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Original Article

Surgery Section

Incidence of UTI and Stent-related Symptoms in Patients with Peri-interventional Antibiotic Prophylaxis Only vs Low-dose Continuous Antibiotic Treatment among Double J Stented Patients: A Randomised Clinical Trial

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ABSTRACT

Introduction: Endourological surgeries like Percutaneous Nephrolithotripsy (PCNL) and Ureteroscopic Lithotripsy (URSL) is the standard of care for upper urinary tract urolithiasis. Placement of Double J stent (DJ stent) is a routine practice, following these surgical interventions. Though endourological surgeries are less invasive, these are not without complications. Main postoperative complications following these procedures, which hamper daily activities are Urinary Tract Infection (UTI) and Stent Related Symptoms (SRS). There is a lack of literature, about appropriate postoperative antibiotic strategy following uncomplicated endourological surgery for upper urinary tract stone disease in patients, who are on DJ stent.

Aim: To evaluate the incidence of UTI and SRS in patients given, a peri-interventional antibiotic prophylaxis only versus a continuous low-dose antibiotic treatment for entire stent indwelling time.

Materials and Methods: This was a randomised clinical study conducted in the Department of Urology, SDM Medical College and Hospital, Dharwad, Karnataka, India from january 2020-march 2021. A total of 70 patients following uncomplicated endourological surgery were randomised, to either receive peri-interventional antibiotic prophylaxis only (group A=31) or low-dose antibiotic treatment for entire stent indwelling time (group B=39). Randomisation was done to allocate sample into two groups using computer randomisation program. All patients received cefotaxime injection 1 gm at the time of anaesthesia induction as peri intervention prophylaxis. Patients in group B, in addition received nitrofurantoine 100 mg tablet at bedtime for entire stent indwelling time. Patients were evaluated for incidence of UTI and SRSs. Statistical analysis was done using Chi-square and Yates corrected Chi-square for analysis of association between attributes. Independent t-test was used for comparison of two groups with numerical variables.

Results: The incidence of UTI was not significantly different between the two groups {group A- 4 (12.9%) and group B- 6 (15.38%)}. UTI was more common following URSL compared to PCNL {group A 24 (77.42%) and group B 29 (74.36%)}, and more common in those with diabetes mellitus. Similarly the incidence and severity of SRSs was very similar in both the groups {group A 28 (90.32%) and group B 37 (94.87%)}.

Conclusion: According to the present study findings, continuous low-dose antibiotic treatment during entire stent indwelling time does not reduce the incidence of UTI and has no effect on SRSs.

Keywords: Antimicrobial prophylaxis, Endourological surgery, Percutaneous nephrolithotripsy, Urinary tract infection

INTRODUCTION

The surgical treatment of upper urinary tract urolithiasis has become less invasive with the development of various endoscopes and lithotripsy machines. Endourological surgeries like, Percutaneous Nephrolithotripsy (PCNL) and Ureteroscopic Lithotripsy (URSL) are now the standard of care for upper urinary tract urolithiasis. Placement of Double J stent (DJ stent) is a routine practice, following these surgical interventions for upper urinary tract stone disease to prevent post operative ureteral obstruction due to oedema, blood clots or stone fragments. Though, endourological surgeries are less invasive, they are not without complications. UTIs and SRSs are the most common postoperative complications following these endourological procedures [1].

These therapeutic upper urinary tract endoscopic procedures have increased the risk of localised and systemic infections, compared to simple diagnostic cystoscopy because of several factors, including increased trauma to the mucosa, increased duration and/or degree of difficulty of most endoscopic procedures, increased pressure of irrigating fluid used in these procedures and manipulation of infected materials like fragmentation of stone [2]. The primary factor leading to UTI is attributed to introduction of bacteria into the urinary tract upon insertion of surgical instruments. Any intravasation of bacteria or endotoxins into the blood stream may lead to urosepsis, a potentially lethal complication. These infections carry significant morbidity and increased healthcare expenditures. Various studies, have reported a rate of UTI following uncomplicated endourological surgeries for upper urinary tract urolithiasis, ranging from 2-34% [3,4]. Risk factors for UTI following these procedures include advanced age, poor nutrition, anatomical anomalies of urinary tract, diabetic mellitus, chronic renal failure, female sex and chronic corticosteroid usage. Additional indwelling hardware like DJ stent, infected endogenous materials like stones, distant infectious sites, and prolonged hospitalisation also increase the risk of infectious complications. Surface of the indwelling stent forms an ideal environment for biofilm formation, bacterial colonisation and antibacterial resistance. This might lead to increased risk of UTI in postoperative period [5].

