


ORIGINAL RESEARCH

Open Access



# The efficacy of alpha-1A blocker (tamsulosin), antimuscarinic (solifenacin) and their combination in the management of double-J stent-related lower urinary tract symptoms: a randomized controlled study

Elsayed M. Salih , Ayman K. Koritenah, Muhamed Yehya and Mourad M. Mourad

## Abstract

**Background:** The insertion of a double-J (DJ) stent is considered a routine and necessary urological procedure. It can cause lower urinary tract symptoms (LUTS). Pharmacologic management is one of many trials that were done to improve these symptoms, particularly the administration of alpha-1A blockers and antimuscarinics medications. This trial aimed to evaluate the efficacy of alpha-1A blocker (tamsulosin), antimuscarinic (solifenacin), and their combination in managing DJ stent-related LUTS.

**Methods:** This prospective, randomized, comparative, and nonblinded trial was conducted between November 2016 and October 2018. Eligible patients were between 18 and 50 years of both genders who underwent temporary retrograde unilateral Double-J stent fixation. Patients were randomized to four groups; group I was control (drug-free), group II received tamsulosin 0.4 mg, group III received solifenacin 5 mg, and group IV received the combination of tamsulosin and solifenacin. All patients completed the IPSS, QoL, and VAS questionnaires at both pre-insertion day of the stent and 2 weeks postoperatively; the data obtained were compared to all four groups.

**Results:** The study included 143 patients (78 males, 65 females). There was no statistically significant difference between the four groups regarding age, sex, side, and DJ placement indications. In comparison with the control group, there were statistically significant differences in all scores in favor of groups II, III, and IV. Compared to groups II and III, there were statistically significant differences in overall IPSS, QoL, and VAS scores in group IV. No significant differences were found between the tamsulosin and solifenacin groups.

**Conclusion:** The alpha-1A blocker (tamsulosin) or antimuscarinic (solifenacin) monotherapy effectively improves the DJ stent-related LUTS and the QoL of patients with no advantage with either drug. The combination therapy of both pharmacotherapies is significantly effective than drug monotherapy.

**Keywords:** Tamsulosin, Solifenacin, Ureteral stent, Quality of life, Lower urinary tract symptoms

## 1 Background

Introducing Double-J (DJ) ureteral stent is a popular urological procedure. More than five decades have passed since the first mention of a temporary ureteric stent inserted cystoscopically in 1967; since then, indications for its use have continued to expand [1]. The insertion

\*Correspondence: elsayedsalih@gmail.com  
Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

of a DJ stent is considered a routine and necessary urological procedure, which can be used in different ways to treat urinary tract diseases [2]. For instance, it is used to relieve ureteral obstruction due to stones or tumors, post-ureteroscopy lithotripsy, pre-shockwave lithotripsy, or post-percutaneous nephrolithotomy (PNL). The DJ ureteral stent can cause lower urinary tract symptoms (LUTS) even with its beneficial effects, such as frequency, dysuria, urgency, urge incontinence, and suprapubic pain that affects sexual health and quality of life (QoL) in 70–80% of cases [3].

Trials to overcome DJ stent-related LUTS included using the DJ stent's precise length, appropriate placement of upper and lower coil, changing stent material from polyurethane to silicone or other polymers, changing the coating substance or stent design [4]. Pharmacologic management is one of many trials that were done to improve these symptoms, particularly the administration of alpha-1A blockers and antimuscarinics medications [5].

The basis for administering alpha-1A blockers based on the DJ stent-related symptoms' resemblance to benign prostatic hyperplasia-related LUTS [6]. The antimuscarinics (tolterodine and solifenacin) stimulate the muscarinic receptors to control the involuntary contractions of vesical smooth muscle that is a cause of LUTS [7, 8].

Therefore, this trial aimed to evaluate the efficacy of alpha-1A blocker (tamsulosin), antimuscarinic (solifenacin), and their combination in the management of double-J stent-related lower urinary tract symptoms using the International Prostate Symptom Score (IPSS), QoL score, and Visual Analog Scale (VAS).

## 2 Methods

This prospective, randomized, comparative, and non-blinded trial was conducted between November 2016 and October 2018. Eligible patients were between 18 and 50 years of both genders who underwent temporary retrograde unilateral Double-J stent fixation.

