

Original Article

Comparison of alpha-blockers and antimuscarinic for the treatment of double-J stent-related lower urinary tract symptoms.

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Abstract

Background: Double-J stent is well known for relieving urinary tract obstruction, but still, some patients might develop double-J stent-related urinary tract infection (UTI), lower urinary tract symptoms (LUTS), lower abdominal pain, and hematuria. This study aims to compare alpha-blockers and antimuscarinics for the treatment of double-j stent-related lower urinary tract symptoms.

Methodology: Patients planned for double-J stent insertion undergoing the urological procedure for ureteric stones were recruited and randomly allocated into two groups. One group was labeled as the tamsulosin (T), and the other was labeled as the solifenacin succinate (S) group. Group "T" patients were prescribed tamsulosin 0.4 mg once at bedtime and solifenacin succinate 10mg once daily to group "S" for 2 weeks. Improvement in symptoms was checked by means of international prostate symptom score (IPSS)/ quality of life (QoL) score charts for LUTS in the out-patient clinic at baseline and at follow-up.

Results: When comparing the absolute changes in IPSS/QoL for LUTS scores, both groups showed significant improvement in double-J stent-related lower urinary symptoms, body pain, generalized body weakness, and sexual function, which affect their quality of life (QoL). The mean index score of all domains in both groups was significantly less ($p < 0.001$). Tamsulosin and solifenacin succinate (S) group was found equally efficacious on urinary symptoms (26.01 ± 5.65 (pre); 5.74 ± 0.99 (post) vs. 26.61 ± 5.7 (pre); 26.01 ± 0.97 (post), ($p \leq 0.001$). Similarly, the score of QoL was also found equally efficacious in both groups in pre and post-insertion on two weeks (4.96 ± 0.7 (pre); 81.58 ± 0.64 (post) vs. 4.99 ± 0.81 (pre); 1.45 ± 0.5 (post) ($p < 0.001$).

Conclusion: On the basis of results, it is said that a combination of alpha-blockers and antimuscarinic agents has shown significant improvement to reduce double-J stent-related lower urinary symptoms, pain, and quality of life than a single drug alone.

Keywords

International Prostate Symptoms Score, Lower Urinary Tract Symptoms, Benign Prostatic Obstruction, Benign Prostatic Hyperplasia.



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Introduction

The double-J stents are widely used as an integral part of endo-urologic practices as they play a major role in relieving urinary tract obstruction^{1,2}. Some patients might develop stent-related problems like urinary tract infection (UTI), lower urinary tract symptoms (LUTS), lower abdominal pain, and hematuria despite the usefulness. These symptoms have considerable effects on substantial general health, QoL, work performance, and sexual problems in both genders³⁻⁵.

Despite the unclear pathophysiology of stent-related symptoms, it is observed that the local irritation of bladder mucosa causes the pain and LUTS by the stent, which ultimately results in bladder spasm⁶. Oral therapeutic agents like alpha-blockers and antimuscarinic are known to relieve LUTS associated with double-J stents⁷⁻¹⁰. Those studies reported the incidence of frequency (45–55%), urgency (55–60%), dysuria (30–40%), incomplete emptying (65%–70%), flank and suprapubic pain (20–30%), and hematuria (25%)²⁻⁴. Joshi and associates demonstrated that stent-related urinary symptoms and lower abdominal pain result in reduced QoL in up to 80% of the patients³.

The symptoms of lower urinary tract among patients with prostate enlargement, are widely assessed by International Prostate Symptom Score (IPSS). However, it can also be used to assess lower urinary tract symptoms other than that. Since it's a known fact that the exact pathophysiology of stent-related symptoms is not cleared yet, but investigators have still made considerable efforts to decrease stent-related symptoms, including improvement in the stent material used, its physical properties, and design^{11,12} but unfortunately, the problem still exists. Considering this problem, several researchers started investigating the effect of drugs in reducing stent-related symptoms. For this purpose, few of them investigated the effect of alpha-blockers on stent-related symptoms. Similarly, the effect of antimuscarinic and a combination of alpha-blockers and antimuscarinic for this purpose was also proposed, but unfortunately, no clear guidelines exist to date.

So the purpose of this study is to get a better choice of drugs to reduce double J stent-related lower urinary tract symptoms in our population in order to have a better modality for the patients of this poor resource country. This study aims to compare alpha-blocker and antimuscarinic and the combination of two for the treatment of lower urinary tract symptoms associated with double-J stent.