SRS like dysuria, haematuria, flank pain, increased urinary frequency are very common following stent placement and can impair daily activities, sexual function and work capacity. Various factors have been proposed for SRSs but most important one's are irritation of the bladder mucosa, especially the trigone by the bladder coil of

the stent, smooth muscle spasm, reflux of the urine during voiding and UTI due to bacterial overgrowth on the surface of the stent. Symptoms due to stent are very similar to symptoms of UTI [6].

European Association of Urology (EAU) recommends, simple peri-interventional antibiotic prophylaxis to prevent UTI. For most procedures, prophylaxis should be initiated between 30 to 120 minutes before the procedure. Efficacious levels should be maintained for the duration of the procedure and, in special circumstances, a limited time (24 hours at most) after the procedure. The type of procedure also helps to direct the timing, duration, and spectrum of antimicrobial prophylaxis needed [7,8]. Most guidelines suggest prophylaxis lasting less than 24 hours with either a fluoroquinolone or trimethoprim-sulpamethoxazole for therapeutic endourological procedures [9,10]. However, there is lack of data about the exact antibiotic strategy for entire stent indwelling time. Many clinicians, give a continuous low-dose antibiotic treatment for entire stent indwelling time to prevent UTI and also possibly to obtain a positive effect on SRS [11]. Non scientific and unproven use of antibiotics, results in antimicrobial resistance which is an important healthcare problem, and also long-term antibiotic treatment might result in unnecessary drug-related side-effects which adversely affect the quality of life [12]. With this background, the present study was conducted with the primary objective, to see the difference in incidence of UTI between two groups and secondary objectives were; to evaluate incidence and severity of SRSs in both the groups and also to note associated drug-related side-effects, in those treated with a continuous low-dose antibiotic treatment for entire stent indwelling time.

MATERIALS AND METHODS

This was a randomised clinical trial, conducted in Department of Urology, SDM Medical College and Hospital, Dharwad, Karnataka, India from January 2020 to March 2021. Patients who had undergone procedures for upper urinary tract calculus disease, like PCNL with DJ stenting and URSL with DJ stenting during the stated period of duration were evaluated in the study. Informed written consent was taken from all the participants. Ethical clearance was taken from Institutional Ethical Committee (SDMIEC2020/134). CTRI registry number (CTRI/2022/01/039389).

Inclusion criteria: Sterile urine culture prior to procedure, complete stone clearance, no fever or antibiotic treatment within past two weeks of procedure.

Exclusion criteria: Incomplete stone clearance, active UTI prior to intervention, recent antibiotic treatment within past two weeks.

