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Efficacy of tamsulosin in improving lower urinary tract symptoms in patients with indwelling double- pigtail ureteral stent: A placebo controlled non-randomized clinical trial

Mohanned Husam Mohammed Saeed[1], Samir Ali Muter[2], Mohammed Bassil Ismail[3], Hasanain Farhan Hasan[4], Noorulhuda Mukhlif Najm[5]

[1] (FICMS), Uro-Surgeon, Urology Department, Tikrit Teaching Hospital. Tikrit, Iraq.

[2] (FICMS), Uro-Surgeon, Urology Department, Medical City Complex, Baghdad, Iraq.

[3] (CABMS), Uro-Surgeon, Urology Department, Medical City Complex, Baghdad, Iraq.

[4] (CABMS), Uro-Surgeon, Urology Department, Medical City Complex, Baghdad, Iraq.

[5] (MBCHB), Baghdad teaching hospital, Medical City Complex, Baghdad, Iraq.

Corresponding Author:

Mohammed Bassil Ismail. Urology Department, Medical City Complex, Baghdad, Iraq.
E mail: mohammed_albassil@yahoo.com

ABSTRACT

INTRODUCTION: Lower urinary symptoms are nearly always associated with placement of ureteral stent. It affect the morbidity of the patients and its wellbeing. Anticholinergic drugs were used to treat these symptoms; however, they have many adverse effects. Alpha-1 adrenoceptor blockers sound to have similar effect but with less adverse effects.

OBJECTIVE: To evaluate the role of tamsulosin in improving urinary symptoms and pain in patients with indwelling double- pigtail ureteral stent.

METHODS: A placebo-controlled non-randomized clinical trial was conducted at the Medical City Directorate in Baghdad from November 2009 to December 2010. Seventy-three patients who underwent ureteral stent placement for 2 weeks due to any reasons were enrolled. Post operatively group A have received tansulosin, and group B have received placebo for 2 weeks then the stent was removed and both groups followed for another week. We assessed lower urinary symptoms by ureteric stent symptoms questionnaire, pain in bladder and or flanks by visual analogue scale, and development of urinary tract infections and number of using analgesics in both groups.

RESULTS: At the end of the second weeks of stent placement, group A showed a significant improvement of urinary symptoms (14.2 versus 27.2 P=0.008) and pain (5.3 v 20.4 P=0.002) than patients in group B. This significant difference has not maintained a week after discontinuation of treatment; urinary symptoms were found in 13.5 in group A versus 14.2 in group B, and pain was reported in 5.4 in group A versus 5.3 in Group B.

CONCLUSION: Our findings indicate that administration of tamsulosin has a significant effect on stent-related urinary symptoms and pain for improving quality of life.

Key words: ureteral stent, double J stent, tamsulosin,

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INTRODUCTION

Since its first description in 1967 by Zimskind et al,[1] the double J ureteral stent has been an indispensable tool in the urologists' surgical armamentarium.

Ureteral stents play a major role in a wide range of situations where urinary drainage is needed. Urgent indications include cases of obstructive pyelonephritis and intolerable acute renal colic;[2] safety indications following endoscopic procedures include ureteral oedema or perforation, steinstrasse, history of renal failure, and solitary or transplanted kidney.[3] Relative indications would still include stone burden larger than 2 cm undergoing extracorporeal shock waves lithotripsy, pregnancy, long-standing impacted stone, recent history of urinary tract infection or sepsis, stenting to passively dilate the ureter and/or ureteral orifice, prolonged endoscopic operative time (over 45 minutes) and any patient with imminent post-operative plans such as a second-look ureteroscopy.[4]

Stent discomfort can vary from one patient to another in an idiosyncratic manner, but it is believed to affect over 80% of patients.[5] Several studies have described the symptoms relat-

ed 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]

