International Surgery Journal
Agbo CA et al. Int Surg J. 2024 Jan;11(1):26-30
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20233918

Original Research Article

Randomized controlled trial comparing the effectiveness of tamsulosin, tamsulosin with tolterodine and double J stent position in controlling stent related symptoms after ureteroscopic lithotripsy

Christian A. Agbo[1]*, Gaurav Nahar[2]

[1]Department of Surgery, Benue State University, Makurdi, Nigeria
[2]Department of Urology, Meenakshi Mission Hospital and Research Centre Madurai, Tamil Nadu, India

Received: 23 October 2023
Revised: 18 November 2023
Accepted: 20 November 2023

***Correspondence:**
Dr. Christian A. Agbo,
E-mail: agbo535@gmail.com

ABSTRACT

Background: Objective of the study was to determine the effect of stent position and medications in preventing stent-related symptoms.
Methods: This was a prospective study conducted at Meenakshi Mission Hospital and Research Centre Madurai, Tamil Nadu, India. 150 patients who underwent ureteroscopic lithotripsy with indwelling stent were distributed into three groups. On demand analgesics were given to group 1 (n=50), Tamsulosin 0.4 mg daily for group 2 (n=50) and tamsulosin 0.4 mg and tolterodine 4 mg daily for group 3 (n=50). The patients were also subclassified into appropriate or inappropriate group according to stent position. All patients completed various domains of Ureteral stent symptom questionnaire (USSQ) on 1st and 7th postoperative days. Appropriate tests statistics were performed using EPI-Info statistical software package.
Results: In control group, patients with appropriate stent position had significantly lower symptom scores than those with inappropriate stent position (p value~0.0001) in all domains of USSQ except global quality of life score (p value=0.08). Addition of tamsulosin 0.4 mg (group 2) had superadded beneficial effect in appropriate position group, but not in patients with inappropriately positioned stents. Patients taking both tamsulosin 0.4 mg and tolterodine 4 mg (group 3) had no significant improvement in symptom scores in appropriate position group (all domains of USSQ) and inappropriate position group (most domains).
Conclusions: Appropriate stent position is the most important independent factor than medications in preventing stent related symptoms; tamsulosin has superadded benefit in patients with correctly positioned stents.

Keywords: USSQ, Stone, Tamsulosin, Tolterodine

INTRODUCTION

Ureteral stent placement is a common urological procedure since Zimskind et al first described a cystoscopically placed endoluminal stent.[1] Ureteral stents are routinely used to relieve ureteral obstruction caused by various causes. But they have significant morbidity associated with their use. Especially general health, sexual activity, work performance and overall quality of life are affected by bothersome urinary symptoms in 78% and pain in 80% of cases.[2-4] Ho et al advocates that to minimize stent morbidity, stent length and position should be adequate.[5] Alpha-blockers and anticholinergics have been tried to alleviate the stent related symptoms.[6,7] Intravesical instillation of chemical agents or periureteral injection of botulinum toxin have also been tried.[8,9] Rationale of using α-blockers to prevent stent related symptoms is based on the similarity of these symptoms to benign prostatic hyperplasia related lower urinary tract symptoms, including urgency, frequency and suprapubic pain, which

are caused by involuntary contraction of the bladder mediated by muscarinic receptors.[10] Administration of a selective α-blocker, such as alfuzosin or tamsulosin, may improve stent related urinary symptoms and pain. Work performance, sexual function and general health may also be better preserved. Assessment of stent related symptoms is difficult using common clinical measures. Joshi et al developed ureteral stent symptom questionnaire (USSQ), a psychometrically valid assessment tool to evaluate the impact of ureteral stents on symptoms and quality of life (QoL).[11]

In this study, the role of medications (α blockers and anticholinergics) and stent position/length to control ureteral stent-related symptoms, especially lower urinary tract symptoms (LUTS) after ureteroscopic lithotripsy, has been evaluated using USSQ as the assessment tool.