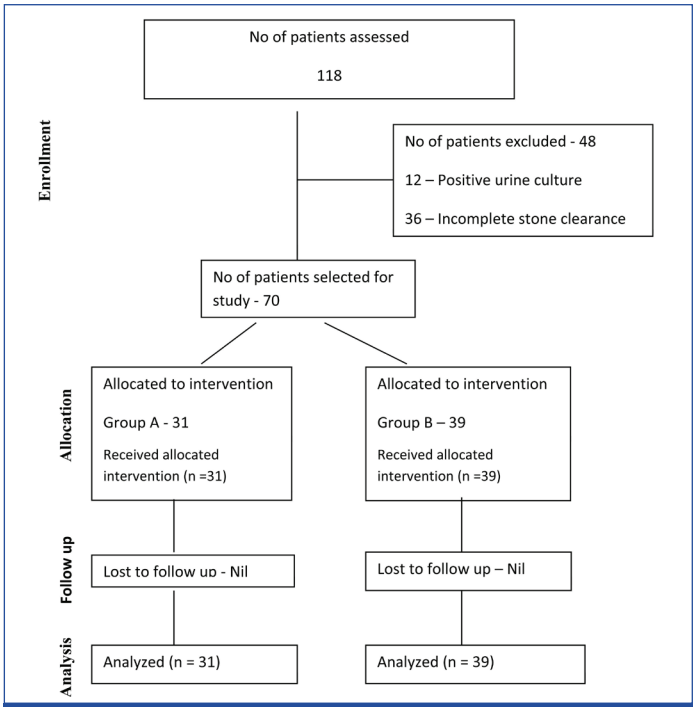
Study Procedure

Baseline evaluation: All patients were evaluated with thorough medical history, physical examination, blood chemistry test, midstream urine sample analysis and culture. All patients received peri-interventional antibiotic prophylaxis that is intravenous cefotaxime 1 gm at the time of anaesthesia induction. Patients were randomised into 2 groups using computer randomization program.

- Group A- No antibiotic treatment from the time of discharge up to removal of the stent.
- Group B- Low-dose continuous antibiotic treatment for entire stent indwelling time, that is nitrofurantoine tablet 100 mg at bedtime from the time of discharge up to removal of stent.

A total of 118 patients were evaluated, out of which 70 patients were selected according to inclusion criteria. 48 patients were excluded, out of which 12 patients had positive urine culture prior to surgery and 36 patients had incomplete stone clearance [Table/Fig-1].

Follow-up evaluation: Patients were evaluated at 1, 2 and 4 weeks for SRS and urine culture evaluation. Clinical symptoms of UTI and SRS are very similar, therefore positive urine culture was used to distinguish UTI from SRS. Clinical symptoms with positive urine culture were considered UTI, and clinical symptoms with negative urine culture were considered as symptoms related to stent in-situ. The primary objective was to determine the prevalence of UTI and secondary objective were SRS and drug side-effects. Any patients with symptomatic UTI were given full dose antibiotic treatment according to antibiotic resistance pattern. Drug side-effects were also evaluated like gastrointestinal symptoms and cough.



[Table/Fig-1]: CONSORT flowchart showing recruitment of participants.

STATISTICAL ANALYSIS

Descriptive statistics was analysed with frequency, percentage, mean, standard deviation, and median of variables. Chi-square and Yates corrected Chi-square was used for analysis of association between attributes. Independent t-test was used for comparison of two groups with numerical variables. The statistical significance was set at 5% level of significance ($p<0.05$). The Statistical Package for Social Sciences (SPSS) version 20.0 was used for analysis.

RESULTS

Mean age in both the groups were similar (group A-44.71±13.89 years, group B-44.33±15.14) years. URSL was the most commonly performed procedure in both the groups {group A 24 (77.42%) and group B 29 (74.36%)}. Co-morbidity like diabetic mellitus was evenly distributed in both the groups (38.71% in group A and 43.59% in group B) with insignificant p-value [Table/Fig-2].

Variables	Group A (n=31)	Group B (n=39)	Total (N=70)	Test values	p-value
Age in years					
Mean±SD	44.71±13.89	44.33±15.14	44.50±14.50	t=0.1071	0.9150
Median (range)	42 (20-70)	42 (18-79)	42 (18-79)		
Sex					
Male	21 (67.74%)	28 (71.79%)	49 (70%)	χ^2=0.1350	0.7130
Female	10 (32.25%)	11 (28.21%)	21 (30%)		
Procedures					
PCNL	7 (22.58%)	10 (25.64%)	17 (24.28%)	χ^2=0.0884	0.7670
URSL	24 (77.42%)	29 (74.36%)	53 (75.71%)		
DM					
Present	12 (38.71%)	17 (43.59%)	29 (41.42%)	χ^2=0.1702	0.6810
Absent	19 (61.29%)	22 (56.41%)	41 (58.57%)		

[Table/Fig-2]: Group specific demographic profiles of the patients.
PCNL- Percutaneous nephrolithotripsy, URSL- Ureteroscopic lithotripsy, DM- diabetic mellitus

