

Evaluate the Effects of Silodosin and Solifenacin Combination with Silodosin Alone in Reducing DJ Stent Related Symptoms

Dr. Prashant Lavania¹, Dr. Akash Sharma², Dr. Nikhil Singh³

Abstract: Background: Ureteral stents play a major role in a wide range of situations where urinary drainage is needed. The placement of stent produces variety of lower urinary tract symptoms. The study was aimed to Evaluate the effects of silodosin and solifenacin combination with silodosin alone in reducing DJ stent related symptoms (SRS). Methods: A total of 150 patients who underwent DJ stenting and developed SRS were randomized into 3 groups [Group A: silodosin (8mg OD) + solifenacin (10mg OD), Group B: silodosin (8mg OD) and group C: placebo]. IPSS, VAS for pain and QOL score were noted at 7th day. All groups received drugs for 14 days and IPSS, VAS for pain and QOL scores were noted at 21st day. Results: Scores were similar in all groups at first week but group A and B had significant reduction in scores as compared to group C on 21st day. On statistical evaluation between A and B groups, score reduction was in favour of group A which was significant. Conclusion: Combination therapy with silodosin and solifenacin is effective for relieving stent related symptoms with improved QOL and less pain.

Keywords: DJ stent, Silodocin, Solefinacin, LUTS

1. Introduction

Since its first description in 1967 by Zimskind et al^[21] the double-j stent has been an indispensable tool in the urologist's surgical armamentarium. Despite its usefulness, morbidity associated with these stents has been considered as a potential health problem and are thought to be overused in contemporary urology practice. Stent discomfort are believed to affect over 80% of patients^[2]. The symptoms related to ureteral stents and their respective estimated incidence: irritative voiding symptoms including frequency (50-60%), urgency (57-60%), dysuria (40%), incomplete emptying (76%), flank pain (19-32%), and suprapubic pain (30%), incontinence, and hematuria (25%) are included.^[6,7,15,16,17] Pharmacological treatment is the simplest and a non invasive option for the management of these symptoms.

Silodosin is a highly selective antagonist for the alpha 1 A adrenergic receptor subtype and has high selectivity, causes much fewer adverse cardiovascular effects. Solifenacin is a competitive cholinergic receptor antagonist, selective for the M3 receptor subtype. The binding of acetylcholine to these receptors particularly M3 plays critical role in contraction of smooth muscles. Solifenacin reduces smooth muscle tone in the bladder, allowing the bladder to retain larger volumes of urine and reducing the number of micturition, urgency and incontinence episodes. Once a day dose can offer 24 hours control.

2. Material and Methods

This prospective randomized placebo controlled study was conducted in Department of Surgery, S.N. Medical College, Agra from January 2018 to June 2019. Informed and written consent was taken from all study participants. All patients above 18 years of age group not having any contraindication for the drugs undergoing routine DJ stenting after an endourological surgery [either unilateral percutaneous nephrolithotomy (PCNL) or ureteroscopic lithotripsy (URSL)] were enrolled in the study for evaluation. History

and physical examination was done in all patients with baseline basic investigations such as serum creatinine, urine analysis and culture, ultrasonography, plain X-ray of the kidneys, ureters and bladder (KUB) and non contrast enhanced computed tomography (NCCT) KUB were performed in every patient before surgery. A 6Fr polyurethane DJ stent was used in all the study participants.

Patients having previous or present history of prostatic or bladder surgery, lower urinary tract surgery, malignancy, neurological disorder, pelvic irradiation, diabetes, acute or chronic renal insufficiency, solitary kidney or congenital urinary abnormality, medical treatment, cardiac disease, post operative residual stone fragments, multiple or bilateral ureteral stones, bilateral stents, history of interstitial cystitis, chronic cystitis or prostatitis, pregnant and lactating women, and patients not available for follow were excluded from this study.

Post operative X-ray KUB and urinary ultrasonography were done in all patients to identify residual stone fragment(s). Foley's catheter was removed on Post operative day 1 in all patients. On post operative day 2, nephrostograms were obtained before removal of nephrostomy tubes in all PCNL patients. Patients were discharged on day 3 with 7 day course of antibiotics and were told to come 7 days later and scoring at first week was carried out to see the severity of DJ stent related symptoms.