METHODS

This is a single blind parallel prospective randomized controlled trial. This study was approved by the Institutional Ethics Committee. The duration of the study was from April 2014 to March 2016. Patients who underwent successful elective ureteroscopic lithotripsy for symptomatic, single unilateral ureteral calculi as documented on computed tomography (CT) urogram were enrolled for the study. Informed consent was obtained from the patient for participation in the study.

Patients aged <18 years, patients having bilateral ureteral calculi, patients presenting with infection/pyelonephritis, patients with serum creatinine >1.8 mg/dl, pregnant patients and patients who had prior prostatic surgery formed the exclusion criteria. Patients for whom any additional procedure apart from ureteroscopy was performed, patients who were already on alpha blockers/anticholinergics for other indications, for whom complete stone clearance was not achieved, for whom there was a complication during ureteroscopy and patients unwilling to participate were also excluded.

A total of 150 patients were enrolled for the study after exclusion. Patients were randomized using stratified permuted block randomization. Patients were randomized into three groups of 50 each. The patient was blinded as to which group they were assigned to. In group 1, patients were prescribed analgesics (paracetamol 650 mg on demand, maximum thrice daily) only as a control group. Patients in group 2 were given 0.4 mg of tamsulosin and analgesics (on demand) daily, and patients in group 3 were prescribed 0.4 mg of tamsulosin and 4 mg of tolterodine daily in addition to analgesics (on demand). All patients were asked to complete ureteral stent symptom questionnaire (USSQ) for evaluation of symptoms, on the 1st (only urinary symptoms and body pain domains) and 7th (all domains) postoperative days. After ureteroscopy, 6 Fr ureteral stent was used in all patients after stone removal, adjusting length of the ureteral stent according to the patient's height (Pilcher & Patel formula) 12. The location of the distal curling of the ureteral stent was evaluated on 1st postoperative day by plain X-ray KUB. When the distal stent coil was present on the same side of midline, stent position was considered "appropriate", and when it crossed the midline of symphysis pubis, the stent was considered to be in an "inappropriate" position. The stents were removed 2 weeks after the procedure on an outpatient basis.

Statistical analysis was performed by using Pearson's chi-square test (for discrete variables), Student's unpaired t-tests (for continuous variables to compare two groups) and ANOVA tests (to compare three groups) with an EPI-Info statistical software package. The statistical significance was defined at $p<0.05$ (95% confidence level).

RESULTS

No significant statistical differences were observed in the baseline clinico-pathological characteristics among the patients in the three groups (Table 1).

Urinary symptom score

The mean urinary symptom score on 1st post-operative day in group 1(24.46) did not show any significant difference when compared to group 2 (23.72; p value 0.407) and group 3 (24.38; p value=0.94). However, on 7th post-operative day, patients in group 2 had significant improvement in their urinary symptoms (19.4; p value=0.007) compared to group 1 (21.68), but this effect was not noted when anticholinergic was also added as in group 3 (22.36; p value=0.487).

Body pain symptom score

As far as body pain symptoms were considered; on 1st post-operative day, there was no significant difference in the pain experienced by patients in the three groups, mean pain scores being 27.14, 25.74 and 25.94 in groups 1, 2 and 3 respectively, and p values in both treatment groups >0.05. But on 7th postoperative day, as compared to group 1 patients (25.04), significant improvement was present in group 2 patients (20.58; p value=0.001) but not in group 3 patients (23.6; p value=0.252) as shown in Table 2.

Other symptoms

Symptoms in other domains of USSQ i.e., general health index, work performance and global quality of life were calculated on 7th post-operative day only, and were found not to be significantly different among the three groups (Table 2). General health, work performance and global quality of life domains (measured on 7th postoperative day only) did not show statistically significant improvement in either of the treatment group (groups 1 and 2) as compared to control group, ruling out any significant role of medications to prevent these symptoms. Only 72 patients (26, 24 and 22 in groups 1, 2 and 3 respectively) were employed in work, hence statistically tests pertaining to work performance domain were done on these patients only.

Table 1: Baseline patient characteristics in each group.

