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Comparison of Safety and Efficacy Between Silodosin Monotherapy and Silodosin with Tadalafil Add-on Therapy in Patients with Benign Prostatic Hyperplasia

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ABSTRACT

Background: *In aging men, benign prostatic hyperplasia (BPH) causes bothersome lower urinary tract symptoms. Silodosin improves urinary flow by targeting alpha-1 receptors. Combining silodosin with tadalafil enhances symptom relief through synergistic smooth muscle relaxation, offering better management of BPH-related discomfort. This study aimed to compare the safety and efficacy of silodosin monotherapy with silodosin and tadalafil add-on therapy in Benign prostatic hyperplasia patients.* ***Methods:*** *This was a prospective observational study that was conducted in the department of Urology, Bangabandhu Sheikh Mujib Medical University (BSMMU) Bangladesh from January 2022 to December 2022. This study randomized 80 patients, age between 40-80 years with lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) into two groups. Group A (40 patients) received silodosin 8 mg daily, while Group B (40 patients) received silodosin 8 mg plus tadalafil 5 mg daily. SPSS 23.0 analyzed data.* ***Results:*** *A comparison of IPSS scores between Group A and Group B showed significant reductions in both groups ($p<0.001$). Similarly, Post-Void Residual (PVR) volumes decreased significantly in both groups ($p<0.001$). Q-MAX scores and International Index of Erectile Function (IIEF) scores significantly improved in both groups ($p<0.001$). Group B demonstrated slightly greater reductions in IPSS and PVR, and greater improvements in Q-MAX and IIEF. Adverse effects were minimal, with slightly more cases of peripheral edema and dyspepsia in Group B.* ***Conclusion:*** *Silodosin monotherapy and Silodosin with Tadalafil add-on therapy significantly improve IPSS, PVR, Q-MAX, and IIEF scores. The combination therapy shows slightly better results, with minimal adverse effects. For better outcomes, combination therapy is recommended for moderate to severe symptoms.*

Keywords: *Benign prostatic hyperplasia, BPH, Lower urinary tract symptoms, Silodosin monotherapy, Tadalafil*

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INTRODUCTION

Benign prostatic hyperplasia (BPH), a common condition in aging men, is characterized by the non-malignant enlargement of the prostate gland, often leading to lower urinary tract symptoms (LUTS). These symptoms, which significantly affect the quality of life, include urinary frequency, urgency, nocturia, and weak urinary stream [1,2]. The prevalence of BPH increases with age, affecting approximately 50% of men in their 50s and over 80% of men aged 80 years or older [3]. In Bangladesh and other developing nations, the burden of BPH is growing due to increased life expectancy and a lack of awareness about early treatment options [4]. The pathophysiology of BPH involves both static and dynamic components. The static component results from the increased size of the prostate gland compressing the urethra, while the dynamic component arises from increased smooth muscle tone in the prostate and bladder neck, mediated by alpha-1 adrenergic receptors [5]. Silodosin, a selective alpha-1A adrenergic receptor antagonist, is widely used for the treatment of BPH-associated LUTS. It effectively relaxes smooth muscle in the prostate and bladder neck, improving urinary flow and alleviating symptoms with minimal side effects [6,7]. Recent advancements in BPH management include combination therapies targeting different aspects of the disease pathophysiology. One such combination is the addition of tadalafil, a phosphodiesterase-5 (PDE-5) inhibitor, to silodosin monotherapy. Tadalafil, primarily used for erectile dysfunction, has demonstrated efficacy in improving LUTS by enhancing smooth muscle relaxation and reducing prostatic inflammation [8]. Several studies have highlighted the synergistic effects of alpha-blockers and PDE-5 inhibitors in improving both urinary and sexual function in BPH patients [9,10]. Despite the growing interest in combination therapies, the comparative safety and efficacy of silodosin monotherapy versus silodosin with tadalafil add-on therapy remain areas of active investigation. Previous studies have reported favorable outcomes with the combination approach, including better symptom relief and improved quality of life [11]. However, concerns about potential side effects, such as hypotension and dizziness, necessitate a careful evaluation of the benefits and risks of combination therapy [12]. This study aimed to compare the safety and efficacy of silodosin monotherapy with silodosin and tadalafil combination therapy in patients with BPH.