Joshi et al[5] reported on the first study to objectively evaluate the symptomatology associated with stents. They prospectively assessed the prevalence and bother of various urinary tract symptoms caused by indwelling ureteral catheters using validated questionnaires [International Prostatic Symptoms Score (IPSS), International Continence Society male questionnaire, Quality of Life questionnaires, and the Bristol Female Lower Urinary Tract Symptoms questionnaire (BFLUTS)]. Although they succeeded in showing the association of urinary symptoms with stents and their negative impact on patients' quality of life, the most important contribution was to bring to attention the need for the development of a stent-specific measuring tool.[5] They later developed and validated a questionnaire to specifically address this purpose. The Ureteral Stent Symptom Questionnaire (USSQ) consists of 38 items examining 6 sections: pain, voiding symptoms, work performance, sexual matters, overall general health, and additional problems.[8] It was shown that 76% of patients had urinary symptoms, 70% had pain severe enough to reduce their activities by 50% and felt less healthy in general, and 32% experienced sexual dysfunction.[9]

LUTS are managed by alpha blockers, anticholinergics, and analgesics . Tamsulosin, a selective α-1a/1d blocker, inhibits contraction of the smooth muscles in distal ureter, bladder trigone, and neck, relieving LUTS and flank pain.[10]

This study aims to recognize the efficacy of alpha-1 adrenoceptor blocker (tamsulosin) in improving lower urinary symptoms and pain in patients with double J ureteric stent.

METHODS

Settings and study design: A prospective, single blinded, placebo-controlled non-randomized clinical trial was conducted at the urology clinic, Surgical subspeciality Hospital, Medical City Complex in Baghdad from November 2009 to December 2010.

Ethical issues: The local ethical committee of the Medical City Directorate has approved the study. Aims of the study; its benefits and potential adverse effects were explained to all participants and their written informed consent was requested prior to enrolment.

Definition of the case, inclusion and exclusion criteria: Patients who were admitted to the Urology Department and underwent ureteral stenting for any reasons during the studied period were the target of this study. Patients who has lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (International Prostate symptom score higher than 8), a history of stent placement, chronic prostatitis and the use of alpha-blockers or analgesic drugs were excluded from this study to avoid the potential serious effect on interpretation of the results. Also we have excluded any patient who needs the ureteral stents for more than 2 weeks.

Sampling: We enrolled all participants who have underwent DJ placement on every Wednesday, the specific weekly day of operations of our section in the department.

Randomization: Patients were divided into two groups; group A, included patients who were prescribed tamsulosin in a dose of 0.4 mg once daily for 3 weeks. Group B has included patients who were prescribed placebo pills. Allocation of patients into either groups were done by using a lottery. Patients in both groups has received ciprofloxacin 500 mg twice daily for 5 days and analgesics were used on demand bases in form of paracetamol 500 mg on each occasion, diclofenac sodium 50 mg has been added if paracetamol alone has not achieved a satisfactory response. Group A has included 37 participants while group B has included 36 participants.

Outcomes of the study: Effectiveness of tamsulosin in controlling lower urinary tract symptoms were assessed in three domains. The first is the urinary symptoms; dysuria, haematuria, urgency, and frequency. The second domain is pain in the flank, bladder or both, while the third domain is about other problems like urinary tract infections and the need for analgesia. Lower urinary tract symptoms were assessed by ureteric stent symptoms questionnaire (USSQ). The answers are based on a four-point rating scale and high score indicates worse outcomes. We calculated the mean score of USSQ at the end of second week where patients in-group A were still using tamsulosin and patients in-