Methodology

This parallel-arm study was conducted at the Department of Urology at Sindh Institute of Urology and Transplantation, Karachi, from July 2017 to Jan 2018. A total of 274 patients between 18-40 years undergoing double J stents, those with flank pain, intermittent micturition for more than 4 weeks, and who had not undergone any intervention of lower urinary tract before unilateral stent were enrolled. While patients with diabetes (RBS < 180 mg/dl at presentation), hypertension (SBS < 140 mmHg at presentation), active UTI (diagnosed on urine detail report showing more than 10 pus cells), bladder pathology (infection, neurogenic bladder, cystitis, etc.) assessed on history and benign prostatic hyperplasia-related LUTS (IPSS > 7) were excluded. In addition, pregnant females, patients administering antimuscarinic or alpha-blockers, or those having a previous history of stenting were excluded from the study sample.

Patients planned for double-J stent insertion undergoing the urological procedure for ureteric stones were selected from the out-patient clinics. The patients were well explained about patients the purpose of the study, procedure, risks and benefits, and data confidentially. Informed consent was also obtained from all the patients. The patients were randomly enrolled into two groups by the sealed opaque envelop method. One group was labeled as the tamsulosin (T), and the other was labeled as the solifenacin succinate (S) group. Patients were given IPSS/QoL for LUTS in the out-patient clinic at baseline. After double-J stent insertion, the consultant performed the procedure, and patients were prescribed medicines on discharge according to the allotted group. At bedtime, a daily oral dose

of tamsulosin (0.4 mg) was provided to group T and solifenacin succinate (10 mg) once daily to S group for 2 weeks. Patients were called up in the out-patient clinic after 2 weeks and asked to fill up the IPSS/QoL for LUTS again. Data including a detailed history, clinical examination, along demographic details were also taken from the patients.

SPSS version 20.0 was used for data analysis, mean and standard deviation was computed for age, duration of stone, size of the stone, height, weight, BMI, and IPSS/QoL. Frequency and percentages were calculated for gender, smoking status, and location of the stone. The outcomes were compared using an unpaired T-test. Effect modifiers like age, gender, size and location of

stones, smoking status were stratified to see the outcomes. Post-stratification T-test was applied, and p-value < 0.05 was considered as significant.

Results

In this study total of 274 patients were enrolled (127 patients in each group) consisted of 166 males and 108 females in whom a double-J stent was placed. All patients completed the IPSS score before and two weeks after the procedure. The study included ages ranging from 18 up to 60 years. The average age was 30.75 ± 6.68 , the weight of the patients was 64.50 ± 13.26 kg, the mean value of the height of the patients was 2.94 ± 7.69 meter, and the BMI of the patients was 24.13 ± 7.35 kg/m² (Table 1).

Table 1: Patient's demographics.

Variables	Treatment Groups (Mean±SD)	
	Solifenacin group	Tamsulosin group
Age	32.01±6.09	29.49±7.03
Height	3.59±10.24	2.30±3.61
Weight	63.63±15.14	65.37±11.06
BMI	24.80±8.08	23.45±6.50
Stone	1.40±0.25	1.43±0.85

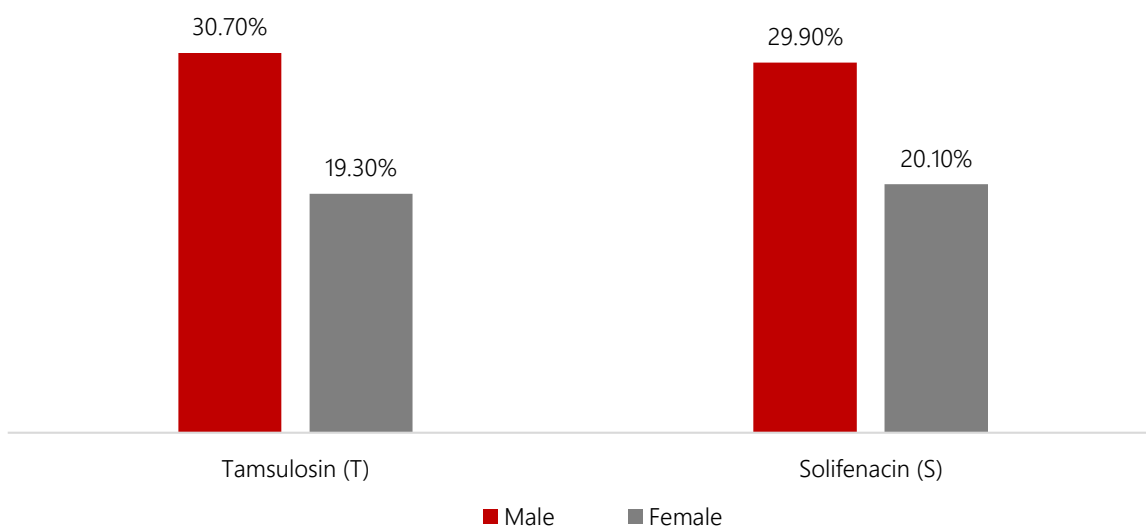


Figure 1: Comparison of Tamsulosin (T) and Solifenacin (S) group with gender.

