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Comparison of Mirabegron and Tamsulosin in Alleviating Symptoms from Ureteral Stents: Insights from a Single-Center Institutional Study

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Abstract

Background: Indwelling ureteric stents commonly induce complications that significantly affect patients' quality of life. Despite the widespread use of pharmacological interventions such as alpha-blockers and anti-muscarinic agents, their efficacy remains debatable. The beta-3 agonist Mirabegron has emerged as a potential alternative, yet comparative studies with Tamsulosin within a single institutional setting are lacking. *Methodology*: This prospective observational study enrolled 60 patients with unilateral DJ stents following various urological procedures. Patients were divided into Mirabegron and Tamsulosin groups based on consultant preference. Symptom assessment was performed using the USSQ questionnaire at 7th and 14th post-operative days. *Results*: Both Mirabegron and Tamsulosin effectively reduced urinary, pain, additional, working, and general health scores. Mirabegron demonstrated superior efficacy in reducing pain and improving working health scores compared to Tamsulosin. However, no significant difference was observed in urinary, general, sexual, and additional scores between the two drugs. *Conclusion*: Mirabegron, particularly at a dosage of 25 mg once daily, emerges as a promising option for relieving ureteral stent-related symptoms, especially pain and working health score. However, further research is needed to optimize treatment strategies and elucidate the underlying mechanisms of action.

Keywords: Fever, Lower Urinary Tract Symptoms, Pain, Quality of Life, Stent.

Introduction

Ureteral stent placement stands as a cornerstone procedure in modern urology, serving to alleviate upper urinary tract obstruction following interventions such as ureteroscopy (URS) and percutaneous nephrolithotomy (PCNL) [1]. By facilitating proper post-operative drainage and mitigating complications such as severe flank pain, fever, and sepsis, these stents play a pivotal role in patient care [1]. However, despite their therapeutic benefits, ureteral stents can induce distressing symptoms that significantly impact patients' quality of life. Studies have reported a spectrum of morbid symptoms including frequency (50-60%), urgency (57-60%), and dysuria (40%), among others, affecting approximately 80% of patients [2-4]. The development of the Ureteral Stent Symptom Questionnaire (USSQ) by Joshi *et al*. emphasizes the need for a standardized tool to assess stent-related symptoms and their impact [5].

Addressing these symptoms often involves pharmacological intervention, with alpha-1 adrenergic receptor antagonists (alpha-1 blockers) and anti-muscarinic agents emerging as potential therapeutic agents. Alpha-blockers, akin to their efficacy in treating benign prostatic hyperplasia-related lower urinary tract symptoms (LUTS), target symptoms such as urgency, frequency, and suprapubic pain attributed to involuntary bladder contractions [5]. Conversely, anti-muscarinic

agents are thought to alleviate symptoms of stent-induced overactive bladder (OAB) by blocking muscarinic receptors on efferent neurons in the detrusor muscles, thus reducing involuntary bladder contractions triggered by trigone discomfort [6].

In this observational study, we aim to compare the efficacy of Mirabegron versus Tamsulosin in ameliorating symptoms and enhancing the quality of life in patients with indwelling ureteral stents. The primary objective was to compare USSQ scores at 7th and 14th post-operative days, while secondary objectives included assessing improvements in general health, work performance, sexual function, additional health, and global quality of life.

Methodology

The study was conducted at Lilavati Hospital and Research Centre, Mumbai, with a total of 60 patients enrolled. Ethical approval was obtained, and patients aged 18 to 50 undergoing unilateral PCNL, ESWL, RIRS, or URS with DJ stenting were considered for inclusion. Exclusion criteria included patients with certain medical conditions, prior medication use, and pregnancy or breast feeding mothers. The sample size was determined using the SAS 9.2 package. Patients were divided into two groups: Group 1 received Tamsulosin, while Group 2 received Mirabegron. The efficacy variable was the average decline of USSQ Urinary Complaint. The null hypothesis (H0) stated that the mean decline of USSQ in Group 1 equalled that in Group 2, while the alternative hypothesis (H1) posited inequality in mean decline. A minimum sample size of 28 patients per group was determined to achieve a power of 90% at an alpha level of 0.05, using a two-sample t-test. Patients were evaluated at the 7th and 14th post-operative days using the USSQ questionnaire.