Overall incidence of UTI in the present study was 14.28%. Incidence of UTI in group A was 12.9% (4 out of 31 patients) and in group B was 15.38% (6 out of 39 patients), which was statistically insignificant (p-value of 0.7680). Majority of patients with UTI were females in both the groups, group A 3 out of 4 patients and 4 out of 6 patients in group B. It was observed that 3 out of 4 patients in group A and 2 out of 6 patients in group B were diabetic. URSL was commonly performed procedure in those with UTI in both the groups (group A- 4 out of 4 patients, group B- 5 out of 6 patients). Majority of patients developed UTI in second week following the procedures (3 out of 4 in group A and 4 out of 6 patients in group B). But none of these values were statistically significant [Table/Fig-3].

Patients characteristics	Group A	Group B	Total	Test values	p-value
Number of patients with UTI	4 (12.90%)	6 (15.38%)	10 (14.28%)	χ^2=0.0870	0.7680
1st week	1	2	3	Yates χ^2=0.0000	1.0000
2nd week	3	4	7	Yates χ^2=0.0000	1.0000
4th week	0	0	0	-	-
UTI associated with DM	3	2	5	Yates χ^2=0.1852	0.6670
URSL/ PCNL	4/0	5/1	9/1	Yates χ^2=0.0000	1.0000
Male/Female	1/3	2/4	3/7	Yates χ^2=0.0000	1.0000

[Table/Fig-3]: Patients specific characteristics in those with UTI.
PCNL- Percutaneous nephrolithotripsy, URSL- Ureteroscopic lithotripsy

Most of the patients in both the groups had some form of SRS (90.32% in group A and 94.87% in group B) but the difference was not statistically significant. Frequency of micturation and pain were the most common symptom (74.19% and 54.8% in group A and 74.36% and 33.3% in group B) [Table/Fig-4]. In those patients who were treated with low-dose continuous antibiotics, 12 patients had mild gastrointestinal symptoms like epigastric discomfort, and symptoms of acid peptic disease at 2nd and 3rd week of follow-up. They were treated with proton pump inhibitors.

Stent related symptoms	Group A	Group B	Total	Test values	p-value
Number of patients with SRS	28 (90.32%)	37 (94.87%)	65	Yates χ^2=0.0710	0.7900
Frequency of micturition	23 (74.19%)	29 (74.36%)	52	χ^2=0.0194	0.8910
Nocturia	7 (22.58%)	9 (23.08%)	16	χ^2=0.0020	0.9610
Urgency	6 (19.35%)	3 (7.69%)	9	Yates χ^2=1.1850	0.2760
Pain	17 (54.84%)	13 (33.33%)	30	χ^2=3.2620	0.0710
DM	12 (38.71%)	17 (43.59%)	29	χ^2=0.1700	0.6810
Male/Female	20/8	27/10	47/18	χ^2=0.0190	0.8900

[Table/Fig-4]: Comparison of SRS in two groups.

DISCUSSION

Development of modern endourological equipments has revolutionised the management of upper urinary tract urolithiasis. UTI is a known complication following surgical treatment for upper urinary tract stone disease. Infectious complications might vary in severity, ranging from febrile cystitis to severe pyelonephritis and urosepsis [13,14].

Surgical antimicrobial prophylaxis is essential, however there is lack of data about exact antibiotic strategy for entire stent indwelling time. To lower the incidence of UTI, it is common practice among urologist to give continuous low-dose antibiotic treatment for entire stent indwelling time [15,16]. However long-term antimicrobial treatment is not without morbidity, it increases rate of bacterial drug resistance, increases overall healthcare cost and drug side-effects like allergic reaction, rashes, gastric disturbances [17-19].