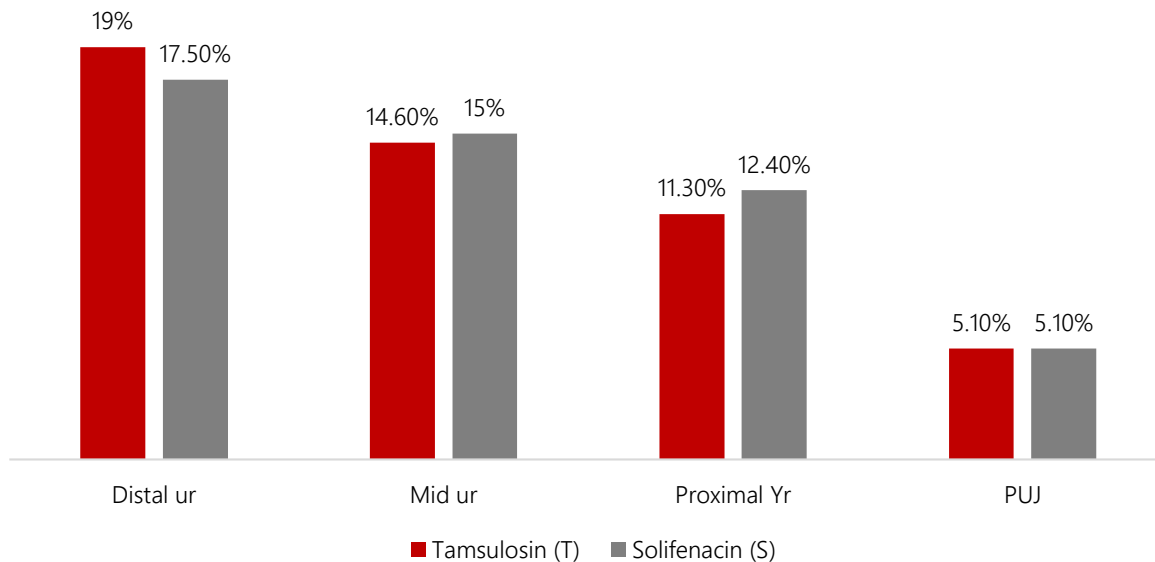


Figure 2: Comparison of Tamsulosin (T) and Solifenacin (S) group with the location.

When comparing the absolute changes in IPSS/QoL for LUTS scores, both groups showed significantly lower urinary symptoms, body pain, general health, work performance, sexual performance, additional problems, and QoL. The mean index score of all domains in both groups was significantly less ($p < 0.001$). Tamsulosin and solifenacin succinate (S) group was found equally efficacious on urinary symptoms (26.01 ± 5.65 (pre); 5.74 ± 0.99 (post) vs. 26.61 ± 5.7 (pre); 6.01 ± 0.97 (post), $p\text{-value} \leq 0.001$). Similarly, the score of QoL was also found equally efficacious in both groups in pre and post-insertion on two weeks (4.96 ± 0.7 (pre); 1.58 ± 0.64 (post) vs. 4.99 ± 0.81 (pre); 1.45 ± 0.5 (post) ($p < 0.001$).

Table 2: Comparison between Solifenacin group and Tamsulosin group pre-insertion and post-insertion of Double-J stent.

Treatment Groups	IPSS		p-value	QOI		p-value
	Pre-insertion	Post-insertion		Pre-insertion	Post-insertion	
In Solifenacin group	26.01 ± 5.65	5.74 ± 0.99	0.001*	4.96 ± 0.78	1.58 ± 0.64	0.001*
Tamsulosin group	26.61 ± 5.72	6.01 ± 0.97	0.001*	4.99 ± 0.81	1.45 ± 0.5	0.001*

*Values are given as mean \pm SD.

Discussion

Double-J stent placement has now become a routine for the management of a various urological procedures. These stents relieve urinary tract obstruction by diverting urine, allowing faster tissue healing by making the ureter less kinetic, dilating the ureter, and assisting in the stone passage. However, the ideal stent is not yet available¹. Many patients experience significant stent-related morbidity, and an additional procedure is required for stent removal¹³. To

minimize stent-related LUTS, the distal end is tapered and made from hydrophilic, biodegradable, or tissue-engineered materials^{14,15}.

