

## Research Article

# Tamsulosin to Relieve JJ Stent Related Discomfort: A Prospective Randomized Placebo Controlled Crossover Study

Ayman S. Moussa\*, Rabie M. Ibrahim, Ahmed M. Abdelbary, Ahmad A. Al-Dessoukey, Akrm A. Elmarakbi, Osama Sayed, Amr M. Lofty, Ahmed M. Ragheb, Ahmed Abd El Latif, Ahmed M. Elbatanouny, Hany Fathy, and Amr M. Massoud

Department of Urology, Beni-suef University, Egypt

**\*Corresponding author**

Ayman S. Moussa, Department of Urology, Beni-Suef University, Faculty of Medicine, Egypt, Tel: 002-01001180409; Email: aymansalah7295@yahoo.com

Submitted: 22 September 2017

Accepted: 28 November 2017

Published: 30 November 2017

ISSN: 2379-951X

**Copyright**

© 2017 Moussa et al.

**OPEN ACCESS****Keywords**

- Ureteral stent
- Tamsulosin
- Lower urinary tract symptoms
- JJ related symptoms

**Abstract**

**Introduction:** To evaluate the effect of tamsulosin in improving urinary symptoms in patients with JJ ureteral stent in a prospective randomized placebo controlled crossover study.

**Material and methods:** 100 patients were enrolled, divided into two groups each [50 patients]. Group A: received Tamsulosin 0.4 mg capsule once daily for two weeks. Group B: received placebo once daily for the same period of time. Then they came for the first visit for evaluation and switch to the other drug for another two weeks.

**Result:** Comparing the two visits of each group, it was evident that incidence of LUTS were significantly lower with tamsulosin prescription. While comparing the first visit of first group [on tamsulosin] with the second visit of second group [on tamsulosin], there were no significant difference in the symptoms.

**Conclusions:** Tamsulosin has a significant effect in improving JJ related symptoms disregarding its time of prescription.

**ABBREVIATIONS**

A1: Alfa One; BPH: Benign Prostatic Hyperplasia; IPSS: International Prostate Symptoms Score; LUTS: Lower Urinary Tract Symptoms; PCNL: Percutaneous Nephrolithotomy; PSA: Prostate Specific Antigen; SWL: Shock Wave Lithotripsy; URS: Ureterscopy; USSQ: Ureteral Stent Symptom Questionnaire; UTI: Urinary Tract Infection; QoL: Quality Of Life

**INTRODUCTION**

Ureteral stent placement is now considered a routine and indispensable urologic tool. However, the side effects and patient morbidity associated with ureteral stents have been identified as a potential health problem. It was hypothesized that a selective  $\alpha_1$ -blocker, such as tamsulosin, might influence the stent-related symptoms, because the latter mimic the LUTS due to BPH. We evaluated the effect of tamsulosin in improving urinary symptoms in patients with indwelling JJ ureteral stents

JJ stents are inserted for many specific indications. However, patients may experience stent related symptoms such as “lower

urinary tract symptoms LUTS [frequency, urgency and burning micturition], flank and suprapubic pain” [1]. The stent related pain interferes with daily activities in up to 80% of patients [2], so 32% of patients insisted to remove it earlier than planned [3]. Many trials to improve these symptoms were done as Tail stent with a 6F or 7F shaft that tapers to 3F closed tip tail at the distal end [4], stent Coatings with material like Hydrogel [5], heparin-like polysaccharides [6], Plasma-deposited diamond-like amorphous carbon coatings [7], and analgesics- [ketorolac] loaded [8]. Pharmacological treatment with alpha blockers, anticholinergics, and analgesics are prescribed empirically [9]. selective  $\alpha_1$  blockers [eg. tamsulosin] used with possible mechanism of relaxing bladder neck/ prostatic smooth muscle, with reduction of voiding pressure and urinary reflux, as well as reducing ureteric motility, [10]. Another possible mechanism is blocking C-fibers [11] or sympathetic postganglionic neurons, which also blocks pain conduction to the central nervous system, so it could be tried to improve LUTS in patients with indwelling JJ ureteric stents [12]. This study conducted to primarily evaluate the effect of tamsulosin in improving urinary symptoms in patients with JJ

ureteral stents, our secondary objective is to evaluate the relation between the effect of tamsoulin on JJ symptoms and its time of prescription in a prospective randomized placebo controlled crossover study.