Overall incidence of UTI in the present study was 14.28% . It was 15.38% in those who were treated with continuous low-dose antibiotic for entire stent indwelling time i.e group B and 12.9% in those with only peri-interventional antibiotic prophylaxis i.e group A. Similar results were seen by Moltzahn F et al., i.e. 9 % in those who were given with low-dose antibiotic treatment versus 10.8% in those without antibiotic treatment [20]. In the present study there was no increased incidence of UTI in those patients who were treated with peri-interventional antibiotic prophylaxis only. Consistent with other reports by Kumar M, Sanchit R et al., [21], this study also found women to be at higher risk of developing UTI (3 in group A and 4 in group B). This finding was irrespective of antibiotic strategy. UTI was more common in patients with Diabetes mellitus (3 out of 4 patients in group A and 2 out of 6 patients in group B). UTI was more common following URSL compared to PCNL in both the groups (4 out of 4 in group A and 5 out of 6 in group B), one possible explanation could be due to better outflow fluid drainage in PCNL compared to URSL which prevents increased fluid pressure within the pelvicalyceal system. Majority of the patients developed UTI in the 2nd week following the surgical intervention in both the groups (3 out of 4 in group A and 4 out of 6 in group B).

Majority of patients on DJ stent will have SRSs. Various factors have been proposed for SRSs but most important ones are irritation of the bladder mucosa, especially the trigone, by the bladder coil of the stent, smooth muscle spasm, reflux of the urine during voiding and UTI due to bacterial overgrowth on the surface of the stent. Frequency, nocturia and urgency of micturition are caused by mechanical stimulation of bladder mucosa by the bladder coil of the stent, dysuria and flank pain are usually experienced at the end of voiding. Dysuria is considered to be result of trigonal irritation by the bladder coil when it crosses the midline or forms an incomplete loop. Flank pain is related to movement of the DJ stent in the ureter and associated ureteral spasm and stretching of renal capsule due to retrograde urine reflux during voiding. However, all these symptoms can also be caused due to UTI. Hence, it is common belief among Urologist, that low-dose continuous antibiotic treatment reduces incidence of UTI along with SRSs [22]. However, in the present study SRSs were very common in both the groups (90.32% in group A and 94.87% in group B). Continuous low-dose antibiotic treatment had no effect on rate of SRSs, nor on the spectrum of symptoms. Similar finding was noted in study conducted by Anup D et al [23]. Frequency and pain were most common symptoms in both the groups, followed by nocturia and urgency. No major drug related side-effects were noted in those treated with continuous low-dose antimicrobial, however 12 out of 39 patients in group B had mild gastrointestinal side-effects.

This study suggests that there is no added advantage of giving long-term antimicrobial agents for entire stent indwelling time. Proper choice of antibiotics for prophylaxis and also the duration of treatment must be included and updated in various medical guidelines.

Limitation(s)

The present study was limited by its small sample size.

CONCLUSION(S)

The study showed that continuous low-dose antibiotic treatment during entire stent indwelling time, following uncomplicated endourological treatment for upper urinary tract urolithiasis, did not reduce incidence of UTI and it also had no effect on SRSs, continuous antibiotic treatment did not have any effect on incidence or severity of SRS. Unnecessary long-term antibiotics will lead to drug resistant bacteria, increase in treatment cost and sometimes undesirable drug related side-effects which might impair work capacity. Proper effort should be made to ensure one is familiar

with local antibiogram and accordingly choose an appropriate preoperative antibiotic.

