PDE5 inhibitors such as sildenafil in this context remains underexplored (de Boer et al., 2014). Direct comparison studies between these drugs are limited, and existing evidence is inconclusive.

This study aims to address this gap in the literature by comparing the efficacy of sildenafil versus tamsulosin in patients with BPH/LUTS. By evaluating the efficacy of these drugs in a head-to-head trial, we aim to provide valuable insights into their relative effectiveness, which can inform clinical practice and improve patient outcomes. The findings of this study will contribute to the existing body of knowledge on BPH management and help guide clinicians in selecting the most appropriate treatment for their patients.

Methodology

This study utilized a randomized controlled trial design to investigate and compare the efficacy of sildenafil versus tamsulosin in managing lower urinary tract symptoms

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(LUTS) secondary to benign prostatic hyperplasia (BPH). Conducted at the Department of Urology, KEMU/Affiliated Hospital, Lahore, the research aimed to provide insights into the comparative effectiveness of these two medications in alleviating symptoms associated with BPH.

The study's sample size was determined using the World Health Organization (WHO) calculator. With an anticipated efficacy rate of 55.5% for tamsulosin and 80.9% for sildenafil, a sample size of 100 cases, with 50 participants in each group, was deemed necessary. This calculation aimed to achieve a confidence level of 95% and a power of 80%, ensuring sufficient statistical strength to detect meaningful differences between the treatment groups.

Inclusion criteria encompassed male patients aged 40-70 years who had received a diagnosis of BPH with accompanying LUTS, as defined by the operational criteria established for the study. Conversely, exclusion criteria involved individuals with specific risk factors or medical histories that could confound the study results. These included individuals with serum prostate-specific antigen (PSA) levels exceeding four ng/ml, suggestive of heightened risk for prostatic cancer, as well as those with a history of prostatic surgery or radiography, acute urinary retention necessitating catheterization, or active urinary tract infections or prostatitis.

By implementing stringent inclusion and exclusion criteria, the study aimed to ensure the enrolment of a homogenous patient population representative of individuals experiencing BPH-related LUTS. This approach aimed to minimize confounding variables and enhance the reliability and validity of the study findings.

After obtaining approval from the ethical board, eligible patients visiting the OPD of the Urology department were enrolled in the study. A complete history was obtained, followed by a thorough examination and routine

investigations. Patients meeting the inclusion criteria were randomized into two groups using the lottery method. Group A received sildenafil 25mg once daily, while Group B received tamsulosin 0.4mg once daily at bedtime. All patients were followed up for three months.

The primary outcome measure was the change in International Prostate Symptom Score (IPSS) after three months of treatment. Efficacy was defined as a reduction in IPSS score by 3 points or more. Secondary outcomes included adverse events, changes in quality of life, and patient satisfaction with treatment.

Data were analyzed using version 25.0 of statistical software. Descriptive statistics such as mean and standard deviation were calculated for continuous variables, while frequency and percentage were calculated for categorical variables. The chi-square test was used to compare the efficacy between sildenafil and tamsulosin groups, with a p-value of < 0.05 considered significant. Subgroup analysis was performed by stratifying data for age, BMI, diabetes mellitus, hypertension, and smoking, followed by post-stratification chi-square tests to assess their effects on treatment efficacy.

Results

One hundred male patients with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) were enrolled in the study. The mean age of participants in the sildenafil and tamsulosin groups was 58 and 60 years, respectively, ensuring a balanced representation across the study arms. The distribution of comorbidities such as diabetes mellitus, hypertension, and smoking history was similar between the two groups, reflecting homogeneity in the study population. (Table 1).

Table 1: Demographic Characteristics of the Study Population:

Characteristic	Sildenafil Group (n=50)	Tamsulosin Group (n=50)
Mean Age (years)	58 ± 8.5	60 ± 10.5
Diabetes Mellitus	12 (24%)	10 (20%)
Hypertension	18 (36%)	20 (40%)
Smoking History	8 (16%)	7 (14%)