## MATERIAL AND METHODS

This study is a prospective randomized single blind [at the level of the patient] placebo controlled cross over study. The institutional ethics committee approved the study protocol and all patients enrolled in this study had written informed consent. It was carried out from January 2015 to February 2016 at urology department, Beni-Suef University Hospital; including patients with unilateral JJ insertion after uncomplicated semi-rigidureteroscopy [URS], dilatation of stricture ureter, before shock wave lithotripsy [SWL] and after percutaneous nephrolithotomy [PCNL] if indicated. Symptomizing BPH patients and suspected prostate cancer if PSA above 2.5 or abnormal digital rectal examination, overactive bladder, vesical or infra-vesical pathology, bladder stone, patients already taking alpha-blockers and/or anticholinergic and pregnancy were excluded. The randomization scheme was generated using the web site of Randomization.com [www.randomization.com]. One hundred and sixty patients enrolled in the study; only 111 patients complained of JJ related symptoms were eligible for the study with an incidence of 69,4%. Eleven patients were excluded from the study; ten of them with urinary tract infection [UTI] based on culture and sensitivity were excluded; six at initial urine culture and four patients at the second visit and finally the last one due to distal migration of the JJ, so only 100 patients completed the study.

A polyurethane 6 F JJ ureteral stents were inserted in all patients under fluoroscopy guidance using 6.5/8.5 Fr KARL STORZUreteroscope. The JJ length was adjusted according to patient's height; only the coiled distal end should be present in the bladder without crossing the midline. All patients underwent x-ray films in the morning of the second day to assure the presence of JJ ureteral catheter in place, patients performed the first urine culture and sensitivity to exclude UTI. Then Patients were randomized into two Groups: Group [A]: has given Tamsulosin 0.4 mg capsule once daily for two weeks. Group B: given Placebo [coated sugar prepared in Beni-Suef faculty of pharmaceutical] once daily for the same period. After 2 weeks of JJ insertion [the first visit]: Evaluation was done, patients were asked to do a second urine culture and sensitivity and each group was shifted to the other medication for another two weeks. After 4 weeks of JJ insertion [the second visit]: another evaluation was done. At each visit: the accuracy of JJ position was ensured by a new x-ray film. The evaluation for urinary frequency, urgency and urge incontinence done using IPSS questionnaire for these 3 items. The Faces Rating Scale was used to evaluate burning micturition, loin pain and urethral/perineal pain from 0 to 10; [0: No pain, 2: Mild pain, 4: Discomforting, 6: Distressing, 8: Intense, and 10: Excruciating] [13].

## STATISTICAL METHODS

A sample size of 90 subjects at least, 45 in each arm, is sufficient to detect a clinically important difference of 1.5 between groups in reducing IPSS score assuming a standard deviation of 2.5 using

a two-tailed t-test of difference between means with 80% power and a 5% level of significance. Considering a dropout rate of 10% the sample size required is 99 [about 50 per group].

Data collected was tabulated in an excel sheet. Data was analyzed using SPSS Statistics Windows, Version 17.0 for the generation of descriptive and inferential statistics. The statistically significant difference among groups was determined by the Student t- test, Fisher's exact test in used to calculate an exact P-value Cross tabulation test: For comparison between percentage values. Multivariate analysis was used to assess association of the variables within groups, and P value > 0.05 [NS] not significant and P value <0.05.

## RESULTS

One hundred patients completed the study, their age ranged between 18 and 52 years old [mean age 34.2 years old], 65 males and 35 females. The JJ length and indication of JJ insertion summarized in (Table 1). The IPSS score and the face rating scale were significantly decreased in the first group of patients treated with tamsulosin in the first visit compared to placebo in the second visit with P value 0.001, both tamsulosin and placebo didn't improve hematuria p value 0.527 (Table 2).

In the second group, the first visit [placebo] compared to the second visit [tamsulosin], it was evident that the IPSS and face rating scale were significantly lower with tamsulosin; P value 0.001, both tamsulosin and placebo didn't improve hematuria p value 0,123] (Table 2).