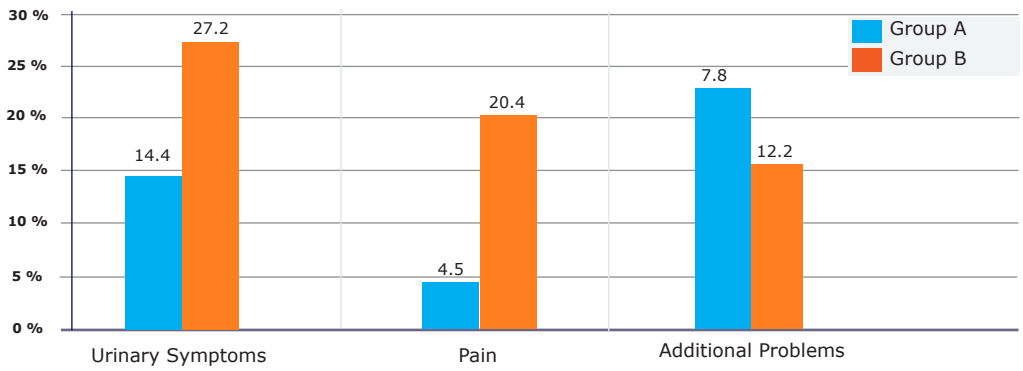

Figure 1: Percentages of urinary symptoms, overall pain, and additional problems like UTI and needs for analgesia at the end of second week from placement of stents in Group A (tamsolosin) and B (placebo).

group B were using the placebo. Then the mean was also calculated for both groups at the end of the third week; a week after discontinuation of drug and placebo.

The second domain was assessed by VAS, we asked patients to express their perception of the intensity of the pain. Patients were requested to define the colicky pain they experienced as a number between 0 and 10 by comparing the pain with the most severe pain they had ever experienced (0, no pain; 10, the most severe pain perceived).

The third domain was measuring by asking patients in both groups how many times they used analgesics and whether its used have alleviated the pain or not. Urinary tract infection was assess by asking about fever and flank pain, then documented by urine analysis. UTI was considered present when Urine analysis has shown more than 5 pus cell per high power field with or without symptoms.

Measurements of the three domains was done at the end of the second week of starting the treatment where patients in-group A were still using tamsulosin and patients in-group B were using the placebo. Then all outcomes were re-measured in both groups at the end of the third week; a week after discontinuation of drug and placebo.

Procedure: In all patients, stent was removed at the end of the second week. Tamsulosin and placebo were stopped at the same time. The ureteral stent used in all patients was 5F polyurethane stents B Braun. On each follow up visit, the position of stent was assessed by doing plain radiography of kidney, ureter and bladder (KUB) and ultrasonography to exclude dislodgement and incorrect placement, which may be another cause for lower urinary tract symptoms.

Positive effects on the reduction of stent-related urinary symptoms and impairment of quality of life were the primary endpoints of the study. A difference of more than 30% was considered a meaningful difference. Tamsulosin was defined as responsible for the reduction of stent-related urinary symptoms and quality of life impairment if its use decreased the expected EQ VAS. To detect a difference of this magnitude with a power of 80% and a significance level 5%, about 35 patients per arm (tamsulosin versus no medication group) were required.

Statistical analysis: All variables were expressed as mean values ± SD or as numbers of patients and percentages. Statistical analyses were performed with Student's T test. A P-value of less than 0.05 was considered significant. Analyses were performed using SPSS software, version13.0 for Windows (SPSS, Chicago, Illinois, USA).

RESULTS

All patients (38 females and 35 males) completed the study, their mean age was 34.6 years (25-58 years), and no stent required manipulation before removal.

At the end of second week, there was a significant difference in the mean symptom score between the 2 study groups with regard to all the 3 domains of symptoms, as shown in figure 1.

On the other hand, comparing the symptoms between the two groups at the end of week 3

Table 1: Detailed outcomes of both groups after 2 weeks of placement of stents.

