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Efficacy of Alpha Blockers in Relieving Symptoms of JJ Stent

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ABSTRACT

Introduction: JJ stenting has been routinely used in endourology with a wide variety of implications. These stents have beneficial effects in postoperative period improving surgical outcome. Though they are widely used in urology practice, JJ stents cause lower urinary tract symptoms (LUTS) in majority of patients.

The objective of this study was to test the hypothesis that alpha blockers reduce lower urinary tract symptoms (LUTS) after rigid ureterorenoscopy in postoperative time period up to 3 weeks.

Study Design: It was a randomized clinical trial (RCT).

Setting: The study was conducted in KRL hospital, Islamabad. Patients presenting in outpatient / emergency department were selected for the study.

Duration of Study: Six months (15th July 2016 to 15th Jan' 2017)

Methods: A prospective randomized study was conducted in total 100 patients undergoing rigid ureterorenoscopy (URS). Patients were randomized into an intervention Group A and Control Group B. In Group A tamsulosin 0.4mg was given after rigid ureterorenoscopy, while in Group B no tamsulosin was given except placebo. Primary outcome were lower urinary tract symptoms (LUTS), which were measured by international prostate symptoms score (IPSS) up to 3 weeks postoperatively.

Results: The mean IPSS at 3rd week in postoperative phase of rigid URS for Group A was 4.76 ± 4.14315 and in Group B was 27.28 ± 5.03879 with the P value of 0.0001 which was statistically significant and also less than 0.05. So IPSS was statistically lower in Group A as compared to Group B up to 3 weeks post operatively. In conclusion, a significant statistical difference was found for Double J (DJ) stent related symptoms between the two groups.

Conclusion: Alpha blockers reduce lower urinary tract symptoms (LUTS) in postoperative period of rigid ureterorenoscopy up to 3 weeks.

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Introduction

The incidence of urolithiasis is about 5 percent in general population and annual incidence can be up to 1 percent overall [1]. Urolithiasis is more common in males than females and average age at which first episode of symptoms occurs is 30 years [2]. There is bimodal age pattern in females at 30 and 55 years. If

proper preventive measures are not taken the risk of recurrence increases with time [2].

Urolithiasis is crystalline mineral deposits that either stay in kidney or slip into the ureter causing symptoms of colic. The process of stone formation depends on pH and volume of urine and formation of substances that either promote or inhibit stone formation [3].

Urolithiasis are divided on the basis of size, location, radiographic

properties, cause of formation, their composition and risk of recurrence [4-7]. Specifically the ureteric stones cause symptoms of colic with severe flank pain, nausea vomiting associated with or without hematuria, though many stones with obstruction may cause the patient to suffer with severe sepsis and in worst cases death.

The gold standard to diagnose the ureteric stones is non-contrast computed tomography because it has the ability to detect stones of all compositions, can find any other incidental finding in abdomen and also there is no chance of contrast related toxicity [8,9].

Usually stones less than 5mm can easily pass in urine with good analgesic control and adequate hydration, but as stone size increases the chances of spontaneous passage decrease, like there is less than 10 percent chance of spontaneous passage of stone size of 1cm [10].

Indications for active intervention in ureteric calculi are stones with less chances of spontaneous passage, recurrent urinary tract infections(UTI), Persistent obstructive symptoms, deranged renal function tests(RFTS), Solitary kidney & Bilateral obstruction [11-13].

The major evolution in the management and active removal of ureteric calculi is the development of ureterorenoscopy, both rigid and flexible. Usually rigid ureterorenoscopes with tip diameter of less than 8 Fr is used. The rigid ureterorenoscopes are used for whole ureter [11]. In rigid ureterorenoscopy(URS) both ultrasound and pneumatic approaches can be used to fragment the ureteric calculi with good disintegration outcome [14,15]. With the advancement in technical equipment, there is tendency towards the use of flexible cystoscopies [16].

Usually post URS the ureteric stents are inserted by most urologists to increase the expulsion rate of residual stones. It is believed that these stents in postoperative phase have reduced ureteric stricture incidence, keep the kidney drained & reduce the pain [17].

Also in some cases ureteric catheters are also placed and then removed at 24 hours postoperatively [18].

The use of JJ stents in endourology has been a worldwide practice after Zimskind et al first described their use in patients via cystoscopy. Finney and Hepperlen in 1978 introduced the use of double J stents or pigtail stents reducing the complications of expulsion and migration [19,20]. DJ stents is a commonly used equipment in endourology and their use in our field has been increased very rapidly [21].

Despite recent advances, these DJ stents cause complications to some extent in some patients. The range of DJ stents vary from stent syndrome to forgotten stents complication causing serious medico legal issues [22,23]. Although there are many genuine indications of DJ stents symptoms, still in many centers there is overuse of these DJ stents [24].