Patients who had bladder pathology (like bladder tumor), age less than 18 years, bilateral stents, urethral stricture, benign prostatic hyperplasia, prior use of alpha-blocker and anticholinergics drugs, urinary tract infection, pregnant women, overactive bladder (OAB), history of previous ureteral stenting or long-term stenting were excluded from the study. The local ethics committee approved the research procedure.

An informed consent form was signed by eligible patients who decided to participate in the trial. Patients that developed complications associated with stents were excluded.

A computer randomization software (<http://www.randomization.com/>) was used to assign patients to four

groups: group I control group did not receive any medications, group II received tamsulosin 0.4 mg once daily, group III received solifenacin 5 mg once daily, and group IV received both tamsulosin and solifenacin. The medication was used until the DJ stent was removed.

All patients were evaluated by medical and surgical history, examination, and routine laboratory investigations. In all cases, Percuflex™ 6F DJ ureteral stents (Boston Scientific, USA) were used. The DJ length was determined by the marks on the ureteric catheter inserted from the ureteral orifice to the renal pelvis before the DJ stent fixation.

Routinely, abdominal X-ray film was done to confirm proper DJ positioning before home discharge. The day before operation and 2 weeks after stent fixation, each patient completed written validated IPSS, QoL, and VAS questionnaires.

The VAS is a validated, subjective measure for pain. Scores are verified by creation a hand-written mark on a 10-cm line that denotes a range between “no pain” and “pain as bad as it could possibly be” [9]. We compare the total scores between groups on the pre-insertion day of the stent and after 2 weeks.

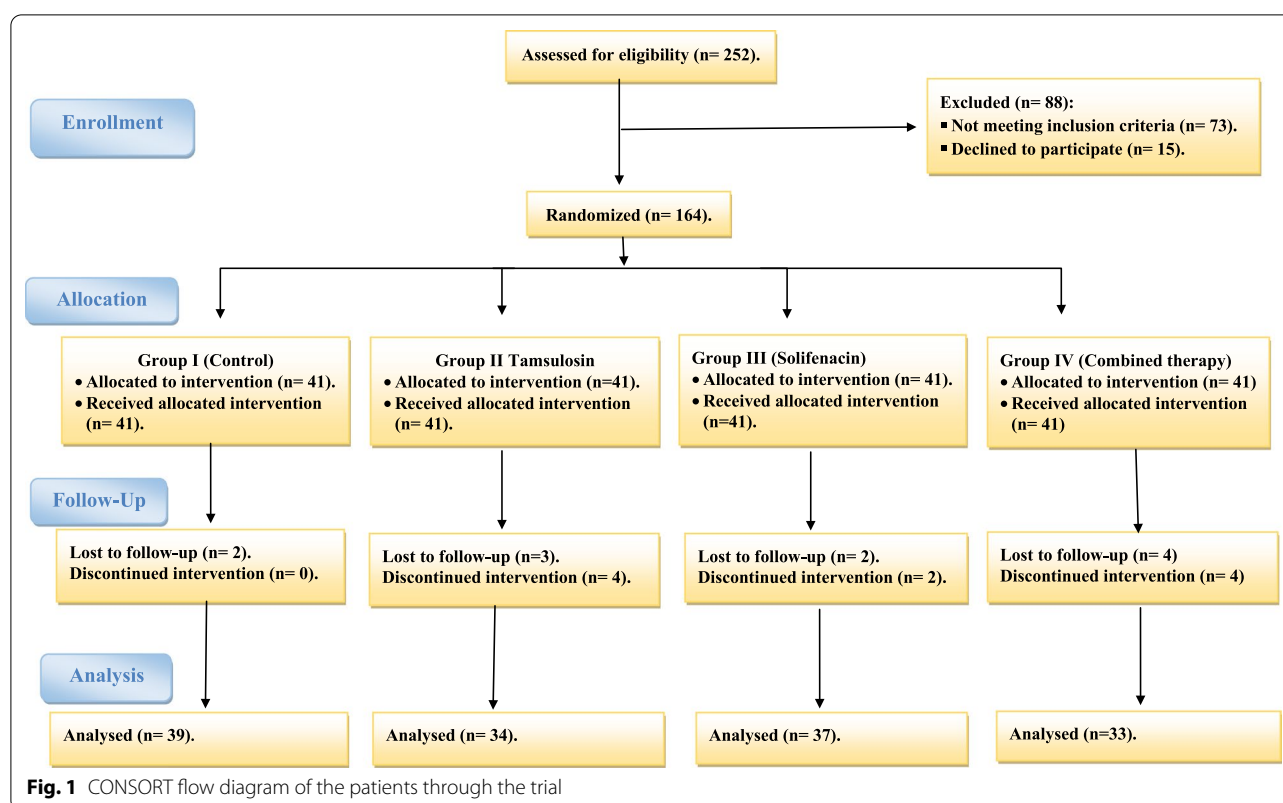
The data collected and analyzed by SPSS (version 24.0, IBM Corporation; Armonk, NY, USA). Categorical variables were compared between treatment groups by Chi-square or Fisher exact tests. Comparisons between multiple groups were made using the Kruskal–Wallis test, and post hoc comparisons were made with adjustment for multiple comparisons. The sample size was calculated with ClinCalc Sample Size Calculator. A sample size of 130 patients was calculated for the power of 0.8, alpha error probability 0.05 and 20% drop-out.