Patients underwent standard pre-operative tests and received intravenous antibiotics before surgery. All stents were 5.5FR/24 CM double J stents. Post-operative medications, either Tamsulosin or Mirabegron, were administered as per consultant preference. USSQ scores were compared between the two groups at the 7th and 14th post-operative days. Follow-up visits were scheduled for all patients at the outpatient clinic on the 7th and 14th days post-stent placement for USSQ assessment.

This prospective observational study aimed to evaluate the effectiveness of Mirabegron and Tamsulosin in relieving ureteral stent-related symptoms using the USSQ questionnaire. Study interventions included the administration of Mirabegron or Tamsulosin according to consultant preference, with data analysis conducted at the study's conclusion.

Results

This prospective observational study was conducted at Lilavati Hospital and Research Centre, a tertiary healthcare center in Bandra, Mumbai, Maharashtra, over a one-year period from October 31, 2021, to October 31, 2022. A total of 60 patients were included in the study based on predefined inclusion and exclusion criteria.

Table 1 presents a comparison of means between two time points in two groups, Mirabegron and Tamsulosin. Significant differences were observed in all variables (except for the Sex Score in the Mirabegron group) between the first and second weeks for both Mirabegron and Tamsulosin groups. Statistical analysis was performed using Student's paired t-test. **Table 2** illustrates the comparison of change (1 week - 2 week) of mean between the two groups, Mirabegron and Tamsulosin. While no significant difference was noted in Urinary Score, Additional Health Scores, Sex Score, and General Health Score between the two groups, significant differences were observed in Pain Score and Working Health Scores. Mirabegron demonstrated greater effectiveness than Tamsulosin in reducing Pain Score and Working Health Score.

Table 1: *Comparison of means between 2 time points in 2 groups.*

	Mirabegron (Mean ± SD)			**Tamsulosin (Mean ± SD)**		
	1st week	*2nd week*	*P value*	*1st week*	*2nd week*	*P value*
Urinary Score	35.33 ± 3.22	20.47 ± 4.17	0.001	35.20 ± 2.58	18.47 ± 3.83	0.001
Pain Score	28.23 ± 2.34	14.43 ± 2.74	<0.001	28.50 ± 2.30	22.47 ± 1.89	0.001
Additional Health Score	12.20 ± 2.46	9.93 ± 2.20	0.001	12.80 ± 2.09	9.80 ± 1.45	0.001
Sex Score	7.57 ± 1.43	7.23 ± 1.65	0.4	8.00 ± 1.39	6.93 ± 1.66	0.005
Working Health Score	23.20 ± 1.67	16.43 ± 3.25	0.001	23.10 ± 1.67	19.07 ± 2.39	0.001
General Health Score	24.33 ± 2.19	17.10 ± 1.73	0.001	23.87 ± 1.70	17.83 ± 3.83	0.001

Table 2: *Comparison of change (1 week - 2 week) of means between 2 groups.*

	Mirabegron (Mean ± SD)	**Tamsulosin (Mean ± SD)**	**P value**
Urinary Score	14.87 ± 5.73	16.73 ± 5.93	0.2
Pain Score	13.80 ± 3.78	6.03 ± 2.55	<0.001
Additional Health Score	2.27 ± 1.84	3.00 ± 2.15	0.2
Sex Score	4.98 ± 2.74	4.43 ± 2.60	0.4
Working Health Score	6.77 ± 3.40	4.03 ± 2.87	0.001
General Health Score	7.23 ± 3.22	6.03 ± 3.92	0.2

Discussion

Indwelling ureteric stents are associated with various complications that significantly diminish patients' quality of life. Joshi *et al*. reported a high prevalence of urinary dysfunction symptoms and stent-related pain among patients with indwelling ureteric stents [8]. The USSQ, developed for evaluating discomfort associated with ureteric stents, has become a widely utilized tool in this context [5]. Although the precise mechanism underlying ureteric stent-related discomfort remains unclear, several factors such as ureteric spasms, ureteric reflux caused by the stent, or trigonal irritation have been proposed by researchers.

