

Original Research Article

Effect of tamsulosin on ureteric stent related morbidity: a double-blind randomized placebo-controlled study

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ABSTRACT

Background: Post ureteral stenting, symptoms occurs of lower urinary tract which impact quality of life in around 80% of patients, urgency, frequency, dysuria, suprapubic pain, hematuria. α 1-Adrenoceptors are found in highest density in the distal ureter. α 1-Adrenoceptor antagonists dilates the lumen of the ureter and reduces the spasms by decreasing the peristaltic frequency and inhibiting basal tone of the ureter, leading to improvement in stent-related symptoms. This study was conducted to study effect of tamsulosin, a selective α 1A- and α 1D-adrenoceptor antagonist in relieving ureteric stent related symptoms

Methods: A randomized double blinded placebo-controlled study conducted from February 2019 to August 2020 in Department of Surgery SGRD University, Amritsar. We enrolled 60 patients with each group of 30 patients (Group A placebo and Group B Tamsulosin 0.4 mg). IPSS (irritative and obstructive), quality of life (QoL) and visual analog scale (VAS) pain score were calculated based on post-operative day one versus at Stent removal day (Post-operative day 21) at 3 weeks observations. analysis was done using Statistical package for social sciences (SPSS) version 23.0. Student 't' test (unpaired) and Chi-square test.

Results: IPSS, QoL and VAS showed improvement with significant relieve of symptoms in patients on tamsulosin compared to placebo at time of stent removal.

Conclusions: The study concluded that administration of tamsulosin a selective α 1-blocker is useful in decreasing lower urinary tract symptoms in patients undergoing ureteral stenting.

Keywords: Ureteral stent, Tamsulosin, Stent syndrome

INTRODUCTION

The prevalence of urolithiasis in Indian Population has been 1-5% with variations due to socioeconomic status and geographic locations.¹

The first endoluminal stent was placed in 1967 by Zimskind et al.² For the advantages like prevention of urinary tract obstruction, drainage of urine, healing of ureteral mucosa and dilatation of ureter leading to passage

of small size ureteric stone.³ It is becoming a routine practice in urology to place a indwelling ureteral stent.

Despite its effectiveness and large scale usage in urological procedures, ureteral stents has been found to cause stent syndrome.⁴ Stent syndrome is common complication which consists low urinary tract symptoms (LUTS) such as frequency (50–60%), urgency (57-60%), dysuria (40%), incomplete emptying (76%) flank pain (19-32%), suprapubic pain (30%), in continence and hematuria

(25%), impacting quality of life in around 80 % of patients.⁵

Even after various studies and trials owing to conflicting theories of its exact cause and mechanism. Studies done so far has attributed stent syndrome to presence of distal end of stent lying in bladder causing irritation of trigonal bladder mucosa, smooth muscle spasm, inflammatory reaction of ureter and bladder or combination of all.

For post double j stent related LUTS symptoms pharmacological treatment has been area of focus which minimizes motor and sensory response to presence of stent.

α 1-Adrenoceptors are found, with highest density in the distal ureter. α 1-Adrenoceptor antagonists dilates the lumen of the ureter and reduces the spasms by decreasing the peristaltic frequency and inhibiting the basal tone of the ureter, which may lead to improvement in stent-related symptoms.

With the use of molecular technology three α 1 ARs (α 1a, α 1b, and α 1d) have been pharmacologically characterised. Since the alpha 1a AR subtype predominates in the prostate smooth muscle and the proximal urethra, this subtype is presumed to be responsible for the dynamic obstruction portion and the resulting voiding symptoms.

Tamsulosin is a selective α 1A- and α 1D-adrenoceptor antagonist, causing relaxation of the smooth muscles in the prostate, bladder neck and distal ureter which decreases bladder outlet resistance and voiding pressure, with beneficial effect on urinary stent symptoms.⁷

This study done to evaluate effect of tamsulosin when compared to placebo in relieving ureteric stent related morbidity.