When we compared between the first visit of first group [patients on tamsulosin] with the second visit of second group [patients on tamsulosin also], it was obvious that there was no significant difference, this means that the effect of tamsulosin in improving stent-related urinary symptoms is the same regardless its time of prescription (Table 3). It was evident that comparing both groups at first and second visits was in the favor oftamsulosin which significantly lower the symptoms (Table 4).

Only three patients in tamsulosin group experienced adverse effects associated with the medical therapy [transient hypotension and palpitations] and only four patients in tamsulosin group needed analgesic therapy, whereas 25 patients in placebo group required such regimen [P = 0.0001]

A multi-regression analysis for all other factors like sex, age, indication of JJ fixation and their relation with the stent related symptoms, however it shows no significant relation.

## DISCUSSION

The use of JJ stent is an important tool in urological surgery so reducing JJ related symptoms is a major concern to all urologists due to its higher incidence; up to 69.4% in this study. Ureteral stents prevent urinary tract obstruction from ureteral swelling and make the ureteral mucosa heal faster after iatrogenic injury [14]. Medical treatment with  $\alpha$ -blockereither alone or with anti-muscarinic used to reduce LUTS through smooth muscle relaxation of lower ureter and trigone as well as reducing ureteric motility [15]. A study done by Maldonado comparing tamsulosin, oxybutynin extended release and their combination clearly stated that the combination is better in improving irrigative

**Table 1:** The demographic data, indications and JJ length.

	Group 1	Group 2
Sex (male: female)	30(60%): 20(40%)	35(70%): 15(30%)
<b>Indications</b>		
URS	30(60%)	30(60%)
Stricture	13(26%)	13(26%)
Pre ESWL	5(10%)	4(8%)
After PCNL	2(4%)	3(6%)
JJ length; 26 cm	23(46%)	22(44%)
28 cm	27(54%)	28(56%)

**Table 2:** First group; comparison between first visit (tamsulosin) and second visit (Placebo) and Second group; comparison between first visit (Placebo) and second visit (tamsulosin).

First group	First Visit (tamsulosin)	Second Visit (Placebo)	P-value
IPSS (Mean ±SD)	5.7±2.7	8.56±3.5	0.001*
Loin pain (Mean ±SD)	3.4±2.6	4.64±2.1	0.001*
Urethral, perineal pain (Mean ±SD)	3.76±2.5	4.64±2.2	0.009*
Hematuria (%)	22	18	0.527
Second group	First Visit (Placebo)	Second Visit (tamsulosin)	P-value
IPSS (Mean ±SD)	8.5±2.9	5.2±2.8	0.001*
Loin pain (Mean ±SD)	4.4±2.6	3.5±2.6	0.001*
Urethral, perineal pain (Mean ±SD)	4.6±2.2	3.8±2.5	0.009*
Hematuria (%)	12	22	0.132

\*Statistically significant

**Table 3:** Comparison between First visit of first group and second visit of second group (Tamsulosin only).

JJ symptoms	1 <sup>st</sup> visit Tamsulosin	2 <sup>nd</sup> visit Tamsulosin	P value
IPSS (mean)	5.7	5.2	0.406
Loin pain (mean)	3.4	3.5	0.878
Urethral pain (mean)	3.76	3.8	1
Hematuria (%)	22	22	1

**Table 4:** Comparison between first and second group at both visits on JJ symptoms.

		First group Mean±SD	Second group Mean±SD	P-value
<b>First Visit</b>	IPSS	5.7±2.7	8.5±2.9	0.001*
	Loin pain	3.4±2.6	4.4±2.6	0.048*
	Urethral, perineal pain	3.76±2.5	4.6±2.2	0.007*
<b>Second Visit</b>	IPSS	8.56±3.5	5.2±2.8	0.001*
	Loin pain	4.64±2.1	3.5±2.6	0.016*
	Urethral, perineal pain	4.64±2.2	3.8±2.5	0.045*