## 3 Results

The total studied patients for eligibility were 252 cases. A total of 164 cases were included in the trial, but 143 patients completed the study. Eleven patients lost to follow up, and ten patients discontinued the treatment. The CONSORT Flow Diagram of the patients through the trial is illustrated in Fig. 1.

The study included 143 patients (78 males, 65 females). There was no statistically significant difference between the four groups regarding age, sex, side, and DJ placement indications. The most frequent indication was ureteroscopy (URS), 65% (Table 1). There was no statistically significant difference between groups as regards stone size and operative time in URS cases.

Regarding IPSS scores, initially (pre-insertion day), there was no statistically significant difference between the four groups. In contrast, after 2 weeks, there was an overall significant difference between the four groups (Table 2). The control group was significantly different

**Table 1** Patients demographics

		Control	Tamsulosin	Solifenacin	Combined therapy	P value
Age	Mean $\pm$ SD	38 $\pm$ 7	39 $\pm$ 1	40 $\pm$ 4	39 $\pm$ 8	0.55
Sex: n (%)	Male	21 (53.8)	20 (58.8)	19 (51.4)	18 (54.4)	0.37
	Female	18 (46.2)	14 (41.2)	18 (48.6)	15 (45.6)	
Side: n (%)	Right	19 (48.7)	16 (47.1)	21 (56.8)	20 (60.6)	0.09
	Left	20 (51.3)	18 (52.9)	16 (43.2)	13 (39.4)	
Indications for stent fixation: n (%)	URS	27 (69.2)	22 (64.7)	21(56.8)	23 (69.7)	0.64
	ESWL	8 (20.5)	9 (26.5)	11(29.7)	7 (21.2)	
	PNL	4 (10.3)	3 (8.8)	5 (13.5)	3 (9.1)	
Stone size (mm) In URS cases	Mean $\pm$ SD	7.7 (1.9)	7.4 (1.9)	8.1 (2.2)	7.8 (1.8)	0.12

URS Ureteroscopy, ESWL extracorporeal shock wave lithotripsy, PNL percutaneous nephrolithotomy

from all the other three groups. The combined therapy group was also statistically significantly different from both tamsulosin and solifenacin monotherapy.

The difference between the tamsulosin and solifenacin groups was not statistically significant. That means tamsulosin alone or solifenacin alone improves DJ stent-related symptoms with no advantage with either medication. At the same time, their combination does a better result than either drug alone in improving DJ stent-related LUTS.

Regarding QoL score and VAS, pre-insertion day of DJ stent, there was no significant difference between the four groups. Meanwhile, after 2 weeks, there was an overall statistically significant difference between the four groups. The control group was statistically significantly different from all the other three groups.

The tamsulosin group was also statistically significantly different from the combination treatment group. The solifenacin group was also statistically significantly different from the combination treatment group. There was