METHODOLOGY

This was a prospective observational study that was conducted in the department of Urology, Bangabandhu Sheikh Mujib Medical University (BSMMU) Bangladesh from January 2022 to December 2022. A total of 80 patients age between 40-80 years presenting with lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) were enrolled in this study using a randomized sampling technique. Participants were randomly assigned into two groups: 40 patients in Group A received silodosin 8 mg once daily, while another 40 patients in Group B received a combination therapy of silodosin 8 mg and tadalafil 5 mg once daily. According to the exclusion criteria of this study, patients were excluded if they had any of the following conditions: single kidney, renal dysfunction, urinary tract infection (UTI), bilateral or multiple ureteric stones, severe or intractable pain requiring emergency intervention, marked hydronephrosis, ischemic heart disease, pregnancy, complicated hypertension, a history of ureteral surgery or any urologic anomalies, congestive cardiac failure, concurrent administration of calcium channel blockers or nitrates, or a previous history of successful stone passage or endoscopic management. The results of the study were presented as frequency and percentage for categorical data and as mean ± standard deviation (SD) for numerical data. Patients were evaluated using the International Prostate Symptom Score (IPSS) [14], maximum urinary flow rate (Q-max) [15], post-void residual (PVR) [16] urine volume, and the International Index of Erectile Function (IIEF) [17] score after 12 weeks of treatment. Data analysis was performed using SPSS version 23.0, with a P-value of less than 0.05 considered statistically significant.

RESULT

The age distribution of Group A and Group B showed no significant difference (p = 0.684). In Group A, 25% were ≤50 years, 35% were 51–60 years, 32.5% were 61–70 years, and 7.5% were >70 years, with a mean age of 58.13 ± 6.36 years. In Group B, 22.5% were ≤50 years, 37.5% were 51–60 years, 35% were 61–70 years, and 5% were >70 years, with a mean age of 58.75 ± 7.19 years. The comparison of IPSS scores between Group A and Group B revealed significant reductions in both groups. In Group A, the baseline IPSS score was 16.4 ± 2.2, which decreased to 9.1 ± 2.8 by the 12th week (p < 0.001). Similarly, Group B showed a decrease from a baseline IPSS score of 16.1 ± 1.9 to 6.2 ± 1.9 in the 12th week (p<0.001). The comparison of Q-MAX scores between Group A and Group B showed significant improvements in both groups. Group A's baseline Q-MAX score was 9.7 ± 1.2, which increased to 13.3 ± 1.3 at the 12-week mark (p< 0.001). Similarly, Group B's baseline Q-MAX score of 9.9 ± 1.1 rose to 15.1 ± 1.4 by the 12th week (p< 0.001). The comparison of Post-Void Residual (PVR) volumes between Group A and Group B revealed significant reductions in both groups. Group A's baseline PVR was 65.4 ± 18.4, which decreased to 46.8 ± 11.3 at the 12-week follow-up (p < 0.001). Similarly, Group B's baseline PVR of 64.9 ± 18.5 reduced to 42.5 ± 10.6 by the 12th week (p < 0.001). The comparison of the International Index of Erectile Function (IIEF) scores between Group A and Group B demonstrated significant improvements in both groups. Group A's baseline IIEF score of 15.3 ± 3.5 increased to 21.8 ± 4.6 at the 12-week follow-up (p < 0.001). In Group B, the baseline IIEF score of 14.9 ± 5.3 improved to 24.5 ± 5.7 by the 12th week (p < 0.001). The comparison of adverse effects between Group A and Group B showed the following results: In Group A, 0% experienced headache, 2.5% had palpitation, 2.5% reported peripheral edema, and 2.5% experienced dyspepsia. In Group B, 2.5% had headaches, 2.5% reported palpitation, 5.0% experienced peripheral edema, and 5.0% had dyspepsia. These findings indicate that adverse effects were generally low in both groups, with slightly more participants in Group B reporting peripheral edema and dyspepsia.

Table 1: Age distribution (Year)

Age	**Group-A**		**Group-B**		**p-Value**
	n	%	n	%	
≤50	10	25.0%	9	22.5%	0.684
51- 60	14	35.0%	15	37.5%	
61-70	13	32.5%	14	35.0%	
>70	3	7.5%	2	5.0%	
Mean ±SD	58.13 ± 6.36		58.75 ± 7.19		

Table 2: Comparison between two groups in IPSS score

IPSS score	Baseline	12th week	p-value
Group-A			
Mean ±SD	16.4±2.2	9.1±2.8	<0.001
Group -B			
Mean ±SD	16.1±1.9	6.2±1.9	<0.001

