

Comparative Study of Tamsulosin, Solifenacin and Combination Therapy in the Treatment of Double –J Stent Related Symptoms

Abhinav Kumar, Vasudevan S

Department of Urology, Government Medical College, Trivandrum, Kerala*

ABSTRACT

Published on 27th March 2017

Introduction: The double-J ureteral stent had been widely used during the endourologic surgery to relieve or prevent ureteral obstruction. Despite the usefulness of stents, however, patients experience various stent related symptoms, such as pain, frequency, and urgency etc. Several attempts to minimize stent-related symptoms have recently been reported. Pharmacologic management is one such trial, especially the prescription of selective alpha-1-blockers and antimuscarinic agents.

Aim: To evaluate the effectiveness of tamsulosin, solifenacin and combination of both drugs in relieving double-J stent related lower urinary tract symptoms.

Materials and Methods: A prospective study of patients with placement of double –J ureteral stent after retrograde ureteroscopy for urinary stone disease is to be conducted. All patients receive polyurethane double-J ureteral stents (5 Fr, 26 cm), which were removed at a mean of 2 weeks duration postoperatively. All patients are to be randomly assigned, post operatively, into 5 groups. Patients in Group I having symptoms receive no treatment and serve as the control group, Group II patients receive tamsulosin 0.4 mg daily, Group III patients receive solifenacin 5 mg daily, Group IV patients receive a combination of both drugs and group V patients being asymptomatic receive no treatment. At 1 day postoperatively and at 2 weeks, all patients complete International Prostate Symptom Score/Quality of Life (IPSS/QoL) and visual analogue pain scale (VAPS) questionnaires.

Results: A total of 168 patients were enrolled in the study, while 8 patients in group 5 being asymptomatic were not included in statistical analysis. There was a significant difference in the IPSS irritative score in group IV as compared to groups I and II but not with group III. There was a significant difference in the IPSS obstructive score and VAPS score in group IV as compared to group I and III, while it was not significant with group III. Group IV showed statistically significant differences in total IPSS, QoL score as compared to groups I, II and III

Conclusion: Combination therapy with tamsulosin and solifenacin should be strongly considered for patients who complain of stent-related symptoms. In the future, large-scale, prospective, and randomized study will be needed.

Keywords: Double J stent, Tamsulosin, Solifenacin, Ureteric calculus, LUT symptoms

*See End Note for complete author details

INTRODUCTION

The double-J ureteral stent had been widely used during the endourologic surgery to relieve or prevent ureteral obstruction.¹ Despite the usefulness of stents, however, patients experience various stent-related symptoms, such as pain, frequency, and urgency, which cause a significant decrease in patient health-related quality of life (HRQoL)² Thomas reported that an important factor of stent-related symptoms is the pressure transmitted to the renal pelvis during urination and trigonal irritation by the intravesicular part of the stent.³ Several attempts to minimize stent-related symptoms have

recently been reported. Pharmacologic management is one such trial, especially the prescription of selective alpha-1-blockers and antimuscarinic agents.

Tamsulosin acts as a selective inhibitor of $\alpha 1A/1D$ -mediated contraction of the smooth muscles in the distal ureter, trigone, and bladder neck; relaxation of these smooth muscles decreases bladder outlet resistance and voiding pressure, with beneficial effect on stent-related LUTS.⁴ Solifenacin acts as a muscarinic receptor antagonist used for treatment of patients with overactive bladder(OAB) and might also be effective for stent-related symptoms.^{5,14}

Cite this article as: Kumar A, Vasudevan S. Comparative Study of Tamsulosin, Solifenacin and Combination Therapy in the Treatment of Double –J Stent Related Symptoms. Kerala Medical Journal. 2017 Mar 27;10(1):25–8.

Corresponding Author:

Dr Vasudevan S, Professor, Department of Urology, Government Medical College, Trivandrum, Kerala.
E-mail: periamana@gmail.com

Combined therapy with tamsulosin and solifenacin has been tried before and was found to significantly improve stent-related symptoms.^{6,7} The purpose of this study was therefore to analyze and assess the effectiveness of a selective alpha-1-blocker (tamsulosin) and antimuscarinic (solifenacin) in improving the lower urinary tract symptoms of patients with indwelling double-J ureteral stents.