**Table 2** IPSS scores (obstructive, irritative, and total)

	Control Median (Range)	Tamsulosin Median (Range)	Solifenacin Median (Range)	Combined therapy Median (Range)	P-value
<i>IPSS obstructive score</i>					
Pre-insertion	1 (0–3)	1 (0–2)	1 (0–4)	1 (0–3)	0.59
After 2 weeks	13 <sup>a,b</sup> (6–19)	7 <sup>a,c</sup> (0–11)	7 <sup>c,d</sup> (3–12)	4 <sup>b,d</sup> (2–8)	< 0.001
<i>IPSS irritative score</i>					
Pre-insertion	2 (0–4)	2 (0–3)	1 (0–3)	2 (0–4)	0.45
After 2 weeks	11 <sup>a,b</sup> (6–15)	6 <sup>c,d</sup> (3–9)	5 <sup>a,c</sup> (3–8)	4 <sup>b,d</sup> (2–5)	< 0.001
<i>Total IPSS score</i>					
Pre-insertion	3 (0–7)	3 (0–5)	2 (0–7)	3 (0–7)	0.836
After 2 weeks	24 <sup>a,b,c</sup> (12–34)	13 <sup>a,d</sup> (6–20)	12 <sup>b,e</sup> (8–20)	8 <sup>c,d,e</sup> (4–15)	< 0.001

Similar letters (a, b, c, d, e) indicate significant difference

IPSS International Prostate Symptom Score

no statistically significant difference between the tamsulosin group and the solifenacin group. That means both tamsulosin and solifenacin improve the QoL and VAS of patients with no advantage of either medication, while their combination is better than either medication alone (Table 3).

#### 4 Discussion

DJ ureteral stenting has become a routine practice for every urologist. The main advantages of stenting are preventing ureteral obstruction, permitting ureteral healing, and preventing ureteral stricture.

Despite its useful effects, short-term use of a double-J stent is associated with mild complications. In contrast, the complications became more severe in long-term usage, particularly when placed for more than 6 months. Patients usually complain of various stent-related symptoms, such as frequency, urgency, dysuria, incomplete emptying, flank pain, suprapubic pain, incontinence, and hematuria. These symptoms negatively affect the patient's activities, work performance, and QoL [10]. The pathogenesis of the DJ stent-related LUTS has not been verified. Multiple theories were proposed to describe these

symptoms' mechanisms; it might be due to smooth muscle spasm in the lower ureter, irritation of nerve endings located in the trigone of urinary bladder submucosa, and bladder instability [11–13].

Trials to overcome the DJ stent-related LUTS included using the suitable length of the stent, appropriate placement of upper and lower coils, changing stent material from polyurethane to silicone or other polymers, changing the coating substance or stent design. Pharmacologic management is one of many trials to improve those problems; many medical drugs have been tested, such as anticholinergics, analgesics, and alpha-blockers.

In this trial, we aimed to evaluate the efficacy of alpha-1A blocker (tamsulosin), antimuscarinic (solifenacin), and their combination in the management of DJ stent-related LUTS, using IPSS, QoL, and VAS questionnaires.

Our analysis found that, relative to the control group, both alpha-1A blocker (tamsulosin) and antimuscarinic (solifenacin) monotherapy improved patients' DJ stent-related LUTS using IPSS, QoL, and VAS questionnaires. However, their combination was much better than either drug alone. These results were consistent with other studies; Lim et al. conducted a retrospective study that stated

**Table 3** QoL score and VAS

	Control Median (Range)	Tamsulosin Median (Range)	Solifenacin Median (Range)	Combined therapy Median (Range)	P-value
<i>QoL</i>					
Pre-insertion	0 (0–0)	0 (0–1)	0 (0–1)	0 (0–1)	0.31
After 2 weeks	5 <sup>a,b,c</sup> (4–6)	3 <sup>a,d</sup> (1–5)	3 <sup>b,e</sup> (1–5)	2 <sup>c,d,e</sup> (1–3)	< 0.001
<i>VAS</i>					
Pre-insertion	1 (0–2)	1 (0–2)	0 (0–1)	1 (0–2)	0.11
After 2 weeks	7 <sup>a,b,c</sup> (4–9)	4 <sup>a,d</sup> (3–6)	4 <sup>b,e</sup> (2–5)	3 <sup>c,d,e</sup> (1–5)	0.021

Similar letters (a, b, c, d, e) indicate significant difference

QoL Quality of life; VAS visual analog scale

that combined treatment with tamsulosin and solifenacin improved LUTS more than in the other groups (control, tamsulosin, and solifenacin monotherapy) [14].

In a prospective, randomized, and controlled study by Shalaby et al., combined treatment with tamsulosin and solifenacin was confirmed to be substantially better than either drug alone in relieving the DJ stents-related LUTS [11]. EL-Nahas et al. indicated that in patients with DJ stents, tamsulosin alone or solifenacin alone could improve the QoL by reducing LUTS related to DJ stents. Solifenacin has shown better efficacy than tamsulosin. They did not study the efficacy of combined treatment [15].