The mechanism involved in JJ stent related symptoms might involve irritation of mucosa in trigone of bladder as it has alpha-1 D receptors and there might be spasms of smooth muscles in lower ureter manifesting symptoms similar to BPH. Another hypothesis postulated is that during voiding, pressure may be exerted on the renal pelvis and produces flank pain [25,26].

DJ stents cause lower urinary tract symptoms in 80% of patients and these symptoms include frequency, urgency, hematuria, suprapubic pain, dysuria and flank pain. In addition to these LUTS, 32% of patients complain of sexual dysfunction and 50% complain of difficulty in doing routine daily activities[27]. Joshi et al made a questionnaire named ureteral stent symptom questionnaire (USSQ) to assess the symptoms caused by DJ stents [27].

There are many studies and researches which have been conducted till date which used international prostate symptom score (IPSS) to assess the irritative and storage symptoms caused by JJ stents. Many drugs have been tried in the past to alleviate the JJ stent related symptoms, and in these drugs alpha blockers are considered to be most beneficial because they not only relax ureteral smooth muscles but also take important part in trigone inhibition [28].

Deliveliotis et al via his study explained that these alpha blockers are beneficial in relieving these lower urinary tract symptoms (LUTS) caused by JJ stents. Wang and associates demonstrated the impact and efficiency of tamsulosin 0.4 mg once daily to relieve the symptoms in patients with JJ stents [29,30].

Material and Methods

The randomized clinical trial (RCT) was conducted in KRL hospital, Islamabad. Patients presenting in outpatient / emergency department were selected for the study. Duration of the study was 6 months (15th July 2016 to 15th Jan' 2017). Sample size was calculated using WHO sample size calculator with the following: Level of significance: 5%, Power of test: 80%, Population pooled SD:1.37, Test value of Population mean: 2.22, Anticipated Population mean: 5.28, Sample Size Calculated: 50 in each group, Total size: 100. The sampling technique used was Consecutive (non-probability) sampling.

Adult male patients in age group of 20-50 years presenting to department of urology undergoing rigid ureterorenoscopy (URS) were included in our study.

Patients having Solitary functioning kidney, Renal insufficiency in terms of deranged urea and creatinine, Ureteric injury during trauma/procedure, Pregnant patients & those having Benign prostatic hypertrophy were excluded from the study

Data Collection Procedure

Study was started after approval from the ethical committee of hospital. Selected patients who gave written informed consent were randomly allocated either of two groups by lottery method.

One group was given alpha blockers at the end of JJ stenting and second group was given placebo.

Preoperative investigations which were done before procedure included complete blood picture (CBC), renal function tests (urea and creatinine) and urinalysis. X-ray KUB and ultrasound KUB were performed in all patients. Rigid ureterorenoscopy was performed in selected patients under spinal or general anesthesia under intravenous antibiotic cover which was 1 gram cefotaxime at the time of induction of anesthesia. Pneumatic lithotripsy was performed with Swiss lithoclast. At the end of procedure JJ stent was inserted in both groups of patients.

All the patients were assessed and evaluated by trainee researcher and final outcome in terms of mean IPSS was measured at the end of three weeks postoperatively. Follow-up was ensured by taking contact numbers of patients.

Data Analysis Procedure

All data was entered and visualized by SPSS version 13. For continuous variables like age, size of calculus and IPSS at the end of 3 weeks, mean + S.D was calculated. For categorical variables like site of calculus, frequency (percentage) was calculated.

Independent samples test was used to compare mean IPSS at the end of 3 weeks between two groups. Effect modifiers like age, site and size of calculus were controlled by stratification. Post stratification independent sample t-test was applied. P value < 0.05 was considered as significant.

Results

A total of 100 patients were included in the study and randomized into two study groups as defined previously. All rigid ureteroscopies were performed in KRL Hospital, Urology Department from 20th July, 2016 to 20th January, 2017.

The mean age in Group A was 34.32 ± 9.65621 and in Group B was 33.34 ± 7.15031 . (Table 1)

The mean IPSS for Group A was 4.76 ± 4.14315 and in Group B was 27.28 ± 5.03879 with the P value of 0.0001 which was statistically different and also less than 0.05. (Table 2)

The mean size of calculus in Group A was 9.52 ± 1.61927 and in Group B was 9.12 ± 1.54708 . (Table 3)

In group A 16% of calculi were proximal, 30% were mid ureteric calculi and 54% were distal calculi. In group B, 26% of calculi were in proximal ureter, 38% were in mid portion of ureter and 36% were distal ureteric calculi.