After applying exclusion and inclusion criteria, 150 patients reported DJ stent related symptoms at 1st week and were randomly divided into three groups. Group A were prescribed combination of silodosin (8mg) and solifenacin (10mg), Group B prescribed silodosin (8mg) and group C prescribed placebo (multivitamin). Patients were advised to take analgesics (diclofenac sodium 50mg) as per requirement. All patients were informed about side effects of the drugs. Patients were asked to come after 14 days of taking these drugs and IPSS, VAS for pain and QOL scores were noted before removal of DJ stent. In every domain a

final score was found by adding the scores obtained and higher score was considered more bothersome.

3. Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (Microsoft Excel), Trial version 23 for Windows statistical software package and Primer. The quantitative data were presented as mean and standard deviation and compared using Student t-test and the categorical data were presented as numbers (percent) and compared among groups using Chi square test. ANOVA Test applied to find out the most significant groups among all the groups. P value <0.05 was considered as statistically significant.

4. Results

In the study, total of 150 eligible patients based on inclusion criteria were randomly assigned into three groups. Out of these 150 patients, groups A (50), B (50) and C (50) contained indicated number of patients. All patients tolerated drug well and none of them were excluded from the study because of drug related side effects.

No statistically significant differences were observed regarding patient's age, gender, body mass index and procedure done (PCNL/URSL) in all the groups.

AT 7 Days:

Table 1: VAS Score at 7th day

Groups	N	Mean	SD
A	50	4.64	0.94
B	50	5.00	1.36
C	50	2.80	0.99

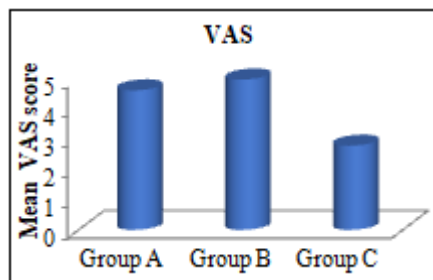


Table-1 shows VAS score for pain at 7 days in all three groups. In group A mean score was 4.64 ± 0.94 , in group B 5.00 ± 1.36 and in group C 2.80 ± 0.99 .

Table 2: IPSS Score at 7th Day

Groups	N	Mean	SD
A	50	11.68	0.96
B	50	13.10	0.84
C	50	12.60	0.93

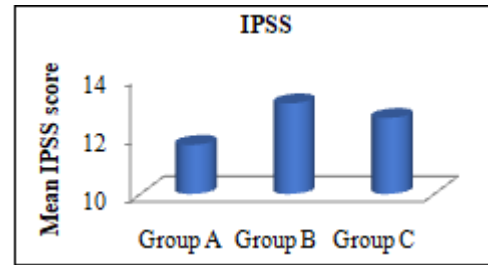


Table-2 shows IPSS score for SRS at 7 days in all three groups. In group A mean score was 11.68 ± 0.96 , in group B 13.10 ± 0.84 and in group C 12.60 ± 0.93 .

Table 3: QOL Score

Groups	N	Mean	SD
A	50	4.48	0.50
B	50	3.40	0.49
C	50	3.60	0.49

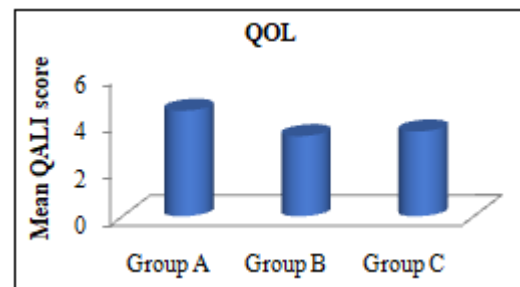


Table-3 shows QOL score at 7 days in all three groups. In group A mean score was 4.48 ± 0.50 , in group B 3.40 ± 0.49 and in group C 3.60 ± 0.49 .