A meta-analysis performed by Zhou et al. proved a substantial advantage of combined treatment of alpha-blockers and antimuscarinics compared with alpha-blockers monotherapy. Also, they stated a beneficial effect of alpha-blockers alone and antimuscarinics alone in relieving the ureteric stent-related LUTS. After all, higher quality, randomized controlled trials have been recommended to deal with this subject [16].

Liu et al. reported that in the first few days, combination therapy was affected quicker than monotherapy. Based on this analysis, the combination treatment was suggested for patients with severe symptoms at the start [17]. Another study by Dellis et al. reported that tamsulosin and solifenacin monotherapy or combined treatment relieve the DJ stent-related LUTS and improve the QoL [18].

In contrast, Lee et al., a prospective randomized study using a combined treatment of tamsulosin and tolterodine, informed no statistically significant difference compared to placebo. The combined treatment showed no benefit when compared to tamsulosin alone. In their view, the DJ stent's correct positioning was more important than pharmacotherapy for relieving the DJ stent-related LUTS [19].

Also, Park et al. have performed randomized clinical trials to test the effectiveness of tamsulosin, solifenacin and combined treatment in relieving DJ stent-related LUTS. They concluded that neither tamsulosin nor solifenacin positively affected relieving the DJ stent LUTS [20].

Another study reported that anticholinergic (tolterodine) was not different from anti-inflammatory, spasmolytic, and alpha-blockers regulating DJ stent-related LUTS [21]. In contrast to this result, a prospective randomized controlled study by Park et al. stated that the anticholinergic (tolterodine ER) and alpha-blocker (alfuzosin) relieving the DJ stent-related urinary symptoms [8].

The heterogeneity due to differences in surgical procedures was the key drawback of our report. For instance,

post-ureteroscopy DJ placement leads to less pain and hematuria than post-PNL.

## 5 Conclusion

The alpha-1A blocker (tamsulosin) or antimuscarinic (solifenacin) monotherapy effectively improves the DJ stent-related LUTS and the QoL of patients with no advantage with either drug. On the other hand, both pharmacotherapies' combination therapy is significantly effective than drug monotherapy in improving DJ stent-related LUTS and the patients' QoL.

## Abbreviations

LUTS: Lower urinary tract symptoms; IPSS: The international prostate symptom score; QoL: Quality of life score; VAS: Visual analog scale; OAB: Overactive bladder; DJ: Double-J; PNL: Percutaneous nephrolithotomy.

## Acknowledgements

Not Applicable.

## Authors' contributions

ES contributed to the conception, design of the work, data analysis and interpretation, and drafted the work. AK contributed to acquisition, interpretation of data, drafted the work. MY substantially contributed to the conception, acquisition. MM contributed to data analysis, work revision. All authors have read and approved the manuscript.

## Funding

None.

## Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available because that is the policy of our university but are available from the corresponding author on reasonable request.

## Ethics approval and consent to participate

In this prospective study, all procedures performed involving human participants were in accordance with the ethical standards of our institution and the Helsinki Declaration of 1964 and its later modifications or equivalent ethical principles. The study was approved by two ethical committees, the first one in the urology department and the other in the faculty of medicine, Al-Azhar University. No. of ethical committee (IRB): Uro-surg./R/2016/0006.

## Informed consent

Written informed consent was obtained from the patients for their anonymized information to be published in this article.

## Consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

Received: 12 November 2020 Accepted: 11 February 2021

Published online: 23 February 2021

## References

1. Zimskind PD, Fetter TR, Wilkerson JL (1967) Clinical use of long-term indwelling silicone rubber ureteral splints inserted cystoscopically. *J Urol* 97(5):840–844
2. Chew BH, Knudsen BE, Nott L et al (2007) Pilot study of ureteral movement in stented patients: first step in understanding dynamic ureteral anatomy to improve stent comfort. *J Endourol* 21:1069–1075