		Never		Occasionally		Frequently		Always	
		Group A*	Group B†	Group A	Group B	Group A	Group B	Group A	Group B
Urinary Symptoms	Dysuria	28	10	7	17	2	8	0	1
	Haematuria	12	16	13	10	9	6	4	4
	Urgency	20	7	8	8	7	18	2	3
	Frequency‡	18	3	13	12	3	11	3	10
Pain	Flank	30	24	4	8	2	1	1	3
	Bladder	27	19	5	8	4	6	0	2
	Both	22	8	11	20	4	6	0	2
Additional Problems	UTI	34	23	2	7	1	4	0	2
	Need for pain killers	14	5	16	22	4	6	3	3

*Number in group A= 37
†Number in group B= 36
‡For frequency never means 1-4 times, occasionally means 5-7 times, frequently means 8-12 times, always mean > 12 times

showed no significant difference. Figure 2

The mean attack of acute colic was 3 ± 1.2 (range 1-5) in group B and 1.5 ± 1 (range 0-3) in group A, and this shows highly statistical difference (P<0.0001). The mean number of Diclofenac injections during therapy was 5.2 ± 2 (range 3-9) for group B and 0.8 ± 1 (range 0-3) (P<0.0001).

DISCUSSION

Since its first description in 1967 by Zimskind, et al the double J ureteral stent has been indispensable tool in the urologists' surgical armamentarium. Ureteral stents play a major role in a wide range of situations where urinary drainage is needed. Despite the limited indications of double J stent placement, they are thought to be overused in a contemporary urology practice.

In a recently published survey among community and academic practicing urologists from worldwide centres, Auge et al have reported that 98% of the responders perform ureteroscopic stone surgery in their routine. Of these, two-thirds would place a stent more than 50% of the time and 13% would always place a postoperative stent, even though intolerance to the stent presence was the most significant problem addressed by patients (98%).[11] Based on a recent meta-analyses, the role of stenting in uncomplicated ureteroscopy remains unclear, even though stent placement results in a considerable morbidity in the form of irritative LUTS.[12] Therefore, patients should be involved in the decision to use or not, once they are made aware of the possibility of a secondary unplanned procedure of for repositioning.[13]

During the last decade, technical advances in stent development and design (e.g., tapered distal ends) and construction (e.g., magnetic, biodegradable and tissue engineered materials) to decreased stent related morbid-

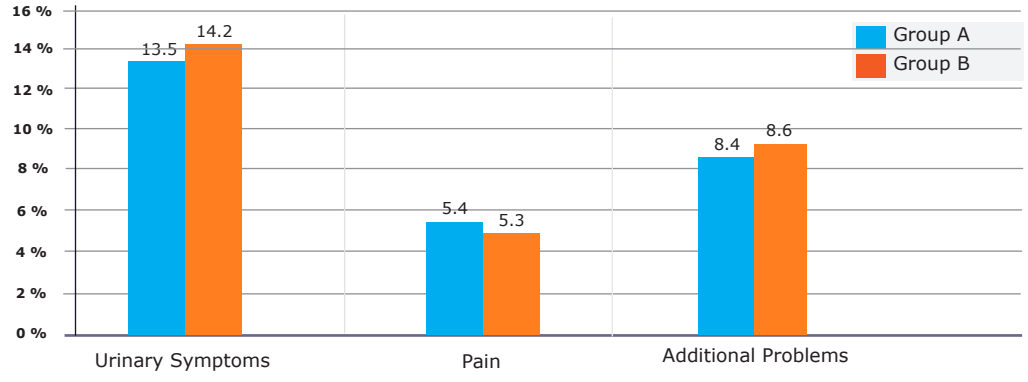

Figure 2: Percentages of urinary symptoms, overall pain, and additional problems like UTI and needs for analgesia at the end of third week from placement of stents in Group A (tamsolosin) and B (placebo).