MATERIALS AND METHODS

This prospective comparative study was carried out between July 2016 and December 2016 in Medical College Hospital Trivandrum, Kerala. Patients were selected among those who underwent retrograde double-J ureteral stent placement after retrograde ureteroscopy for ureteric stones. Patients' ≥ 18 years of age with unilateral double-J ureteral stent who agreed to random allocation of treatment were eligible for enrolment. Patients were excluded if they met any of the following criteria: (1) age less than 18 years, (2) pregnant women, (3) history of previous ureteral stenting, (4) bilateral stents, (5) long-term stenting (on regular exchange), (6) bladder pathology, (7) benign prostatic hyperplasia, (8) overactive bladder, (9) urinary tract infection, or (9) previous use of selective alpha-1-blocker and/or antimuscarinic agent. Surgery was performed under spinal anesthesia and the position of the stent was confirmed by plain X-ray. The stents were removed at a mean of 2 wks after surgery. All patients receive polyurethane double-J ureteral stents (5 Fr, 26 cm). All patients were randomly assigned, post operatively, into 5 groups.

Patients in Group I having symptoms receive no treatment and serve as the control group, Group II patients receive tamsulosin 0.4 mg daily, Group III patients receive solifenacin 5 mg daily, Group IV patients receive a combination of both drugs and group V patients being asymptomatic receive no treatment. At 1 day postoperatively and at 2 weeks, all patients completed International Prostate Symptom Score/quality of life (IPSS/QoL) and visual analogue pain scale (VAPS) questionnaires. The IPSS was divided into the total score, obstructive symptom score, and irritative symptom score, and each was compared. Each group's postoperative day 1, and stent removal day scores were compared.

Statistical analysis

Statistical analysis was performed with SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA). Chi-square test, one-way ANOVA were used for comparisons between each of four groups followed by post hoc analysis- Tuckey's test

RESULTS

A total of 168 patients were enrolled in the study, while 8 patients in group 5 being asymptomatic were not included in statistical analysis. The main indication of ureteral double-J stent placement was after retrograde ureteroscopy for urinary stone disease.

There were no statistically significant differences between groups regarding patient's age and sex distributions (**table 1**).

Table 1. Group wise gender and age distribution of the study participants

Variable	Group 1 (N=40)	Group 2 (N=41)	Group 3 (N=36)	Group 4 (N=43)	P value
GENDER					0.772 *
Male	30 (75)	29 (70.7)	24 (66.7)	28 (65.1)	
Female	10 (25)	12 (29.3)	12 (33.3)	15 (34.9)	
Age	43.75 (7.66)	43.32 (8.69)	43.00 (8.37)	42.49 (9.18)	0.922 #

*pvalue based on chi square test #p value based on one way ANOVA

Based on one way ANOVA there was significant difference in all domains of the groups on the day of stent removal (**table 2**). We proceeded with post hoc analysis- Tuckey's test in between groups (**table 2**).

There was a significant difference in the IPSS irritative score in group IV as compared to groups I and II but not with group III. There was a significant difference in the IPSS obstructive score and VAPS score in group IV as compared to group I and III, while it was not significant with group III. Group IV showed statistically significant differences in total IPSS, QoL score as compared to groups I, II and III.

Thus overall there was a statistically significant difference between Groups I, II and III vs Group IV, denoting that the outcome was in favour of combination therapy.

The side effects of tamsulosin and solifenacin were minimal. No patients discontinued the medication because of side effects.

DISCUSSION

Ureteral stents have become a fundamental tool in today's urologic armamentarium. Ureteroscopy, especially after ureteroscopic lithotripsy, routinely make use of ureteral stents⁸ Lower urinary tract symptoms such as frequency, urgency, dysuria, and pain (flank or suprapubic) occur almost universally as stent related symptoms. Joshi et al reported that, because of these stent-related symptoms, 80% of patients have

Table 2. Comparative analysis of IPSS, QoL and VAPS Scores in all groups

		Group 1 (N=40)	Group 2 (N=41)	Group 3 (N=36)	Group 4 (N=43)	P value*	P value#
IPSS Total score	Day 1	9.80 (1.77)	10.15 (2.11)	10.19 (1.92)	10.21 (1.95)	0.757	0.772 *
	After 2 wks.	10.28 (1.88)	9.00 (1.89)	7.97 (1.81)	6.26 (1.44)	<0.001	<0.001 ^a <0.001 ^b <0.001 ^c
IPSS Irritative score	Day 1	7.02 (1.33)	7.15 (1.31)	7.47 (1.23)	7.44 (1.22)	0.318	
	After 2 wks.	7.25 (1.31)	7.07 (1.38)	5.25 (1.25)	4.77 (1.10)	<0.001	<0.001 ^a <0.001 ^b 0.339 ^c
IPSS Obstructive score	Day 1	2.78 (0.92)	2.98 (1.21)	2.72 (0.88)	2.77 (0.97)	0.683	
	After 2 wks.	3.02 (1.14)	1.88 (0.87)	2.72 (0.88)	1.49 (0.55)	<0.001	<0.001 ^a 0.184 ^b <0.001 ^c
QoL	Day 1	3.58 (0.67)	3.56 (0.70)	3.50 (0.60)	3.86 (0.74)	0.084	
	After 2 wks.	3.60 (0.67)	3.41 (0.59)	3.50 (0.60)	2.70 (0.63)	<0.001	<0.001 ^a <0.001 ^b <0.001 ^c
VAPS	Day 1	3.72 (0.78)	3.95 (0.83)	3.81 (0.82)	4.09 (0.71)	0.161	
	After 2 wks.	3.78 (0.73)	3.46 (0.95)	3.81 (0.82)	2.93 (0.76)	<0.001	<0.001 ^a 0.018 ^b <0.001 ^c