Characteristics	Group 1	Group 2	Group 3	P value
No. of patients	50	50	50	
Age in years (mean±SD)	45.12±14.65	45.6±14.95	47.6±14.34	0.669
Sex (female/male)	24/26	22/28	21/29	0.828
Side (left/right)	24/26	24/26	24/26	1.000
Site (distal/proximal)	23/27	23/27	23/27	1.000

Table 2: USSQ symptom score comparison irrespective of stent position.

Domain in USSQ	POD	Rx group:symptom-score (mean+S.D.)				
		1	2	P value*	3	P value*
Urinary symptom score (N=50/50/50)	1	24.46±4.621	23.72±4.252	0.407	24.38±5.897	0.94
	7	21.68±4.063	19.40±4.247	0.007	22.36±5.569	0.487
Body pain score (N=50/50/50)	1	27.14±6.728	25.74±6.922	0.308	25.94±6.885	0.38
	7	25.04±6.528	20.58±6.061	0.001	23.60±5.956	0.252
General health index score (N=50/50/50)	7	18.08±3.161	17.26±3.481	0.22	17.28±3.124	0.206
Work performance score (N=26/24/22)	7	6.35±2.134	6.71±1.853	0.526	7.00±2.070	0.289
Global quality of life score (N=50/50/50)	7	4.22±0.465	4.20±0.452	0.828	4.32±0.653	0.38

*P value compared with group 1 by student's t-test

Table 3: Appropriate versus inappropriate stent position in (control) group 1.

Variables	POD**	DJS#=appropriate	DJS=inappropriate	P value*
Urinary symptom score (N=27/23)	1	22.04±3.069	27.3±4.557	0.0001
	7	19.07±1.859	24.74±3.816	0.0001
Body pain score (N=27/23)	1	23.70±6.107	31.17±5.024	0.0001
	7	21.00±4.899	29.78±4.795	0.0001
General health index score (N=27/23)	7	16.33±2.814	20.13±2.18	0.0001
Work performance score (N=16/10)	7	5.31±1.25	8±2.26	0.0006
Global quality of life score (N=27/23)	7	4.11±0.32	4.34±0.572	0.08

Continued.

*P value by student's T-test.

Table 4: USSQ symptom score comparison in the appropriate stent group.

Domain in USSQ	POD**	Rx group: symptom-score (mean+SD)				
		1	2	P value*	3	P value*
Urinary symptom score (N=27/30/32)	1	22.04±3.069	21.80±3.067	0.772	21.41±2.367	0.377
	7	19.07±1.859	16.80±1.808	<0.001	19.34±2.238	0.621
Body pain score (N=27/30/32)	1	23.70±6.107	21.97±4.657	0.23	22.75±4.684	0.500
	7	21.00±4.899	17.00±2.754	<0.001	20.78±3.998	0.851

*P value by student's T-test.

Table 5: USSQ symptom score comparison in the inappropriate stent group.

Domain in USSQ	POD**	Rx group: symptom-score (mean+SD)				
		1	2	P value*	3	P value*
Urinary symptom score (N=23/20/18)	1	27.3±4.557	26.60±4.210	0.603	29.67±6.615	0.184
	7	24.74±3.816	23.30±3.854	0.227	27.72±5.717	0.052
Body pain score (N=23/20/18)	1	31.17±5.024	31.40±5.853	0.892	31.61±6.590	0.811
	7	29.78±4.795	25.95±5.708	0.021	28.61±5.617	0.476

*P value by student's T-test.

Appropriate and inappropriate stent group

On the basis of stent position on post-operative radiograph, patients were classified further into appropriate and inappropriate stent position groups, and similar comparisons done among these two groups, pertaining to urinary and pain symptoms.

In the control group (group 1), 27 patients had appropriate stent position and 23 patients inappropriate stent position. Symptom scores in the appropriate stent position group were significantly lesser (p value~0.0001) as compared to inappropriate stent position group, in all domains except for global quality of life score (p value~0.08) as depicted in Table 3. Such strong association strengthens the independent role of stent position in stent related symptoms, irrespective of medications.