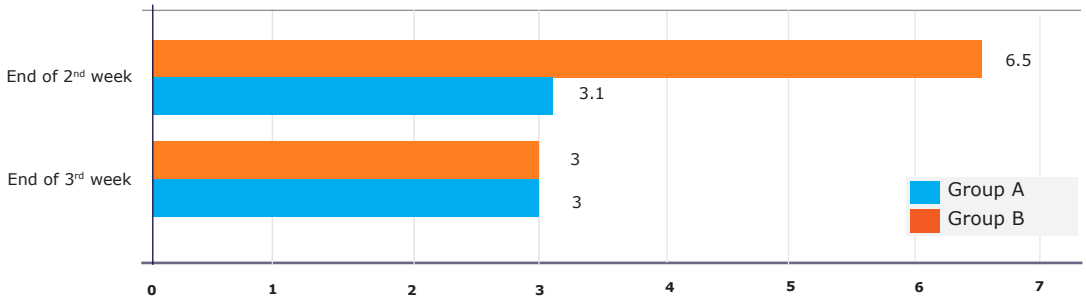

Figure 3: Mean value of visual analogue scale for pain of group A (tamsolosin) and group B (control) at weeks end of second and third weeks

ity. The ideal biomaterial has yet to be discovered. Recently, Joshi and coworkers[8] found no difference in the impact on patients' quality of life between ureteral stents of different compositions. The USSQ, first developed by Joshi and colleagues,[5] has shown satisfactory validity with good evaluative and discriminative properties it showed incontinence and haematuria in 78% of patients and stent related pain in 80% of patients. Our results are in accordance with their findings. At end of the second week following stent insertion about 70% of the control patients reported stent related pain in the loin or bladder region.

According to our results, the use of tamsulosin significantly reduced stent related urinary symptoms (70%) and pain (80%) therefore improving quality of life, because tamsulosin acts as a competitive antagonist of alpha-1 adrenoceptor-mediated contraction of prostatic, bladder and proximal urethral smooth muscle, it can reduce urethral pressure and resistance, bladder outlet resistance, bladder hyperactivity and lower urinary tract symptoms.[14]

In the evaluation of general health, analyses of questionnaires reveals an association between tamsulosin use and responses regarding the different domains particularly pain-discomfort being the most bothering of all domains. Our results were found to be superior into what was founded by Deliveliotis and coworkers who used alfuzosin 10 mg once daily and found that the pain was reduced at fourth week by 33%, also it was superior to what was found by Beiko and colleagues who proposed a novel approach by relieving LUTS by using intravesical administration of various agents (oxybutynin, alkalinized lidocaine, or ketorolac).[15] Ketorolac appeared to be the safest and most effective intravesical agent in reducing stent related discomfort. We found that our results was very close into what was found by Damiano and colleagues[13] who used tamsulosin in preventing ureteral stent related morbidity.

We observed that patients who were given tamsulosin had significantly better outcome in that they had less VAS (Visual Analogue Scale) scores, less attacks of acute colic, and they used less NSAIDs injection during therapy (P<0.0001, P<0.0001, and P<0.0001 respectively). These findings made obvious that the effect of tamsulosin on the ureter was probably to decrease the frequency and amplitude of phasic peristaltic contractions that accompanying ureteric obstruction.

Additional problems (e.g. Symptoms of urinary tract infection) were reduced in both groups at end of second week, with no statistically significant differences between men and women. Symptoms of overactive bladder and concomitant detrusor hyperactivity have been treated with alpha-1 blockers because of their effects on bladder smooth muscle[10] through their action on unmyelinated c fibres of the urethral afferent mechanism.

CONCLUSIONS

Our findings indicate that administration of tamsulosin has a significant effect on stent-related urinary symptoms and pain for improving quality of life. Further clinical research in this field is needed to better define the role of α1-blockers in current clinical practice.

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Abbreviation list: Bristol Female Lower Urinary Tract Symptoms questionnaire (**BFLUTS**), Double J (**DJ**), International Prostatic Symptoms Score (**IPSS**), Kidney, Ureter and Bladder (**KUB**), Lower Urinary Tract Symptoms (**LUTS**), Non-Steroidal Anti Inflammatory Drugs (**NSAID**), Standard Deviation (**SD**), Statistical Package for the Social Sciences (**SPSS**), United States of America (**USA**), Ureteral Stent Symptom Questionnaire (**USSQ**), Visual Analogue Scale (**VAS**)

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