*p values based on one way ANOVA#p value based on post hoc analysis-Tuckey's test

a- comparison between group 1 and 4; b- comparison between group 2 and 4; c-comparison between group 3 and 4

a reduced HRQoL and need continue understanding and interest about their symptoms.⁹ Studies have been run in several ways to solve these problems like changing stent material or length. But the safe and convenient ways to improve stent-related symptoms is pharmacologic management. Wang and his colleagues suggested that relaxation of bladder neck/prostatic smooth muscle,with consequent reduction in voiding pressure and urinary reflux, is other possible mechanisms for control of stent-related symptoms, setting a rationale behind using alpha blockers in overcoming ureteral stent symptoms.¹⁰ In addition, Damiano et al reported that the administration of tamsulosin improved urinary symptoms, VAPS, and QoL.¹¹ Kuyumcuoglu et al. reported in a prospective randomized study that tamsulosin was not different than placebo in controlling stent-related symptoms.¹² Another mechanism was thought to be related to stent

itself which may unmask or exacerbate preexisting subclinical detrusor overactivity causing involuntary bladder contraction, which induces overactive bladder symptoms, setting a rationale behind using antimuscarinic agents to improve stent-related symptoms.¹³ Lee et al. reported in a prospective, randomized, and placebo-controlled study that postoperative solifenacin use was effective and well tolerated for the treatment of LUTS, stent-related body pain, and hematuria irrespective of gender in patients undergoing ureteroscopic lithotripsy (URSL) and double-J stent indwelling.¹⁴ Kuyumcuoglu et al. reported that tolterodine SR 4mg was not different than anti-inflammatory and alpha blocker in controlling stent-related symptoms.¹² In contrast, Lee et al. in their prospective randomized study over 20 patients using a combination of Tamsulosin and tolterodine reported no statistically significant difference when compared to placebo, and also when combination therapy was compared to tamsulosin monotherapy, no beneficial effect was reported. They stated that correct stent positioning and verification of its location were more important than medication for lessening stent-related storage symptoms.¹⁵

The efficacy of combined therapy of both drugs in different doses has been assessed in multiple studies. Lim et al. assessed the effectiveness of a selective a1-blocker (tamsulosin 0.2 mg) and antimuscarinic (solifenacin 5 mg) in improving LUTS in patients with ureteric stents using the IPSS, IPSS/QoL and VAPS questionnaires.⁶ In another study tamsulosin OCAS 0.4 mg daily, solifenacin 10 mg daily, and combination of both medications were tried in a RCT using IPSS/QoL, overactive bladder questionnaire (OAB-q), and VAPS questionnaire.⁷

A recent study has been done to evaluate the efficacy of solifenacin, tamsulosin and the combination of both drugs on JJ stent-related symptoms using the validated Arabic version of the ureteric stent symptom questionnaire (USSQ)¹⁶ Thus several studies concluded that combined therapy with tamsulosin and solifenacin have been shown to have a synergistic effect and be more effective than either medication alone in reducing stent-related symptoms.^{17,18} The results of the present study show that combination therapy significantly improved stent-related symptoms compared with monotherapy with either one of the drugs. The dose of solifenacin was reduced to 5 mg to decrease the potential side-effects of these medications; especially

with elderly patients. The patient homogeneity was maintained by including only those patients in whom stent was placed after ureteroscopic lithotripsy. Comparison with the similar studies revealed the following differences.

- Lim et al. (2011)
 - Retrospective study
 - Non randomized study
- Small groups
- Shalaby et al. (2013)
 - lack of patient homogeneity
 - High dose(10mg) of solifenacin
- Abdelaal et al.(2016)
 - lack of homogeneity of patients
 - elderly patients inclusion
- Our study(2016)
 - Prospective and randomized study
 - Patients homogeneity

The limitations of this study are as follows. The small groups of each scale make it difficult to verify the statistical significance. Some patients did not complete the symptom questionnaire. So further large-scale studies are needed to get more accurate information.