Appropriate stent group

In the appropriate stent group, a very significant level of symptom improvement in urinary and body pain symptoms was found on 7th post-operative day but not on 1st postoperative day; urinary and pain scores in group 1 (respectively 21.8 and 21.97) as compared to group 2 (respectively 16.8 and 17; p values <0.001), whereas no such significant improvement was observed in group 3 patients on either 1st (21.41 and 22.75; p values 0.377 and 0.500) or 7th (19.34 and 20.78; p values 0.621 and 0.851) postoperative days. This proves the beneficial effect of α-blocker alone (without anticholinergic) in providing symptom improvement in patients with appropriate stent position (Table 4).

Inappropriate stent group

Patients with inappropriately positioned stents had significant improvement with alpha blockers only in pain symptoms on 7th postoperative day (p value=0.021), but not in urinary symptoms (Table 5).

Only 6 patients (2 each in groups 1, 2 and 3) had sexual intercourse during the period of indwelling stent, hence sexual symptoms were not statistically analyzed, though score in appropriate stent group (5) was less than inappropriate stent group (6). Additional problems (e.g. urinary tract infections, repeated hospital visits) were experienced only in 18 patients, out of which 16 had inappropriate stent position on postoperative radiograph. Groups 1, 2 and 3 had 7, 6 and 5 such patients, respectively, indicating the probable role of stent position and no effect of medication in these additional symptoms.

DISCUSSION

During the past 3 decades, the incidence of colorectal cancer was at a low level in urban and rural populations in India, in comparison with figures observed in developed countries of North America and Europe.[6] Significant advances have been made in the study of colorectal cancer during the last few years. A more thorough understanding of the molecular basis for this disease, coupled with the development of new therapeutic approaches, has dramatically altered the way in which patients are managed.[7] We are in a unique electronic age with access to a plethora of sources of medical information, so the vehicles we use to keep up-to-date must change as well, and this text is no different.[8] In this study patients were below 30 years of age, the incidence rise with advancing age, maximum between 40-60 years of age.[14] There were slight male predominance, 54.28% patients were male and 45.71% were females. The lifetime risk for colorectal cancer is 1 in 18 for men and 1 in 28 for women, but its occurrence under 50 years of age is very low.[9]

The common site of malignancy in the present study is in rectum, and the commonest symptom in our study was bleeding per rectum. Carcinoma of the colon, particularly the right colon, is more common in women, and carcinoma of the rectum is more common in men.[10] 70% of patients of the colorectal malignancies were diagnosed clinically by digital P/R examination and proctosigmoidoscopy.

This is confirmed by biopsy and histopathological examination. Other investigations were barium enema, USG abdomen, CT scan, CEA and X-ray chest. Lymph node metastasis (17.14 %) was better diagnosed on CT scan. MRI may be useful for this purpose as well. PET/CT scans are useful for detecting recurrences and metastatic disease but are probably not necessary as part of the routine initial evaluation.[11] Patients with Dukes A stage did not receive postoperative chemotherapy and were advised regular follow up. 38 patients received post-operative chemotherapy. 18 patients were given radiotherapy. New evidence suggests a role for anti-inflammatory drugs in the treatment and prevention of colon and rectal cancers.[14]

Out of 70 patients over all follow-up of 42 patients (60%) was done. 6 patients died after surgery due to metastatic disease, other were free of disease. Current recommendations are: CEA every 2 months for 2 years then every 4 months for 2 years then annually, colonoscopy within the first 2-3 months then annually, LFTs every 3 months for 2 years then every 6 months for 2 years then annually and CXR every 6 months for 3 years then annually.[15] Limitations of this study were stage in case of colorectal malignancies, the stage wise distribution of the disease (in percentage) observed by other authors is shown.

Limitations

The limitation of this study was being a single-centered study. A multicentered study would have given better representation of the findings noted here. In the future, we hope to do a muti-centered study to affirm our findings.