At 21 Days:

Table 4: VAS Score

Groups	N	Mean	SD	f-value	p-value	CD
A	50	0.64	0.94	13.842	<0.0001	0.15
B	50	1.60	0.81			
C	50	1.20	0.99			

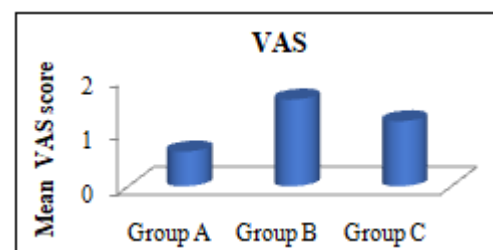


Table-4 shows VAS score for pain at 21 days in all three groups. In group A mean score was 0.64 ± 0.94 , in group B 1.60 ± 0.81 and in group C 1.20 ± 0.99 . F value 13.842 calculated by analysis of variance (ANOVA), p value <0.0001 with CD 0.15. These results shows statistically significant difference between three groups i.e. least pain score in group A (combination of silodosin and solifenacin).

Table 5: IPSS Score

Groups	N	Mean	SD	f-value	p-value	CD
A	50	2.48	0.50	1930.66	<0.0001	0.12
B	50	5.00	0.78			
C	50	11.60	0.93			

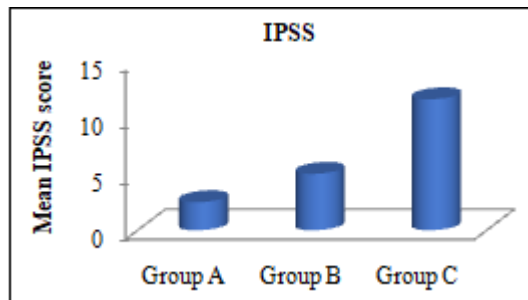


Table-5 shows IPSS score for SRS at 21 days in all three groups. In group A mean score was 2.48 ± 0.50 , in group B 5.00 ± 0.78 and in group C 11.60 ± 0.93 . F value 1930.66 calculated by analysis of variance (ANOVA), p value < 0.0001 with CD 0.12. These results shows statistically significant difference between three groups i.e. least IPSS score in group A (combination of silodosin and solifenacin).

Table 6: QOL

Groups	N	Mean	SD	f-value	p-value	CD
A	50	1.34	0.48	29.553	<0.0001	0.08
B	50	2.10	0.54			
C	50	1.70	0.46			

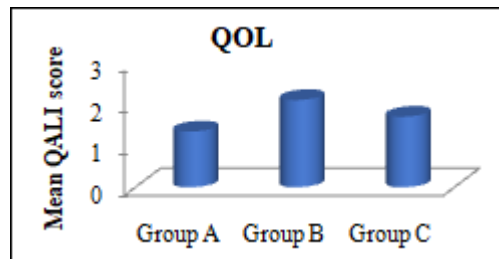


Table-6 shows QOL score at 21 days in all three groups. In group A mean score was 1.34 ± 0.48 , in group B 2.10 ± 0.54 and in group C 1.70 ± 0.46 . F value 29.553 calculated by analysis of variance (ANOVA), p value < 0.0001 with CD 0.08. These results show statistically significant difference between three groups i.e. least QOL score in group A (combination of silodosin and solifenacin). Lower the QOL score suggests better quality of life.

5. Discussion

Indwelling double J (DJ) stents are routinely used for resolution/prevention of ureteral obstruction caused by different etiologies and they are in use for more than three decades.^[21] However SRS is an important issue with the use of these stents and can present in majority of patients with a significant negative impact on patients' QOL.^[9,4] Many theories have been suggested to understand the pathophysiology of these symptoms but still the exact mechanism is not completely understood.^[2]

Various strategies have been applied for better compatibility of these stents based on preventive and pharmaceutical methods. Preventive strategies include minimum use of stents, stent length adjusted according to patients' height, proper positioning of stents, changes in stent design like biodegradable stents, hydrophilic material coating tapered distal end of these stents, stent coating, drug-eluting stents and proper patient counseling regarding symptoms. It had

been suggested that drugs like alpha-blockers and anticholinergics decrease the pressure transmitted toward the renal pelvis during micturition, reduce the peak contraction pressure leading to ureteral dilation and decrease the bladder irritation with the intravesical portion of the stent that will lead to less discomfort related to stents.^[12]

Alpha-blockers, anticholinergics and their combinations can be used for the management of SRSs with good results.^[5,7-10,13-18] Our study shows that combination of silodosin with solifenacin improved SRS and better QOL with less requirement for analgesics as compared to any other group. Kim et al.^[12] had also shown the benefit of silodosin in patients with SRS.