Table 1: Age distribution of patients

	Group A	Group B
N	50	50
Mean	34.32	33.34
Standard Deviation	9.65621	7.15031

Overall Mean: 34.09, Standard Deviation: + 8.4615

Table 2: IPSS Status of patients

	Group A	Group B
N	50	50
Mean	4.76	27.28
Standard Deviation	4.14315	5.03879

Overall Mean: 16.02, Standard Deviation: + 15.92

Table 3: Size of calculus

	Group A	Group B
N	50	50
Mean	9.52	9.12
Standard Deviation	1.61927	1.54708

Overall Mean: 9.32, Standard Deviation: + 0.283

Table 4: Frequency and percentage for site of calculus

Location of calculus	Frequency	Percentage
Group A:		
Proximal	8	16%
Mid	15	30%
Distal	27	54%
Group B:		
Proximal	13	26
Mid	19	38
Distal	18	36

Table 5: Stratification for patients IPSS after 3 weeks with regard to age

Age group	Mean IPSS after 3 weeks		P-VALUE
	Group A N=50	Group B N=50	
20 to 35 years	Mean=4.52 SD +4.22	Mean=26.63 SD=+4.84	0.0001
35 to 50 years	Mean=5.10 SD= +4.11	Mean=28.80 SD= +5.33	0.0001

Table 6: Stratification for patients IPSS after 3 weeks with regard to size & location of calculus

Size of calculus	Mean IPSS after 3 weeks		P-VALUE
	Group A N=50	Group B N=50	
7 to 9mm	Mean=5.42 SD +4.91	Mean=25.67 SD=+6.35	0.0001
10 to 12mm	Mean=4.15 SD= +3.27	Mean=28.65 SD= +5.51	0.0001
Proximal ureter	Mean=3.88 SD= +5.03	Mean=27.08 SD=+5.12	0.0001
Mid ureter	Mean=5.13 SD= +3.44	Mean=28.05 SD= +4.87	0.0001
Distal ureter	Mean=4.26 SD= +3.62	Mean=26.61 SD=+5.33	0.0001

Table 7: Comparison of mean IPSS at the end of 3 weeks between two groups

Group	Mean IPSS	SD	P-Value
A	4.76	+4.35	0.0001
B	26.88	+6.14	

*P value significant only if < 0.05

Discussion

The incidence of urolithiasis is about 5 percent in general population and annual incidence can be up to 1 percent overall. Urolithiasis are divided on the basis of size, location, radiographic properties, cause of formation, their composition and risk of recurrence [4-7].

Usually post URS the ureteric stents are inserted by most urologists to increase the expulsion rate of residual stones. It is believed that these stents in postoperative phase reduce ureteric stricture incidence, keep the kidney drained and reduce the pain [17].

The use of JJ stents in endourology has been a worldwide practice after Zimskind et al first described their use in patients via cystoscopy [19]. Finney and Hepperlen in 1978 introduced the use of double J stents or pigtail stents reducing the complications of expulsion and migration [20].

DJ stents cause lower urinary tract symptoms in 80% of patients and these symptoms include frequency, urgency, hematuria, suprapubic pain, dysuria and flank pain. There are many studies and researches which have been conducted till date which used international prostate symptom score (IPSS) to assess the irritative and storage symptoms caused by JJ stents.

Deliveliotis et al. via his study explained that these alpha blockers are beneficial in relieving these lower urinary tract symptoms (LUTS) caused by JJ stents [29]. Wang and associates demonstrated the impact and efficiency of tamsulosin 0.4 mg once daily to relieve the symptoms in patients with JJ stents [30].

Alpha blockers are routinely prescribed to patients in post-operative period of ureterorenoscopy because it reduces the colicky episode, reduces JJ stent related symptoms and increases the passage of residual calculi [31]. Important mode of action of alpha blockers is to relieve voiding symptoms of JJ stents in alpha blockers by decreasing frequency, urgency and urge incontinence and this effect has been well proved by urodynamics studies [32].

Beddingfield et al. demonstrated that alpha blocker like alfuzocin given daily significantly improves LUTS in patients having JJ stents [33]. Wang et al. showed the effect of tamsulosin in managing lower urinary tract symptoms and also the pain in flank which patient experiences during micturition [34].

Various other studies have been conducted clearly showing the beneficial role of alpha blockers to improve JJ stent symptoms, so they are the frequently prescribed drugs for patients who undergo JJ stenting after rigid ureterorenoscopy [35-38].

Various comparative studies have been done which tried to prove the efficacy of other drugs like anticholinergics in relieving the JJ stent related symptoms but no such effect could be established by the use of anticholinergics like oxybutynin as compared to alpha blockers [39].

Conclusion

Alpha blockers i.e tamsulosin 0.4mg reduce lower urinary tract symptoms (LUTS) including both storage and voiding symptoms caused by Double J (JJ) stents in postoperative period of rigid ureterorenoscopy as compared to placebo. Therefore it is safe to establish that alpha blockers should be prescribed in patients undergoing ureteric stenting after rigid ureterorenoscopy.

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