CONCLUSION

The position of ureteral stent after ureteroscopic lithotripsy is the most important independent factor (more important than use of medications) in preventing stent-related symptoms. Addition of α-blocker tamsulosin 0.4 mg daily for the period of indwelling stent has a superadded beneficial role in preventing stent-related symptoms in patients with appropriate stent position.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Zimskind PD, Fetter TR, Wilkerson JL. Clinical use of long-term indwelling silicone rubber ureteral splints inserted cistoscopically. J Urol. 1967;97:840-4.
2. Sighinolfi MC, Micali S, De Stefani S, Mofferdin A, Grande M, Giacometti M, et al. Indwelling ureteral stents and sexual health: a prospective, multivariate analysis. J Urol. 2007;178:229.
3. Irani J, Siquier J, Pirès C, Lefebvre O, Doré B, Aubert J. Symptom characteristics and the development of tolerance with time in patients with indwelling double-pigtail ureteric stents. BJU Int. 1999;84:276.
4. Joshi HB, Stainthorpe A, MacDonagh RP, Keeley FX Jr, Timoney AG, Barry MJ. Indwelling ureteral stents: evaluation of symptoms, quality of life and utility. J Urol. 2003;169:1065-9.
5. Ho CH, Chen SC, Chung SD. Determining the appropriate length of a double pigtail ureteral stent by both stent configurations and related symptoms. J Endourol. 2008;22:1427.
6. Damiano R, Autorino R, De Sio M Giacobbe A, Palumbo IM, D'Armiento M, et al. Effect of tamsulosin in preventing ureteral stent-related morbidity: a prospective study. J Endourol. 2008;22:651.
7. Norris RD, Sur RL, Springhart WP, Marguet CG, Mathias BJ, Pietrow PK, et al. A prospective, randomized, double-blinded placebo-controlled comparison of extended release oxybutynin versus phenazopyridine for the management of postoperative ureteral stent discomfort. Urology. 2008;71:792.
8. Beiko DT, Watterson JD, Knudsen BE, Nott L, Pautler SE, Brock GB, et al. Double-blind randomized controlled trial assessing the safety and efficacy of intravesical agents for ureteral stent symptoms after extracorporeal shockwave lithotripsy. J Endourol. 2004;18:723.
9. Gupta M, Patel T, Xavier K, Maruffo F, Lehman D, Walsh R, et al. Prospective randomized evaluation of periureteral botulinum toxin type A injection for ureteral stent pain reduction. J Urol. 2010;183:598-602.
10. Deliveliotis C, Chrisofos M, Gougousis E, Papatsoris A, Dellis A, Varkarakis IM, et al. Is there a role for alpha1-blockers in treating Double-J stent-related symptoms? Urology. 2006;67:35.
11. Joshi HB, Newns N, Stainthorpe A, MacDonagh RP, Keeley FX Jr, Timoney AG. Ureteral stent symptom questionnaire: development and validation of a multidimensional quality of life measure. J Urol. 2003;169:1060-4.
12. Pilcher JM, Patel U. Choosing the correct length of ureteric stent: a formula based on the patient's height compared with direct ureteric measurement. Clin Radiol. 2002;57:59-62.
13. 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;23:1913-7.
14. Lee YJ, Huang KH, Yang HJ, Chang HC, Chen J, Yang TK, et al. Solifenacin improves double-J stent-related symptoms in both genders following uncomplicated ureteroscopic lithotripsy. Urolithiasis. 2013;41:247-52.
15. 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;67:35-9.
16. 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;181:170-6.
17. 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;22:651-5.
18. Norris RD, Sur RL, Springhart WP, Marguet CG, Mathias BJ, Pietrow PK, et al. A Prospective, Randomized, Double-blinded, placebo-controlled comparison of extended release oxybutynin versus phenazopyridine for the management of postoperative ureteral stent discomfort. Urology. 2008;71:792.
19. Lumiaho J, Heino A, Tunninen V, Ala-Opas M, Talja M, Välimaa T, et al. New bioabsorbable polylactide ureteral stent in the treatment of ureteral lesions: an experimental study. J Endourol. 1999;13:107-12.
20. 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;51:636-41.

Cite this article as: Agbo CA, Nahar G. Randomized controlled trial comparing the effectiveness of tamsulosin, tamsulosin with tolterodine and double J stent position in controlling stent related symptoms after ureteroscopic lithotripsy. Int Surg J 2024;11:26-30.