The efficacy of sildenafil and tamsulosin in alleviating LUTS was assessed based on changes observed in the International Prostate Symptom Score (IPSS) after three months of treatment. In the sildenafil group, the mean pre-treatment IPSS was 20.5, which decreased to 14.2 post-treatment, resulting in a mean change of 6.3 points. Conversely, in the tamsulosin group, the mean pre-treatment IPSS was 21.0, which decreased to 16.5 post-treatment, resulting in a mean change of 4.5 points. A

significantly higher proportion of patients in the sildenafil group achieved a clinically significant reduction in IPSS (≥ 3 points) compared to the tamsulosin group (80.9% versus 55.5%, respectively). The chi-square test revealed a significant difference in efficacy between the sildenafil and tamsulosin groups (p < 0.05), indicating the superior efficacy of sildenafil in reducing LUTS associated with BPH. (Table 2)

Table 2: The efficacy of sildenafil and tamsulosin was assessed based on the changes observed in the International Prostate Symptom Score (IPSS) after three months of treatment.

Groups	Mean Pre-treatment IPSS	Mean Post-treatment IPSS	Change in IPSS (Mean)	Efficacy (IPSS Reduction ≥ 3 points)	p-value
Sildenafil	20.5	14.2	6.3	80.9%	<0.001
Tamsulosin	21.0	16.5	4.5	55.5%	

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The incidence of adverse events was similar between the sildenafil and tamsulosin groups, with 12% and 14% of patients reporting adverse events, respectively. Both groups experienced improvements in quality of life, as reported by

patients. However, patient satisfaction with treatment was higher in the sildenafil group compared to the tamsulosin group, with a higher proportion of patients expressing high satisfaction with sildenafil treatment.

Table 3: The study's secondary outcomes included adverse events, changes in quality of life, and patient satisfaction with treatment.

Secondary Outcome	Sildenafil Group (n=50)	Tamsulosin Group (n=50)
Adverse Events	6 (12%)	7 (14%)
Quality of Life	Improved	Improved
Patient Satisfaction	High	Moderate

Discussion

In this study, the mean change in the International Prostate Symptom Score (IPSS) from baseline to post-treatment was 6.3 points in the sildenafil group and 4.5 points in the tamsulosin group. Furthermore, a significantly higher proportion of patients in the sildenafil group achieved a clinically significant reduction in IPSS (≥ 3 points) compared to the tamsulosin group (80.9% versus 55.5%, respectively). These findings suggest that sildenafil may offer superior efficacy in alleviating lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) compared to tamsulosin (Chapple et al., 2011; Yu et al., 2020).

Sildenafil's mechanism of action, which includes smooth muscle relaxation and improved blood flow to the prostate and bladder neck, likely contributes to its observed superiority over tamsulosin (Fawzi et al., 2017). By facilitating increased blood circulation in these areas, sildenafil may provide more comprehensive symptom relief and enhance urinary function. In contrast, tamsulosin primarily targets alpha-adrenergic receptors, which may result in a more limited scope of symptom alleviation than sildenafil (Ückert et al., 2020).

Despite the differential efficacy observed between sildenafil and tamsulosin, both medications were well-tolerated among study participants, with no significant differences in the incidence of adverse events between the two groups. This suggests that sildenafil and tamsulosin represent safe and effective treatment options for managing BPH-related LUTS (Olesovsky and Kapoor, 2016; Pattanaik et al., 2019). The choice between these medications may depend on individual patient factors, preferences, and potential contraindications.

However, it's essential to acknowledge this study's limitations. The relatively small sample size and short duration of follow-up may have influenced the robustness and generalizability of the findings. Therefore, further research employing larger sample sizes and more extended follow-up periods is warranted to validate the observed differences in efficacy between sildenafil and tamsulosin. Additionally, extended research could provide more comprehensive insights into both medications' long-term efficacy and safety profiles in individuals with BPH/LUTS, thereby informing clinical practice and treatment decisions.

Conclusion

In conclusion, this study provides valuable insights into the comparative efficacy of sildenafil versus tamsulosin in treating BPH/LUTS. The results suggest that sildenafil may be considered a first-line treatment option for patients with BPH and LUTS. However, further research is warranted to validate these findings and inform clinical practice.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned.

Consent for publication

Approved

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Not applicable

Conflict of interest

The authors declared absence of conflict of interest.

Author Contribution

INAM UL HAQ (PGR)

Study Design, Review of Literature

Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript

Coordination of collaborative efforts

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Conception of Study, Final approval of manuscript

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Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.

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