CONCLUSION

Combination therapy with tamsulosin and solifenacin should be strongly considered for patients who complain of stent-related symptoms. In the future, large-scale, prospective, and randomized studies will be needed.

END NOTE

Author Information

1. Dr. Abhinav Kumar, Senior Resident, Department of Urology, Government Medical College, Trivandrum, Kerala.
2. Dr. Vasudevan S, Professor, Department of Urology, Government Medical College, Trivandrum, Kerala.

Conflict of Interest: None declared

Editor's Remarks: Troublesome symptoms like painful voiding, increased frequency of voiding, haematuria, strangury and occasionally retention of urine are often reported in patients with double J stent placed for various indications. The paper tries to find a medical solution to DJ stent related symptoms after ureteroscopy

REFERENCES

1. Knudsen BE, Beiko DT, Denstedt JD. Stenting after ureteroscopy: pros and cons. *Urol Clin North Am.* 2004 Feb;31(1):173–80.
2. Joshi HB, Stainthorpe A, Keeley FX, MacDonagh R, Timoney AG. Indwelling ureteral stents: evaluation of quality of life to aid outcome analysis. *J Endourol.* 2001 Mar;15(2):151–4
3. Thomas R. Indwelling Ureteral Stents: Impact of Material and Shape on Patient Comfort. *Journal of Endourology.* 1993 Apr 1;7(2):137–40.
4. Wang C-J, Huang S-W, Chang C-H. Effects of specific alpha-1A/1D blocker on lower urinary tract symptoms due to double-J stent: a prospectively randomized study. *Urol Res.* 2009 Jun;37(3):147–52.
5. Vardy MD, Mitcheson HD, Samuels T-A, Wegenke JD, Forero-Schwanhaeuser S, Marshall TS, et al. Effects of solifenacin on overactive bladder symptoms, symptom bother and other patient-reported outcomes: results from VIBRANT - a double-blind, placebo-controlled trial. *Int J Clin Pract.* 2009 Dec;63(12):1702–14.
6. 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 Jul;52(7):485–8.
7. 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;2013:752382.
8. Halebian G, Kijvikai K, de la Rosette J, Preminger G. Ureteral stenting and urinary stone management: a systematic review. *J Urol.* 2008 Feb;179(2):424–30.
9. Joshi HB, Stainthorpe A, MacDonagh RP, Keeley FX, Timoney AG, Barry MJ. Indwelling ureteral stents: evaluation of symptoms, quality of life and utility. *J Urol.* 2003 Mar;169(3):1065–1069; discussion 1069.
10. Wang C-J, Huang S-W, Chang C-H. Effects of tamsulosin on lower urinary tract symptoms due to double-J stent: a prospective study. *Urol Int.* 2009;83(1):66–9.
11. Damiano R, Autorino R, De Sio M, Giacobbe A, Palumbo IM, D'Armiato M. Effect of tamsulosin in preventing ureteral stent-related morbidity: a prospective study. *J Endourol.* 2008 Apr;22(4):651–6.
12. Kuyumcuoglu U, Eryildirim B, Tuncer M, Faydaci G, Tarhan F, Ozgül A. Effectiveness of medical treatment in overcoming the ureteral double-J stent related symptoms. *Can Urol Assoc J.* 2012 Dec;6(6):E234–7.
13. Agarwal A, Dhiraj S, Singhal V, Kapoor R, Tandon M. Comparison of efficacy of oxybutynin and tolterodine for prevention of catheter related bladder discomfort: a prospective, randomized, placebo-controlled, double-blind study. *Br J Anaesth.* 2006 Mar;96(3):377–80.
14. 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 Jun;41(3):247–52.
15. Lee SJ, Yoo C, Oh CY, Lee YS, Cho ST, Lee SH, et al. 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 Sep;51(9):636–41.
16. Abdelaal AM, Al-Adl AM, Abdelbaki SA, Al Azab MM, Al Gamal KA. Efficacy and safety of tamsulosin oral-controlled absorption system, solifenacin, and combined therapy for the management of ureteric stent-related symptoms. *Arab J Urol.* 2016 Feb 22;14(2):115–22.
17. Zhou L, Cai X, Li H, Wang K-J. Effects of α -Blockers, Antimuscarinics, or Combination Therapy in Relieving Ureteral Stent-Related Symptoms: A Meta-Analysis. *J Endourol.* 2015 Jun;29(6):650–6.
18. Chew BH, Seitz C. Impact of ureteral stenting in ureteroscopy. *Curr Opin Urol.* 2016 Jan;26(1):76–80.