3. El-Nahas AR, El-Assmy AM, Shoma AM et al (2006) Self retaining ureteral stents: analysis of factors responsible for patients' discomfort. *J Endourol* 20:33–37
4. Lingeman JE, Preminger GM, Goldfischer ER et al (2009) Assessing the impact of ureteral stent design on patient comfort. *J Urol* 181:2581–2587
5. Tehranchi A, Rezaei Y, Khalkhali H et al (2013) Effects of terazosin and tolterodine on ureteral stent related symptoms: a double-blind placebo-controlled randomized clinical trial. *Int Braz J Urol* 39:832–840
6. Deliveliotis C, Chrisofos M, Gougousis E, Papatsoris A, Dellis A, Varkarakis IM (2006) Is there a role for alpha1-blockers in treating Double-J stent-related symptoms? *Urology* 67:35–39
7. Lee YJ, Huang KH, Yang HJ, Chang HC, Chen J, Yang TK (2013) Solifenacin improves double-J stent-related symptoms in both genders following uncomplicated ureteroscopic lithotripsy. *Urolithiasis* 41:247–252
8. Park SC, Jung SW, Lee JW, Rim JS (2009) The effects of Tolterodine extended release and alfuzosin for the treatment of Double-J stent-related symptoms. *J Endourol* 23:1913–1917
9. Downie WW, Leatham PA, Rhind VW, Wright V et al (1978) Studies with pain rating scales. *Ann Rheum Dis* 37:378–381
10. Joshi HB, Newns N, Stainthorpe A, MacDonagh RP, Keeley FX Jr, Timoney AG (2003) Ureteral stent symptom questionnaire: development and validation of a multidimensional quality of life measure. *J Urol* 169:1060–1064
11. Shalaby E, Ahmed AF, Maarouf A, Yahia I, Ali M, Ghobish A (2013) Randomized controlled trial to compare the safety and efficacy of tamsulosin, solifenacin, and combination of both in treatment of double-j stent-related lower urinary symptoms. *Adv Urol* 2013:752382
12. Duvdevani M, Chew BH, Denstedt JD (2006) Minimizing symptoms in patients with ureteric stents. *Curr Opin Urol* 16(2):77–82
13. Thomas R (1993) Indwelling ureteral stents: impact of material and shape on patient comfort. *J Endourol* 7(2):137–140
14. Lim KT, Kim YT, Lee TY, Park SY (2011) Effects of tamsulosin, solifenacin, and combination therapy for the treatment of ureteral stent related discomforts. *Korean J Urol* 52:485–488
15. El-Nahas AR, Tharwat M, Elsaadany M, Mosbah A, Gaballah MA (2016) A randomized controlled trial comparing alpha-blocker (tamsulosin) and anticholinergic (solifenacin) in treatment of ureteral stent-related symptoms. *World J Urol* 34(7):963–968
16. Zhou L, Cai X, Li H, Wang KJ (2015) Effects of  $\alpha$ -blockers, antimuscarinics, or combination therapy in relieving ureteral stent-related symptoms: a meta-analysis. *J Endourol* 29:650–656
17. Liu Q, Liao B, Zhang R et al (2016) Combination therapy only shows short-term superiority over monotherapy on ureteral stent-related symptoms - outcome from a randomized controlled trial. *BMC Urol* 16(1):66
18. Dellis AE, Papatsoris AG, Keeley FX Jr et al (2017) Tamsulosin, solifenacin, and their combination for the treatment of stent-related symptoms: a randomized controlled study. *J Endourol* 31(1):100–109
19. Lee SJ, Yoo C, Oh CY et al (2010) Stent position is more important than alpha-blockers or anticholinergics for stent-related lower urinary tract symptoms after ureteroscopic ureterolithotomy: a prospective randomized study. *Korean J Urol* 51(9):636–641
20. Park J, Yoo C, Han DH, Shin DW (2015) A critical assessment of the effects of tamsulosin and solifenacin as monotherapies and as a combination therapy for the treatment of ureteral stent-related symptoms: a 2 × 2 factorial randomized trial. *World J Urol* 33(11):1833–1840
21. Kuyumcuoglu U, Eryildirim B, Tuncer M, Faydacı G, Tarhan F, Özgül A (2012) Effectiveness of medical treatment in overcoming the ureteral double-J stent related symptoms. *Can Urol Assoc J* 6(6):E234–E237

# Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

**Submit your manuscript to a SpringerOpen<sup>®</sup> journal and benefit from:**

- Convenient online submission
- Rigorous peer review
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

---

Submit your next manuscript at ► [springeropen.com](https://www.springeropen.com)