These symptoms may be alleviated by inducing relaxation of ureteric and local trigonal smooth muscles, reducing ureteric motility, relaxing the bladder neck and prostatic smooth muscles, and decreasing voiding pressure and urinary reflux [9,10]. Alpha-blockers have been postulated to mitigate ureteral stent-related symptoms through mechanisms involving reduced muscle tone in the ureter, bladder trigone, and prostatic urethra by blocking alpha-adrenergic receptors [11]. However, common side effects associated with alpha-blockers include dizziness and orthostatic hypotension, while anti-muscarinic agents can lead to dry mouth, constipation, blurred vision, and dyspepsia, making adherence to treatment challenging [12,13]. To address these limitations, researchers have explored novel treatment approaches, leading to the development of the beta-3 agonist Mirabegron. Acting as an agonist of the beta-3 adrenergic receptor, Mirabegron is believed to induce detrusor smooth muscle relaxation during storage, thereby enhancing bladder capacity without affecting micturition pressure, post-void residual urine volume, or voiding contractions [14,15]. The potential effectiveness of Mirabegron may be attributed to its actions on both the ureter and bladder smooth muscles.

In our study, both Mirabegron and Tamsulosin demonstrated efficacy in reducing urinary, pain, additional, working, and general

health scores, consistent with findings reported by Alexander *et al*. [7]. Notably, Mirabegron was more effective than Tamsulosin in reducing pain and working health scores, aligning with previous studies [19]. However, conflicting results have been reported regarding the comparative effectiveness of Mirabegron and Tamsulosin in improving urinary symptoms [20]. Our findings indicate no statistically significant difference in urinary score between the two drugs, contrasting with previous studies suggesting superiority of Tamsulosin in this regard [21].

Conclusion

Both Mirabegron and Tamsulosin exhibit efficacy in alleviating ureteral stent-related symptoms. Mirabegron, particularly at a dosage of 25 mg once daily, emerges as superior in relieving body and overall pain and improving working health score. However, no statistical difference was observed between the two drugs in reducing urinary, general, sexual, and additional scores. Therefore, Mirabegron may be recommended for reducing stent-related discomfort, although further research is warranted to elucidate the optimal treatment approach.

