Effect of tamsulosin for reduction of lower urinary tract symptoms after double J stent insertion

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Key words:- Double J stent, lower urinary tract symptoms, Tamsulosin

Abstract:

Ureteral stent implantation is a common procedure in urological practice, due to the in endourological procedures and extracorporeal lithotripsy. Problems following stent insertion such as stent-related symptoms, migration, fragmentation and encrustation of the stent. The level of complications differs among patients, but mostly it will affect quality of life.al-Adrenergic receptors have been expressed in the human ureter, and specially in the distal ureter. all blockers dilate the lumen and decrease spasms leading to improve stent-related symptoms. The present study was done to evaluate the effect of tamsulosin in improving lower urinary tract symptoms in patients with double-J ureteral stents implantation. This prospective study was performed in Iraq-Babylon in the period from July 2016 to December 2016. Fourty eight patients were enrolled in this study all patients completed the follow up period which was 2 weeks, range of age was (25-50) years . The patients were divided into 2 groups: Group 1: consists of (24) patients include (10) males (14) females were treated with double J stent insertion and analgesic on need without Tamsulosin. <u>Group 2</u>: consists of (24) patients include (13) males (11) female were treated with double J stent insertion and drug therapy (tamsulosin 0.4 mg) daily(by oral rout) for 2 weeks. The results show that there was a significant improvement in lower urinary tract symptoms after the treatment period in the second group of patients (p<0.01), while the first group of the patients without tamsulosin use experience the lower urinary tract symptoms for longer duration. The results also reveal that there is no significant relationship between the patients age and gender with the incidence of lower urinary tract symptoms (p>0.01). In conclusion the use of tamsulosin 0.4 mg daily for 14 days is a safe and well tolerated for stent-related symptoms improvement.

تأثير التامسولوسين في علاج أعراض الجزء الأسفل من الجهاز البولي بعد زراعة دعامة "JJ"

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كلمات المفتاح: - دعامة JJ , اعراض الجزء الاسفل من الجهاز البولي , التامسولوسين

الخلا□ة:

تعد عملية زرع الدعامات في الحالب عملية شائعه من عمليات الجهاز البولي ، بسبب تطور العمليات البولية الداخلية واكتشاف طرق لتفتيت الحصى عن طريق موجات خارجية ، لكن هناك مشاكل تحدث بعد عملية ادخال الدعامة مثل : الاعراض المصاحبة للدعامة ، او تحركها من مكانها او تفتتها او تصدؤها. وان درجة تعقيد هذه المشاكل تختلف باختلاف المرضى ، ولكن غالبا سوف تؤثر على جودة ونمط الحياة الطبيعية .ومن الجدير بالذكر ان مستقبلات الفا-1 الادرينالينية توجد في منطقة الحالب وبصورة خاصة في الجزء البعيد من الحالب ، لذلك فأن استخدام الادوية التي تعمل على غلق هذه المستقبلات سوف توسع تجويف الحالب تقلل التشنج وبالتالي يؤدي الى تخفيف الأعراض المصاحبة لعملية زراعة الدعامة بصورة عامة .

تهدف هذة الدراسة الى تقييم تأثير التامسولوسين من أجل تحسين أعراض الجهاز البولي السفلي للمرضى الذين تم زرع دعامة الحالب "JJ" لهم.

تمت هذه الدراسة المحتملة في بابل – العراق في الفترة من تموز 2016 الى كانون الأول 2016 اخضع ثماني واربعون مريضا للدراسة واكمل جميع المرضى فترة المتابعة والبالغة اسبوعين . المرضى قسموا الى مجموعتين : 100مريض يشملون (10) رجال و 100 نساء تم عملية زرع دعامة "100" لهم .

المجموعة الثانية : 24 مريض يشملون (13) رجال و (11) نساء تم زرع الدعامة لهم مع جرعة تامسولوسين يوميا (0,4)ملغم لمدة اسبوعين .

اظهرت النتائج ان هناك تحسنا كبيرا في الأعراض بعد فترة العلاج للمجموعة الثانية بينما اظهرت نتائج المجموعة الاولى بدون استخدام التامسولوسين أعراض الجهاز البولي السفلي لفترة اطول . بينت النتائج كذلك انه ليست هناك علاقة مهمة بين عمر وجنس المريض مع ظهور هذه الأعراض .

نستنتج من ذلك ان استخدام 0,4 ملغم من التامسولوسين يوميا لمدة 14 يوم هو امن وجيد لتحسين الأعراض المصاحبة لزراعة دعامة 1J.