Aim

To study ureteral stent morbidity. To compare the effect of tamsulosin with placebo in patients undergoing ureteral stenting.

METHODS

After institutional ethical committee clearance, a randomized double blinded placebo study conducted from February 2019 to August 2020 at Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar. A total of 60 patients were enrolled in this study with 30 patients in Group A (placebo) and 30 patients in group B (Tamsulosin 0.4 mg). For all patients, history taking and clinical examination were done. Laboratory investigations and radiological imaging including intravenous urography (IVU) or Computed Tomography (CT) were used in evaluation of the patients who were presenting with ureteral stone.

Inclusion criteria

Patients undergoing uncomplicated ureteric lithotripsy for ureteric calculi.

Exclusion criteria

Patients with growth in Urine culture or having symptomatic urinary tract infection. Patients who may need bilateral stent insertion for acute obstruction / obstructive uropathy. Male patients with history of prostatic enlargement, prostatitis or obstruction related to malignancy. History of chronic or recent α -blocker or analgesic drug use, pregnancy, bleeding disorders. Patients who underwent open surgery for ureteric calculi previously.

Patients were randomized by alternatively allotting each patient during study period into group A (n:30) and group B (n:30). It was double blinded as both patients and junior resident doctor giving the drug were completely unaware of contents of pack which were given to patients.

Group A comprised of patients who received tablet Cefpodoxime 200 mg twice daily and tablet Diclofenac 100 mg twice daily for seven days and tablet Placebo for 21 days.

Group B comprised of patients who received Cefpodoxime 200 mg twice daily and tablet Diclofenac 100 mg twice daily for seven days and tablet Tamsulosin 0.4 mg once daily for 3 weeks (21 days).

Questionnaire based on IPSS Scores, Quality of Life (QOL) and Visual Analog Pain Scale was filled on Post-operative day one after stent insertion and than on 21st day at stent removal. IPSS scores were divided into four obstructive IPSS (incomplete emptying, intermittency, weak stream, straining), and three irritative IPSS scores (frequency, urgency, nocturia). This division is to evaluate each sub-score alone to determine which part of IPSS is the most affected in this trial. These scores were compared of both groups (Placebo and Tamsulosin).

Sample size calculation

Assumptions

Precision = 5.00 %

Prevalence = 4.00 %

Population size = infinite

95% Confidence Interval specified limits [0%-9%]

(These limits equal prevalence plus or minus precision)
estimated sample size: n = 60

95% Binomial exact confidence interval with n=60 and n *prevalence=2 observed events: [0.406263%-11.5281%]

Statistical method was done using statistical package for social sciences (SPSS) version 23.0. Student 't' test (unpaired) and Chi-square test. P values less than 0.05 are considered statistically significant.

Ethical clearance from Institutional Ethical Committee of Sri Guru Ram Das University of Health sciences.

RESULTS

In a Group A the mean age of patients is 49.57 years with 2 (6.67%) below 30 years, 5 (16.67%) 31-40 years, 8 (26.67%) 41-50 years, 11 (36.67%) 51-60 years and 4 (13.33%) above 60 years of age. In group B the mean age of patients is 45.53 years with 4 (13.33%) below 30 years,

7 (23.33%) 31-40 years, 7 (23.33%) 41-50 years, 8 (26.27%) 51-60 years and 4 (13.33%) above 60 years of age.

IPSS score at baseline i.e. post-operative day 1 the mean score of Group A was 7.70 (SD 2.336) and Group B was Mean 7.93 (SD 1.818) with p value 0.668, indicating not much difference at baseline. At stent removal IPSS in group A had mean 13.40 (SD 2.027) and Group B had mean 5.00 (SD 0.643) with P value 0.001, indicating significant statistical difference in IPSS score in between both groups at stent removal.

Irritative score at baseline the mean score of Group A was 3.23 (SD 1.040) and Group B was Mean 3.53 (SD 1.008) with p value 0.261, indicating not much statistical difference between two groups at baseline.