We conducted this study to compare the Tamsulosin (T), a specific α -1A/1D blocker, versus solifenacin succinate (S) as an antimuscarinic agent in order to improve the lower urinary symptoms and quality of life in patients with indwelling double-J stents. For this purpose, we used IPSS (IPSS/QoL) to look for the improvement in stent-

related lower urinary tract symptoms and quality of life.

Our study showed high statistical significance in the mean index score of all domains and QoL in IPSS between both groups at week 2 (with the stent in place). These results are comparable with those reported by Park et al.¹⁶, who studied the effects of Alfuzosin and Tolterodine extended-release to treat double-J stent-related symptoms. Similar to our results, both groups, Tamsulosin (T) solifenacin succinate (S) in all domains, were found equally significant after two-week insertion. However, the evaluation was performed much equally (2 weeks after the procedure).

In order to improve the ureteral stent-related symptoms, different drug trials are under investigation to make therapeutic protocols. The present study found that both tamsulosin and solifenacin effectively improved the poorly controlled ureteral stent-related symptoms ($p=0.0001$). Similarly, Wang et al.⁷ in a prospective randomized study focusing on the effectiveness of alpha-blockers (tamsulosin) in comparison to placebo, they reported that tamsulosin improved stent-related urinary symptoms and QoL. As a result, its routine use was recommended. Also, Damiano et al.¹⁷ reported that administration of tamsulosin significantly improves stent-related urinary symptoms and QoL. But the limitation of this study was that it was not double-blinded or placebo-controlled. Furthermore, several studies reported that other alpha-blockers like alfuzosin improved stent-related symptoms and quality of life and reduced analgesic demand compared to the placebo group^{18,19}. However, so far, to our knowledge, not a single study compared the effectiveness of different alpha-blockers or antimuscarinic agents on stent-related symptoms. Kuyumcuoglu et al. reported in a prospective randomized study that the results of tamsulosin and placebo were not comparable¹⁰.

In our study, solifenacin monotherapy has been associated with significant improvement in symptoms related to stent, as shown by significant differences in the IPSS total score, storage sub-

score, and quality of life pre-and post-stent insertion. Similarly, Lee and colleagues reported that post-operative solifenacin use was also very effective and well-tolerated by the patients irrespective of gender who are undergoing ureteroscopic lithotripsy (URSL) and double-J stent placement for the treatment of stent-related LUTS, lower abdominal pain, and hematuria⁹.

There are certain limitations of the present study including lack of patient homogeneity as patients with different urologic procedures were included. However, the indications of double-J stent insertion were almost similar in all four groups. Our main focus was to check the efficacy of alpha-blocker and antimuscarinic with combination therapy, which has not been studied much. Lim and his colleagues reported the superiority of combination therapy of alpha-blocker and antimuscarinic previously; at that time, tamsulosin was already being used with significantly better results in reducing stent-related symptoms²⁰. Since the study was conducted on small groups of patients, it was very difficult to verify the statistical significance.

In contrast, to all the supporting literature, Lee et al.²¹, reported no statistically significant difference associated with the combination treatment of tamsulosin and tolterodine when compared to placebo, and when combination therapy was compared to tamsulosin monotherapy, no beneficial effect was reported. But again, it was a small study. Furthermore, it was also observed in a few cases that the correct position of the stent is also an important factor in reducing stent-related symptoms.

Conclusion

In this study, we found that the alpha-blocker and antimuscarinic agent, Tamsulosin (T) and solifenacin succinate (S), respectively, both improved the double-J stent-related lower urinary tract symptoms, pain, and quality of life. There was a significant difference between symptoms in both the groups on pre and post-insertion using IPSS. A combination of these two is significantly better than either drug alone in reducing LUTS associated

with double-J stents; hence it is strongly recommended.

Conflicts of Interest

The authors have declared that no competing interests exist.