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References

1. Chew BH, Knudsen BE, Denstedt JD. The use of stents in contemporary urology. Current Opinion in Urology. 2004;14(2):111-115.
2. Joshi HB, Okeke A, Newns N, Keeley FX, Timoney AG. Characterization of urinary symptoms in patients with ureteral stents. Urology. 2002;59(4):511-516.
3. Thomas R. Indwelling ureteral stents: Impact of material and shape on patient comfort. Journal of Endourology. 1993;7(2):137-140.
4. Joshi HB, Stainthorpe A, Macdonagh RP, Keeley FX, Timoney AG. Indwelling ureteral stents: Evaluation of symptoms, quality of life and utility. Journal of Urology. 2003;169(3):1065-1069.
5. Joshi HB, Newns N, Stainthorpe A, Macdonagh RP, Keeley FX, Timoney AG. Ureteral Stent Symptom Questionnaire: Development and validation of a multidimensional Quality of Life Measure. Journal of Urology. 2003;169(3):1060-1064.
6. Betschart P, Zumstein V, Piller A, Schmid H-P, Abt D. Prevention and treatment of symptoms associated with indwelling ureteral stents: A systematic review. International Journal of Urology. 2017;24(4):250-259.
7. Alexander K, Palinrungi A, Palinrungi M, Kholis K, Syahrir S, Syarif S, *et al*. Effectiveness of Tamsulosin compared with Mirabegron in treatment of Double-J Stent-Related Lower Urinary Tract Symptoms. International Journal of Medical Reviews and Case Reports. 2020;4(8):8-13.
8. Joshi HB, Okeke A, Newns N, Keeley Jr FX, Timoney AG. Characterization of urinary symptoms in patients with ureteral stents. Urology. 2002;59(4):511-516.
9. Lamb AD, Vowler SL, Johnston R, Dunn N, Wiseman OJ. Meta-analysis showing the beneficial effect of α-blockers on ureteric stent discomfort. BJU International. 2011;108(11):1894-1902.
10. Yakoubi R, Lemdani M, Monga M, Villers A, Koenig P. Is there a role for α-blockers in ureteral stent related symptoms? A systematic review and meta-analysis. Journal of Urology. 2011;186(3):928-934.
11. Dellis AE, Keeley FX, Manolas V, Skolarikos AA. Role of α-blockers in the Treatment of Stent-related Symptoms: A Prospective Randomized Control Study. Urology. 2014;83(1):56-62.
12. Lowe FC. Summary of clinical experiences with tamsulosin for the treatment of benign prostatic hyperplasia. Reviews in Urology. 2005;7(Suppl 4):S13.
13. Hoffstetter S, Che Leong F. Solifenacin succinate for the treatment of overactive bladder. Expert Opinion on Drug Metabolism & Toxicology. 2009;5(3):345-350.
14. Wuest M, Eichhorn B, Grimm MO, Wirth MP, Ravens U, Kaumann AJ. Catecholamines relax detrusor through β2-adrenoceptors in mouse and β3-adrenoceptors in man. Journal of Pharmacology and Experimental Therapeutics. 2009;328(1):213-222.
15. Leon LA, Hoffman BE, Gardner SD, Laping NJ, Evans C, Lashinger ES, *et al*. Effects of the β3-adrenergic receptor agonist disodium 5-[(2R)-2-[[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl] amino] propyl]-1, 3-benzodioxole-2, 2-dicarboxylate (CL-316243) on bladder micturition reflex in spontaneously hypertensive rats. Journal of Pharmacology and Experimental Therapeutics. 2008;326(1):178-185.
16. Sigala S, Dellabella M, Milanese G, Fornari S, Faccoli S, Palazzolo F, *et al*. Evidence for the presence of α1 adrenoceptor subtypes in the human ureter. Neurourology and Urodynamics. 2005;24(2):142-148.

17. Shen H, Chen Z, Mokhtar AD, Bi X, Wu G, Gong S, *et al*. Expression of β-adrenergic receptor subtypes in human normal and dilated ureter. International Urology and Nephrology. 2017;49(10):1771-1778.
18. Khullar V, Amarenco G, Angulo JC, Cambronero J, Høye K, Milsom I, *et al*. Efficacy and tolerability of mirabegron, a β3-adrenoceptor agonist, in patients with overactive bladder: results from a randomised European–Australian phase 3 trial. European Urology. 2013;63(2):283-295.
19. Tae B, Jeon BJ, Shim JS, Cho S, Choi H, Park JY, *et al*. Can Mirabegron relieve double-J stent-related discomfort: a multicenter, randomized, open-label study. Journal of Urology. 2018;17(2):e930-932.
20. Yavuz A, Kilinc MF, Aydin M, Ofluoglu Y, Bayar G. Does tamsulosin or mirabegron improve ureteral stent-related symptoms? A prospective placebo-controlled study. LUTS: Low Urin Tract Symptoms. 2020;13(1):17-21.
21. Aggarwal SP, Priyadarshi S, Tomar V, Yadav SS, Gangkak G, Vyas N, *et al*. A Randomized Controlled Trial to compare the safety and efficacy of Tadalafil and Tamsulosin in relieving Double J stent related symptoms. Advances in Urology. 2015;2015:1-6.