Table 1: Age distribution.

Age group (years)	Group A		Group B		Total	
	No.	%	No.	%age	No.	%
<30	2	6.67	4	13.33	6	10.00
31-40	5	16.67	7	23.33	12	20.00
41-50	8	26.67	7	23.33	15	25.00
51-60	11	36.67	8	26.67	19	31.67
>60	4	13.33	4	13.33	8	13.33
Total	30	100	30	100	60	100
Mean age	49.57±12.27		45.53±12.75		47.55±12.57	

P=0.217

Table 2: Sex distribution.

Gender	Group A		Group B		Total	
	No.	%	No.	%	No.	%
Female	10	33.33	11	36.67	21	35.00
Male	20	66.67	19	63.33	39	65.00
Total	30	100	30	100	60	100

X²: 0.073; df:1; p=0.787.

Table 3: Stone characteristics.

Stone characteristics	Group A		Group B		Total	
	No.	%	No.	%	No.	%
Lower ureteric calculi	16	53.33	15	50	31	51.67
Middle ureteric calculi	8	26.67	9	30	17	28.33
Upper ureteric calculi	6	20	6	20	12	20
Total	30	100	30	100	60	100

X²: 0.091; df:2; p=0.955

Table 4: Comparison of IPSS in both groups.

IPSS	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	7.70	2.336	7.93	1.818	0.668
Stent removal	13.4	2.027	5.00	0.643	0.001
Total	10.55	3.60	6.47	2.004	0.001

Table 5: Comparison of irritative score.

Irritative	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	3.23	1.04	3.53	1.008	0.261
Stent removal	8.93	1.596	2.33	0.547	0.001
Total	6.08	3.169	2.93	1.006	0.001

Table 6: Comparison of obstructive score.

Obstructive	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	4.47	1.456	4.40	1.133	0.844
Stent removal	4.53	0.776	2.63	0.615	0.001
Total	4.50	1.157	3.52	1.269	0.001

At stent removal Irritative in group A had mean 8.93 (SD 1.596) and Group B had Mean 2.33 (SD 0.547) with P value 0.001, indicating significant statistical difference in Irritative score in between both groups at stent removal.

Obstructive score at baseline the mean score of Group A was 4.47 (SD 1.456) and Group B was mean 4.40 (SD 1.133) with p value 0.844, indicating not much statistical difference between two groups at baseline. At stent removal obstructive score in group A had mean 4.53 (SD 0.776) and Group B had Mean 2.63 (SD 0.615) with p

value 0.001, indicating significant statistical difference in obstructive score in between both groups at stent removal.

VAS score at baseline the mean score of Group A was 4.20 (SD 0.961) and Group B was Mean 4.07 (SD 1.172) with p value 0.632, indicating not much statistical difference between two groups at baseline. At stent removal VAS score in group A had mean 5.60 (SD 0.814) and Group B had Mean 2.83 (SD 0.747) with P value 0.001, indicating significant statistical difference in VAS score in between both groups at stent removal.

Table 7: Comparison of visual analog scale of both groups.

VAS	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	4.20	0.961	4.07	1.172	0.632
Stent removal	5.60	0.814	2.83	0.747	0.001
Total	4.90	1.130	3.45	1.156	0.001

Table 8: Comparison of quality-of-life score among both groups.

QOL	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	3.03	0.669	3.07	0.521	0.830
Stent removal	3.47	0.819	1.97	0.669	0.001
Total	3.25	0.773	2.52	0.813	0.001

QOL score at baseline the mean score of Group A was 3.03 (SD 0.669) and Group B was mean 3.07 (SD 0.521) with p value 0.830, indicating not much statistical difference between two groups at baseline. At stent removal QOL score in group A had mean 3.47(SD 0.819) and Group B had mean 1.97 (SD 0.669) with p value 0.001, indicating significant statistical difference in QOL score in between both groups at stent removal.

DISCUSSION

Urolithiasis is the earliest known problem of urinary tract. Ureteroscopic lithotripsy and ureteroscopy has emerged as one of the commonest endourological procedures performed by urologists across world.