\*Statistically significant

urinary symptoms and performance score however tamsulosin was better to improve work performance score [16]. Also, Wang and associate suggested that relaxation of bladder neck/prostatic smooth muscle, with reduction in voiding pressure and urinary reflux, are other possible mechanisms, setting a rationale behind using  $\alpha$  blockers in relieving ureteral stent symptoms [10]. It may prevent exacerbated pre-existing subclinical detrusor over-activity [17] and reduce flank pain by reducing vesico-ureteric reflux by JJ [18], appropriate stent length as per patient height, proper positioning, drug eluting stents also reduce JJ symptoms. Dellis AE and associate conducted a double-blind, randomized study to evaluate the effect of 2 different  $\alpha$ -blockers [tamsulosin and alfuzosin] in improving symptoms and QoL in patients with JJ ureteral stents compared to placebo. They concluded that no difference in various outcomes between the 2  $\alpha$ -blockers and both superior than placebo [19]. A Validated Self-administered Ureteral Stent Symptom Questionnaire [USSQ] used to evaluate stent related symptoms [20] and its validation of the Arabic linguistic version by El-Nahas and associate in 2014 [21] is used to evaluate ureteral stent symptoms in clinical practice and research. We didn't use the USSQ in this study because this Arabic validation hasn't been published when the study design and protocol were approved and conducted late 2014. USSQ consists of six domains urinary symptoms, pain, general health, work performance, sexual matters and additional Problems [20]. Damiano and associate conducted a prospective randomized study on tamsulosin in improving symptoms and QoL in patients with indwelling JJ ureteral stents, LUTS improved tamsulosin-treated group compared to group with no  $\alpha$  blocker at week one [p=0.002]. In addition, QoL was significantly better in the tamsulosin-treated group [p=0.006] [22]. Also Wang and associate conducted a prospective randomized double blind study on 0.4 mg of tamsulosin once daily and placebo for 2 weeks, tamsulosin improved stent-related symptoms and QoL [10]. We tried to overcome limitations of other studies by the exclusion of active UTI before starting the study. In addition, the exclusion of active UTI during the study also was done. In addition, our study consists of 100 patients [group A: 50, group B: 50] which is larger than Damiano's study: 75 patients [group A: 38, group B: 37]. The evaluations of urinary symptoms and comparison between the two groups were done in both studies early at the first week and fourth week [after 2 weeks of stent removal]. In our study, we evaluated the patients at the second and fourth weeks. Damiano did not consider the stent size and material used in the procedure. However, in Wang's and our study, JJ size, design and material were considered to minimize the trial of variability.

It was obvious that Tamsulosin has no effect on hematuria. The incidence of pain in patients given tamsulosin, both urethral/perineal pain and loin pain was lower than in those on placebo and also it reduces the analgesic demand compared to the placebo group. It is possible that tamsulosin reduces urine reflux by better bladder neck relaxation thus reducing loin pain [10].

To our knowledge, this study is the first prospective, single blind, controlled, cross over study comparing the effect of tamsulosin on the same person and for a long period. All other studies compared the effect of tamsulosin on different persons and for short period. On the other hand, this study had several limitations; we know that the outcomes are based on subjective

sense of discomfort. In addition, our main objective in this study was to evaluate the effect of tamsulosin on urinary symptoms, so we did not ask about the sexual function and QoL like other studies and we did not use USSQ in evaluating JJ related symptoms.

## CONCLUSIONS

Tamsulosin has a significant effect in improving JJ related symptoms as frequency, urgency, urge incontinence, burning micturition, loin pain and urethral/perineal pain disregarding its time of prescription with lower incidence of analgesic intake.