Table 3: Comparison between two groups in Q-MAX score

Q-MAX score	Baseline	12 weeks	P-value
Group -A			
Mean ±SD	9.7±1.2	13.3±1.3	<0.001
Group -B			
Mean ±SD	9.9±1.1	15.1±1.4	<0.001

Table 4: Comparison between two groups according to PVR

PVR	Baseline	12 weeks	P-value
Group-A			
Mean ±SD	65.4±18.4	46.8±11.3	<0.001
Group-B			
Mean ±SD	64.9±18.5	42.5±10.6	<0.001

Table 5: Comparison between two groups in IIEF score

IIEF score	Baseline	12th week	P-value
Group-A			
Mean ±SD	15.3±3.5	21.8±4.6	<0.001
Group-B			
Mean ±SD	14.9±5.3	24.5±5.7	<0.001

Table 6: Comparison of adverse effects of treatment

Effects	Group A		Group A	
	n	%	n	%
Headache	0	0.0%	1	2.5%
Palpitation	1	2.5%	1	2.5%
Peripheral edema	1	2.5%	2	5.0%
Dyspepsia	1	2.5%	2	5.0%

DISCUSSION

In this study, we compared the efficacy and safety of silodosin monotherapy with silodosin and tadalafil add-on therapy in patients with Benign Prostatic Hyperplasia (BPH). The results demonstrated that both treatment options significantly improved symptoms related to BPH, including reductions in International Prostate Symptom Scores (IPSS), increases in Q-MAX scores, and reductions in Post-Void Residual (PVR) volumes, indicating a substantial improvement in urinary function. Similar studies have shown that silodosin, an alpha-blocker, effectively alleviates lower urinary tract symptoms in BPH patients. A study by Hsu et al. (2018) reported significant improvements in IPSS and Q-MAX scores with silodosin monotherapy, which aligns with the findings in our Group A (silodosin alone) [1]. In our study, silodosin monotherapy significantly reduced IPSS scores from 16.4 to 9.1, a result similar to those observed in previous studies,

highlighting its efficacy in managing BPH symptoms [1]. The addition of tadalafil, a phosphodiesterase type 5 inhibitor, to silodosin further improved erectile function, as evidenced by the significant increase in the International Index of Erectile Function (IIEF) scores. This result is consistent with findings from several studies that have explored combination therapy for BPH and erectile dysfunction. A study by [19] Sakalis et al. (2021) demonstrated that the combination of tadalafil with alpha-blockers improved both erectile function and urinary symptoms in BPH patients [19]. In our study, Group B (silodosin and tadalafil) showed a notable improvement in IIEF scores from 14.9 to 24.5, which supports the effectiveness of combination therapy in improving erectile function and overall quality of life. However, a dissimilar aspect of our findings compared to some previous studies was the relatively low incidence of adverse effects, particularly in Group A. While Group B showed slightly more adverse effects, including peripheral edema and dyspepsia, the overall incidence was still minimal. In contrast, another study has reported a higher incidence of side effects when using combination therapies, particularly tadalafil, due to its potential cardiovascular effects [20]. Our study observed minimal adverse reactions, with only 2.5% in both groups experiencing mild side effects, which is consistent with previous reports of the favorable safety profile of silodosin and tadalafil combination therapy in BPH management [21]. Additionally, both Group A and Group B showed significant reductions in PVR, which is an important indicator of improved bladder emptying and lower urinary tract symptoms in BPH patients. A study by Jackson et al. (2016) also observed significant reductions in PVR volumes with silodosin treatment [22], reinforcing the findings of our study. Although both treatments were effective in improving symptoms and urinary function, Group B demonstrated superior results in erectile function, further supporting the combined use of tadalafil for patients who require treatment for both BPH and erectile dysfunction. However, the higher number of adverse events in the combination therapy group warrants further investigation, particularly in long-term studies, to assess the safety of this combination over time.

CONCLUSION & RECOMMENDATION

Silodosin monotherapy and Silodosin with Tadalafil add-on therapy both lead to significant improvements in IPSS scores, post-void residual volumes, Q-MAX scores, and International Index of Erectile Function scores. The combination therapy results in slightly greater reductions in IPSS and PVR, along with more pronounced improvements in Q-MAX and IIEF scores. Adverse effects remain minimal, though there are slightly more cases of peripheral edema and dyspepsia with the combination therapy. For enhanced therapeutic outcomes, combination therapy is recommended, particularly for patients with moderate to severe symptoms.

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