Placement of indwelling ureteral stents has become a routine urological practice, as it prevents urinary tract

obstruction, help drainage of urine, allow ureteric mucosa to heal faster after ureteric injury, help dilate the ureter, and facilitate in small sized ureteric stone passage. Treatment strategies in management of stent-related symptoms can be classified into two different approaches: prevention of stent-related symptoms and management of stent-related symptoms. For the first category, accurate stent indications and improvements in both stent design and structures have been the focus. For the second category, pharmacology has focused on minimizing the motor and sensory bladder response to presence of stent.

Post ureteral stenting symptoms of lower urinary tract impacts quality of life in around 80 % of patients, incomplete emptying (76%), urgency (57%), frequency (50-60%), dysuria (40%), suprapubic pain (30 %), flank pain (19-32%), incontinence and hematuria (25%), The underlying mechanisms leading to stent related symptoms are not explained exactly and it is believed to involuntary contraction of the bladder secondary to irritation of the trigone contributes to the bothersome urinary symptoms. Additionally, increase in resistance to bladder outlet and pressure generated during micturition lead to reflux of urine. Alpha blockers have been found to reduce flank pain by its action of muscle tone reduction of ureter, bladder trigone and prostatic part of urethra as it acts as antagonist of alpha – adrenergic receptors leading to decrease in the bladder outlet resistance and the pressure developed during micturition.⁸

Wang et al used IPSS and QoL questionnaire to evaluate the effect of tamsulosin in improving symptoms in patients with indwelling double-J ureteral stents.⁹ They divided patients into 2 groups. Group 1 received tamsulosin 0.4 mg once daily until stent removal and group 2 received placebo. on stent removal patients of group 1 on Tamsulosin had less IPSS score and Better quality of Life Score as compared to group 2.

Singh et al who prescribed alpha blocker to ureteral stent post-operative patients and kept them for follow up for 4 weeks.¹⁰ They found significant decrease (p<0.05) in VAS score at loin area, VAS score at flank, VAS score at suprapubic area, average VAS score as compared to placebo prescribed patients.

So stent related morbidity a common problem faced by every urologist, which puts them through a dilemma, in which case every scenario has to weighed against the pros and cons. Stenting per se causes unnecessary increase in cost in the form of extra procedure to remove it and the cost towards the stent and the cost involved in treating the complications and the lingering odd risk of forgotten stent which might present at a later date with a variety of problems like encrustation, renal calculi, infection, sepsis and the difficult scenario of renal failure. At same time in cases where stenting is done for genuine causes the related symptoms can be treated effectively by α -blockers like Tamsulosin.

Lim KT et al, reported that the IPSS total score, irritative subscore, QoL, and VAPS had show no statistically significant differences. However, the difference in the obstructive subscore was statistically significant.¹¹

Navanimikul et al in there study divided patients into group 1 (placebo) and group 2 (tamsulosin 0.4 mg given) and made observations in terms of irritative and obstructive scores at baseline and at 4 weeks at stent removal.¹² Group 1 mean irritative score at baseline was 7.81 and at 4 weeks 8.19 (p 0.044) whereas in group 2 mean irritative score at baseline 5.48 and at 4 weeks 3.81 (p<0.001). They observed obstructive score in group 1 mean at baseline 4.86 and at 4 weeks mean score 4.00 (p 0.003) whereas in group 2 baseline obstructive mean score 1.38 and at 4 weeks 1.24 (p<0.001).

The result of this randomized placebo control study shows that ureteral stent related symptoms including irritative, obstructive, QoL and pain scale are significantly reduced with the use of tamsulosin.

Limitations

Small sample size, same stent size applied to all patients and only patients of ureteric calculi were taken for study.

CONCLUSION

The study concluded that administration of tamsulosin a selective α 1-blocker is useful in decreasing lower urinary tract symptoms in patients undergoing ureteral stenting.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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