REFERENCES

[1] Saltzman B. Ureteral stents, Indications, variations, and complications. Urol clin North Am. 1988;15(3):481-91.
[2] Joshi HB, Newns N, Stainthorpe A, Keeley. Ureteral stent symptom questionnaire: Development and validation of multidimensional quality of life measure. J Urology. 2003;169(3):1060-64.
[3] Klis R, Korczak E, Denys A, Rozanski W. Relationship between UTI and dj stent colonization. J Endourology. 2009;23(6):1015-19.
[4] Akay AF, Aflay, Gedik A, Sahin H. Risk factors for lower urinary tract infection and bacterial stent colonization in patients with double J stent. Int Urol Nephrol. 2007;39:95-98.
[5] Ozgur BC, Ekici M, Yuceturk CN, Bayrak O. Bacterial colonization of double J stents and bacterial frequency. Kaohsiung J med Sci. 2013;29(12):658-661.
[6] Miyaoka R, Monga M. Ureteral stent discomfort: Etiology and management. Indian J Urol. 2009;25(4):455-60.
[7] Grabe M, Bjerklund-Johansen TE. EAU Guidelines, edition presented at the 25th EAU annual congress, Barcelona 2010. ISBN 978-90-79754-70-0.
[8] Grabe M. The effect of a short antimicrobial course in TURP. Scand J Urol Nephrol. 1984;18:37-42.
[9] Fischbach MA, Walsh CT. Antibiotics for emerging pathogen. Science 2009;325(5944):1089-93.
[10] Olsen JH, FM Alice, KJ Søren, K Bent, H Valdemar. Cefotaxime for prevention of infectious complications in bacteriuric men undergoing TURP. A controlled comparison with methenamine. Scand J urol Nephrol. 1983.17(3):299-301.
[11] Kutlu SS, Z Aybek, Tekin K, Okke D, Akalin S, Altintas S, et al. Is short course of antimicrobial therapy for asymptomatic bacteriuria before urological surgical procedures sufficient? J infect Dev Ctries. 2012;6(2):143-47.
[12] Tenke P, Kovacsa B, Johansenb TE, Matsumotoc T, Tambyahd PA, Nabere KG. European and Asian guidelines on management and prevention of catheter associated urinary tract infection. Int J Antimicrob Agents. 2008;31(1);68-78. suppl 1:s68.
[13] Chen L, Xu QQ, Li JX, Xiong LL, Wang XF, Huang XB. Systemic inflammatory response syndrome after Percutaneous nephrolithotomy: AN assessment of risk factors. Int J Urology. 2008;15(12):1025-28.
[14] Wolf JS, Bennett CJ, Dmochowski RR, Hollenbeck BK, Pearle MS, Schaeffer AJ. Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol. 2008;179(4):1379-90.
[15] Chew BH, Flannigan R, Kurtz M, Gershman B, Arsovska O, Paterson RF, et al. A single dose of Intraoperative antibiotics is sufficient to prevent urinary tract infection during ureteroscopy. J Endourol. 2016;30(1):63-68.
[16] Leaper D, Burman Roy S, Palanca A, Cullen K, Worster D, et al. Prevention and treatment of surgical site infection: Summary of NICE guidance. BMJ. 2008;337:a1924.
[17] Ramaswamy K, Shah O. Antibiotic prophylaxis after uncomplicated Ureteroscopic stone treatment: is there a difference? J Endourol. 2012;26(2):122-25.
[18] Grabe M. Controversies in antibiotic prophylaxis in urology. Int J Antimicrob Agents. 2004;1:S17-23.
[19] Silver S, Laura B, Andrew E. Positive urine cultures: A major cause of inappropriate antimicrobial use in hospitals? Can J infect Diseas Med Microbiol. 2009;20(4):107-11.
[20] Moltzahn F, Katharina H, Frederic D, Roth B, Thalmann GN, Zehnder P. Peri-interventional antibiotic prophylaxis only Vs continuous low dose antibiotic treatment in patients with JJ stent: A prospective randomised trial analyzing the effect on UTI and SRS. BJU. 2013;111(2):289-295.
[21] Kumar M, Sanchit R, Rahul J, Singh U, Ansari M, Srivastava A, et al. A prospective randomized study to define the role of low dose continuous prophylactic antibiotics and anti-adherence agents in altering the microbial colonization related to indwelling double j stent. Asian Journal of Urology. 2021;8(3):269-74.
[22] Joshi HB, Newns N, Stainthorpe A, MacDonagh RP, Kelley FX, Timoney AG. Ureteral stent symptom questionnaire: Development and validation of multidimensional quality of life measure. J Urology. 2003;169(3):1060-64.
[23] Anup D, VS Kundargi, SB Patil, Ranka K, Patil N. Continuous low dose antibiotic prophylaxis versus no antibiotics with respect to urinary tract infection and biofilm formation in the patients with double-j stents: A prospective randomized study International Journal of Surgery Science. 2019;3(3):194-197.

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