Alpha-blockers are commonly used drugs for SRS and various other researchers have also found that these drugs are effective in reducing SRSs.^[5, 8,14, 13] Similarly in our study, silodosin alone was effective in reducing SRS as compared to placebo.

Anticholinergics alone and in combination with alpha-blockers have been found to be effective in patients with SRS but combination therapy is more effective than monotherapy.^[5, 9,10, 12-14, 18]

However our study is also not free from limitations like use of single stent design and material and being a single center study. Although the sample size was adequately calculated, it was still small in each group.

Combination therapy should be strongly considered for patients who complain of stent related symptoms. However, in our opinion, there is need for further studies to compare the effectiveness of combination of different alpha blockers and antimuscrinic agents in order to optimize medical therapy for treatment of symptoms related to stent placement.^[7]

Alpha-blockers, anticholinergics and their combinations can be used for the management of SRSs with good results.^[5, 7-10,13-18]

The combination of tamsulosin and solifenacin appears to significantly improve stent-related irritable and obstructive symptoms compared to monotherapy with either agent alone.

SRS has major impact on patient's daily life and combination of silodosin and solifenacin (Group A) was an effective drug treatment for relieving these symptoms with improved QOL and less requirement of analgesic than all other groups. However, study with multicentre design can be more helpful to validate our results.

6. Conclusion

This study show that combination treatment with silodosin (selective alpha blocker) and solifenacin (anti Cholinergic) significantly improved DJ stent related lower urinary tract symptoms in terms of IPSS, Pain and Quality of life.

Stent related symptoms have high prevalence. Management should focus on prevention and management of symptoms. In this sense research has focused on new material and stent

designs that would be more compatible to physiologic properties of the urinary tract and medications that can ameliorate the sensitivity of motor response of bladder.

Medications to decrease morbidity should be regarded as palliative adjustment approach but seem to be a more reachable solution in the short term.