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References

- Knudsen BE, Beiko DT, Denstedt JD. Stenting after ureteroscopy: pros and cons. *Urol Clin North Am.* 2004;31(1):173-180.
- Chew BH, Knudsen BE, Denstedt JD. The use of stents in contemporary urology. *Curr Opin Urol.* 2004;14(2):111-115.
- Joshi H, Stainthorpe A, MacDonagh R, Keeley F, Timoney A. Indwelling ureteral stents: evaluation of symptoms, quality of life and utility. *J Endourol.* 2003;169(3):1065-1069.
- Joshi H, News N, Stainthorpe A, MacDonagh R, Keeley F, Timoney A. Ureteral stent symptom questionnaire: development and validation of a multidimensional quality of life measure. *J Urol.* 2003;169(3):1060-1064.
- Sighinolfi MC, Micali S, De Stefani S, Mofferdin A, Grande A, Giacometti M, Ferrari N, Rivalta M, Bianchi G. Indwelling ureteral stents and sexual health: a prospective, multivariate analysis. *J Urol.* 2007;178(1):229-231.
- Thomas R. Indwelling ureteral stents: impact of material and shape on patient comfort. *J Endourol.* 1993;7(2):137-140.
- Wang C-J, Huang S-W, Chang C-H. Effects of specific α -1A/1D blocker on lower urinary tract symptoms due to double-J stent: a prospectively randomized study. *Urol Res.* 2009;37(3):147-152.
- Choo MS, Lee JZ, Lee JB, Kim YH, Jung HC, Lee KS, Kim JC, Seo JT, Paick JS, Kim HJ, Na YG. Efficacy and safety of solifenacin succinate in Korean patients with overactive bladder: a randomised, prospective, double-blind, multicentre study. *Int J Clin Pract.* 2008;62(11):1675-1683.
- Lee Y-J, Huang K-H, Yang H-J, Chang H-C, Chen J, Yang T-K. Solifenacin improves double-J stent-related symptoms in both genders following uncomplicated ureteroscopic lithotripsy. *Urolithiasis.* 2013;41(3):247-252.
- Kuyumcuoglu U, Eryildirim B, Tuncer M, Faydaci G, Tarhan F, Ozgöl A. Effectiveness of medical treatment in overcoming the ureteral double-J stent related symptoms. *Can Urol Assoc J.* 2012;6(6):E234.
- Dellis A, Joshi HB, Timoney AG, Keeley FX. Relief of stent related symptoms: review of engineering and pharmacological solutions. *J Urol* 2010;184(4):1267-1272.
- Shalaby E, Ahmed A-f, Maarouf A, Yahia I, Ali M, Ghobish A. Randomized controlled trial to compare the safety and efficacy of tamsulosin, solifenacin, and combination of both in treatment of double-j stent-related lower urinary symptoms. *Adv Urol.* 2013; Article ID 752382.
- Paz A, Amiel GE, Pick N, Moskovitz B, Nativ O, Potasman I. Febrile complications following insertion of 100 double-J ureteral stents. *J Endourol.* 2005;19(2):147-150.
- Beiko DT, Knudsen BE, Denstedt JD. Advances in ureteral stent design. *J Endourol.* 2003;17(4):195-199.
- Lingeman JE, Preminger GM, Berger Y, Denstedt JD, Goldstone L, Segura JW, Auge BK, Watterson JD, Kuo RL. Use of a temporary ureteral drainage stent after uncomplicated ureteroscopy: results from a phase II clinical trial. *J Urol.* 2003;169(5):1682-1688.
- Park SC, Jung SW, Lee JW, Rim JS. The effects of tolterodine extended release and alfuzosin for the treatment of double-J stent-related symptoms. *J Endourol.* 2009;23(11):1913-1917.
- Damiano R, Autorino R, De Sio M, Giacobbe A, Palumbo IM, D'Armiento M. Effect of tamsulosin in preventing ureteral stent-related morbidity: a prospective study. *J Endourol.* 2008;22(4):651-656.
- Deliveliotis C, Chrisofos M, Gougousis E, Papatsoris A, Dellis A, Varkarakis IM. Is there a role for alpha1-blockers in treating double-J stent-related symptoms? *Urology.* 2006;67(1):35-39.
- Beddingfield R, Pedro RN, Hinck B, Kreidberg C, Feia K, Monga M. Alfuzosin to relieve ureteral stent discomfort: a prospective, randomized, placebo controlled study. *J Urol.* 2009;181(1):170-176.
- Lim KT, Kim YT, Lee TY, Park SY. Effects of tamsulosin, solifenacin, and combination therapy for the treatment of ureteral stent related discomforts. *Korean J Urol.* 2011;52(7):485.
- Lee SJ, Yoo C, Oh CY, Lee YS, Cho ST, Lee SH, Yang DY, Lee SK, Cho JS. Stent position is more important than α -blockers or anticholinergics for stent-related lower urinary tract symptoms after ureteroscopic

ureterolithotomy: a prospective randomized study.
Korean J Urol. 2010;51(9):636-641.