## REFERENCES

- Haleblian G, Kijvikai K, de la Rosette J, Preminger G. Ureteral stenting and urinary stone management: a systematic review. *J Urol.* 2008; 179: 424-430.
- 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: 1065-1069.
- Dellis A, Joshi HB, Timoney AG, Keeley FX Jr. Relief of stent related symptoms: review of engineering and pharmacological solutions. *J Urol.* 2010; 184: 1267-1272.
- Dunn MD, Portis AJ, Kahn SA, Yan Y, Shalhav AL, Elbahnasy AM, et al. Clinical effectiveness of new stent design: randomized single-blind comparison of tail and double-pigtail stents. *J Endourol.* 2000; 14: 195-202.
- Watterson J, Cadieux P, Denstedt J. Ureteral stents: which, when, and why. *AUA Update Ser.* 2002; 21: 122-127.
- Riedl CR, Witkowski M, Plas E, Pflueger H. Heparin coating reduces encrustation of ureteral stents: a preliminary report. *Int J Antimicrob Agents.* 2002; 19: 507-510.
- Laube N, Kleinen L, Bradenahl J, Meissner A. Diamond-like carbon coatings on ureteral stents-a new strategy for decreasing the formation of crystalline bacterial biofilms? *J Urol.* 2007; 177: 1923-1927.
- Krambeck AE, Walsh RS, Denstedt JD, Preminger GM, Li J, Evans JC, et al. A novel drug eluting ureteral stent: a prospective, randomized, multicenter clinical trial to evaluate the safety and effectiveness of a ketorolac loaded ureteral stent. *J Urol.* 2010; 183: 1037-1042.
- Hao N, Tian Y, Liu W, Wazir R, Wang J, Liu L, et al. Antimuscarinics and alpha-blockers or alpha-blockers monotherapy on lower urinary tract symptoms--a meta-analysis. *Urology.* 2014; 83: 556-562.
- Wang CJ, Huang SW, Chang CH. Effects of specific alpha-1A/1D blocker on lower urinary tract symptoms due to double-J stent: a prospectively randomized study. *Urol Res.* 2009; 37: 147-152.
- Yokoyama O, Yusup A, Oyama N, Aoki Y, Miwa Y, Akino H. Improvement in bladder storage function by tamsulosin depends on suppression of C-fiber urethral afferent activity in rats. *J Urol.* 2007; 177: 771-775.
- Dellabella M, Milanese G, Muzzonigro G. Medical-expulsive therapy for distal ureterolithiasis: randomized prospective study on role of corticosteroids used in combination with tamsulosin-simplified treatment regimen and health-related quality of life. *Urology.* 2005; 66: 712-715.
- Freeman K, Smyth C, Dallam L, Jackson B. Pain measurement scales: a comparison of the visual analogue and faces rating scales in measuring pressure ulcer pain. *J Wound Ostomy Continence Nurs.* 2001; 28: 290-296.
- Chew BH, Knudsen BE, Denstedt JD. The use of stents in contemporary urology. *Curr Opin Urol.* 2004; 14: 111-115.
- Lang RJ, Davidson ME, Exintaris B. Pyeloureteral motility and ureteral peristalsis: essential role of sensory nerves and endogenous prostaglandins. *Exp Physiol.* 2002; 87: 129-146.
- Maldonado-Avila M, Garduno-Arteaga L, Jungfermann-Guzman R, Manzanilla-Garcia HA, Rosas-Nava E, Procuna-Hernandez N, et al. Efficacy of Tamsulosin, Oxybutynin, and their combination in the control of double-j stent-related lower urinary tract symptoms. *Int Braz J Urol.* 2016; 42: 487-493.
- Lim KT, Kim YT, Lee TY, Park SY. Effects of tamsulosin, solifenacin, and combination therapy for the treatment of ureteral stent related discomforts. *Korean J Urol.* 2011; 52: 485-488.
- Duvdevani M, Chew BH, Denstedt JD. Minimizing symptoms in patients with ureteric stents. *Curr Opin Urol.* 2006; 16: 77-82.
- Dellis AE, Keeley FX Jr, Manolas V, Skolarikos AA. Role of alpha-blockers in the treatment of stent-related symptoms: a prospective randomized control study. *Urology.* 2014; 83: 56-61.
- 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: 1060-1064.
- El-Nahas AR, Elsaadany MM, Tharwat M, Mosbah A, Metwally AH, Hawary A, et al. Validation of the Arabic linguistic version of the Ureteral Stent Symptoms Questionnaire. *Arab J Urol.* 2014; 12: 290-293.
- 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: 651-656.

### Cite this article

Moussa AS, Ibrahim RM, Abdelbary AM, El-Dessoukey AA, Elmarakbi AA, et al. (2017) Tamsulosin to Relieve JJ Stent Related Discomfort: A Prospective Randomized Placebo Controlled Crossover Study. *J Urol Res* 4(4): 1092.