References

- [1] Aggarwal, S.P., Priyadarshi, S., Tomar, V., Yadav, S.S., Gangkak, G. and Vyas, N. 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;592175. <https://doi.org/10.1155/2015/592175>.
- [2] Beddingfield, R., Pedro R.N., Hinck, B., Kreidberg, C., Feia, K. and Monga, M. (2009). Alfuzosin to relieve ureteral stent discomfort: a prospective, randomized, placebo controlled study. *Journal Of Urology* jan (2009)181: 170–176. <http://doi.org/10.1016/j.juro.2008.09.026>.
- [3] Bregg, K. and Riehle, R.A. Jr. (1989). Morbidity associated with indwelling internal ureteral stents after shock wave lithotripsy. *Journal of Urology* 141: 510-512. [http://doi.org/10.1016/s0022-5347\(17\)40875-5](http://doi.org/10.1016/s0022-5347(17)40875-5).
- [4] Chew, B.H., Knudsen, B.E. and Denstedt J.D. (2004). The use of stents in contemporary urology. *Current Opinion In Urology* 4: 111-115. <http://doi.org/10.1097/00042307-200403000-00011>.
- [5] Clifford, G.M. and Farmer, R.D. (2000). Medical therapy for benign prostatic hyperplasia: a review of the literature. *European Journal Of Urology* 38: 2–19. <http://doi.org/10.1159/000020246>.
- [6] Deliveliotis, C., Chrisofos, M., Gougousis, E., Papatsoris, A., Dellis, A. and Varkarakis, I.M. (2006). Is there a role for alpha1-blockers in treating double-J stent-related symptoms?. *Urology* 67: 35–39. <http://doi.org/10.1016/j.urology.2005.07.038>.
- [7] Dellis, A.E., Keeley, F.X. Jr, Manolas, V. and Skolarikos, A.A. (2014). Role of α blockers in the treatment of stent-related symptoms: a prospective randomized control study. *Urology* 83: 56–61. <http://doi.org/10.1016/j.urology.2013.08.067>.
- [8] Denstedt, J.D., Reid, G. and Sofer M. (2000). Advances in ureteral stent technology.
- [9] *World Journal Of Urology* 18: 237-242. 17. <http://doi.org/10.1007/pl00007074>.
- [10] Dyer, R.B., Chen, M.Y., Zagoria, R.J., Regan, J.D., Hood, C.G. and Kavanagh, P.V. (2002). Complications of ureteral stent placement. *Radiographics* 2002;22:1005-22. <http://doi.org/10.1148/radiographics.22.5.g02se081005>.
- [11] Joshi, H.B., Newns, N., Stainthorpe, A., MacDonagh, R.P., Keeley and F.X. Jr. (2000) Ureteral stent symptom questionnaire: development and validation of a multidimensional quality of life measure. *Journal Of Urology* 169: 1060–1064. <http://doi.org/10.1097/01.ju.0000049198.53424.1d>
- [12] Joshi, H.B., Stainthorpe, A., MacDonagh, R.P., Keeley, F.X. Jr, Timoney, A.G. and Barry M.J. Indwelling ureteral stents: evaluation of symptoms, quality of life and utility. *Journal Of Urology* 2003;169:1065-9. <http://doi.org/10.1097/01.ju.0000048980.33855.90>.
- [13] Kim, H.W., Lee, J.H., Shin, D.G. and Lee, J.Z. The effects of silodosin in the treatment of ureteral stent related symptoms. *JIPM Chem* 2015;82:259-63. <http://doi.org/10.1007/s10847-015-0494-y>.
- [14] Lingeman, J.E., Preminger, G.M., Berger, Y., Denstedt, J.D. and Goldstone, L. (2003). Use of a temporary ureteral drainage stent after uncomplicated ureteroscopy: results from a phase II clinical trial. *Urology* 169: 1682-1688. <http://doi.org/10.1097/01.ju.0000055600.18515.a1>.
- [15] Michel, M.C. (2010). The pharmacological profile of the α 1A-adrenoceptor antagonist silodosin. *European Journal Of Urology* 4: 486–490. <https://doi.org/10.1016/j.eursup.2010.03.006>.
- [16] Paz, A., Amiel, G.E., Pick, N., Moskovitz, B. and Nativ, O. (2005). Febrile complications following insertion of 100 double-J ureteral stents. *Journal of Endourology* 19: 147-150. <http://doi.org/10.1089/end.2005.19.147>.
- [17] Richter, S., Ringel, A., Shalev, M. and Nissenkorn, I. (2000). The indwelling ureteric stent: a “friendly” procedure with unfriendly high morbidity. *British Journal Of Urology International* 85: 408-411. <http://doi.org/10.1046/j.1464-410x.1998.00543.x-i1>
- [18] Shalaby, E., Ahmed, A.F., Maarouf, A., Yahia, I. and Ali, M. (2013). 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. *Advanced Urology* 2013: 752382. <http://doi.org/10.1155/2013/752382>.
- [19] Shibata, K., Foglar, R., Horie, K., Obika, K. and Sakamoto A. (1995). KMD-3213, a novel, potent, α 1a adrenoceptor-selective antagonist: characterization using recombinant human α 1-adrenoceptors and native tissues. *Molecular Pharmacology* 1995 Aug;48(2):250-8.
- [20] Tolley, D. (2000). Ureteric stents, far from ideal. *The Lancet* 356: 872–873. [http://doi.org/10.1016/S0140-6736\(00\)02674-X](http://doi.org/10.1016/S0140-6736(00)02674-X).
- [21] Wang, C.J., Huang, S.W. and Chang, C.H. Effects of specific α -1A/1D blocker on lower urinary tract symptoms due to double-J stent: a prospectively randomized study. *Urology Resources* 2009;37:147-52. <http://doi.org/10.1007/s00240-009-0182-8>.
- [22] Zimskind, P.D., Fetter, T.R. and Wilkerson J.L. (1967). Clinical use of long-term indwelling silicone rubber ureteral splints inserted cystoscopically. *Journal Of Urology*, 97(5):840-4. [https://doi.org/10.1016/S0022-5347\(17\)63130-6](https://doi.org/10.1016/S0022-5347(17)63130-6).