INTRODUCTION

Urinary tract "Double J" stent (JJ) is a thin, hollow tube placed inside the ureter during surgery to ensure drainage of urine from the kidney into the bladder. J shaped curls are present at both ends to hold the tube in place and prevent migration, it allows the kidney to drain urine by temporarily relieving any blockage, or to assist the kidney in draining stone fragments freely into the bladder if definitive kidney stone surgery is carried out [1]. In spite of thousand advances in stent biomaterials and structure, JJ stents are not free of complications and problems and the search for an ideal JJ stent may remain until this time. JJ stents are usually made from silicon or polyurethran. Ideal stent characteristics are easy insertion, completely internal placement, resistance to migration, easy removing, radio-opacity, biological insertion, and chemical stability, resistance to encrustations, excellent flow characteristics and reasonable price [2]. Stents are used in temporary situations and must be removed from the body. Occasionally, some events occur where communication and follow

up is lost and the patient must be aware that these stents should be removed within six months from the date of insertion [1]. Complications including stent encrustation, stone formation, fragmentation and migration .Stent migration is an uncommon complication. It may occur proximally near the kidney or distally near the bladder. Contributors related to distal stent migration include design and stent material. Stents with a complete coil are less subjected to migrate than those with a J-shape [3].

Factor related to proximal stent migration is stent length .Proximal migration occurs when the stent is too small for the ureter; therefore an adequate choice of the stent length is recommended [4].

Various explanations were proposed to explain the stent breakage. Interaction with urine and extensive inflammatory reaction in situ may play an important role in the initiation and promotion of degradation [5].

Common risk factors for stent encrustations are long indwelling time, urinary sepsis, history of stone disease, chemotherapy, pregnancy, chronic renal failure and metabolic or congenital abnormalities [6].

Stent insertion believed to affect over 80% of patient result in stent discomfort and can vary from one patient to another in an idiosyncratic manner [11],[12]. Several studies in literature describe the symptoms related to ureteral stents such as irritative voiding symptoms including frequency, urgency, dysuria, flank and suprapubic pain, incontinence, and hematuria are included [3],[4]. Stent length seems to play a relevant role in stent-related symptoms since it is directly related to bladder irritation. Many different ways to assess the perfect stent length have been suggested [9].

Frequency is attributed to a mechanical irretation that comes from the bladder coil. Together with urgency, it affects a significant proportion of patients 60%. Daytime frequency characterized by the absence of coexisting nocturia suggests that mechanical stimulation relates to physical activities and awareness of this triggering during the day, which would not be noticeable during the night [7].

urgency is thought to be a direct result from the presence of the stent, which may potentiate pre-existing subclinical detrusor over activity [7]. Dysuria is mainly distinguished at the end of voiding. It was approved that dysuria is secondary due to trigonal irritation by the terminal end of the stent when it pass through the midline or forms an incomplete loop [10].

Flank pain is most likely a result of urine reflux towards the kidney that leads to an excessive rise in intra pelvic pressure that ultimately translates into pain [11], [12]. Supra pubic pain can result from local bladder irritations by the distal coil or as a secondary sign due to complications such as encrustation or infections [13]. Incontinence typically occurs in association with episodes of urgency, or as a result of stent movement beyond the bladder neck into the proximal urethra across the urethral sphincter mechanism of continence [14].

Tamsulosin act by blocking $\alpha 1A$ -adrenoceptors in the prostate and also by blocking $\alpha 1A$ -and $\alpha 1D$ -adrenoceptors in the bladder, which inhibit detrusor muscle contractions. Blocking of adrenergic receptors cause relaxation of bladder neck and prostate smooth muscles,

resulting in improved urine flow rate and limiting lower urinary tract symptoms (LUTS) [15], [16]. Tamsulosin is primarily used for benign prostatic hyperplasia (BPH), but can also assist the passage of kidney stones by the same mechanism of smooth muscle relaxation via alpha antagonism [17].

PATIENTS AND METHODS

This is a prospective follow up study was performed in AL-Hilla teaching hospital in the period from July 2016 to December 2016. 48 patients with double J stent insertion were enrolled in this study; all patients completed the follow up period. Each patient received midazolam I.V. (0.01 mg/kg), ketamine I.V. (0.5 mg/kg), propofol I.V. (2mg/kg), and intubation was done with assist of muscle relaxant rocuronium (0.5 mg/kg) and maintains of anesthesia with isoflurane.

Inclusion criteria patients with double J stent insertion due to different causes . Exclusion criteria were patients with renal or liver dysfunction, hypertension and diabetic.

From each patient the following data were taken: Age, Gender, History , Physical examination as well as Renal and Liver Function Tests. The patients were divided into 2 groups:

- Group 1 consists of (24) patients include (10) males (14) females were treated with double J stent insertion only.
- Group 2 consists of (24) patients include (13) males (11) females were treated with double J stent insertion and drug therapy (tamsulosin 0.4 mg) daily(by oral rout) for 2 weeks. All patients were followed up 2 weeks after treatment.

Outcome measures:

- For measuring lower urinary tract symptoms, the lower urinary tract symptoms questioner was used.
- Outcome measures of tamsulosin efficacy include mean changes of frequency, urgency, nocturia, urge incontinence, small voided volume and dysuria from baseline and their corresponding variation.

Statistical analysis:-

For continuous data; Mean \pm Standard error was implemented.

Mean difference (MD) was used for the continuous outcome data: mean changes for frequency, urgency, urge incontinence, small voided volume, nocturia and dysuria. Data analysis was done by SPSS. Statistical differences were done by using T-test and a *P-value* of less than 0.01 was considered as significant.

RESULTS:-

Table (1) and (2) show the relation of age and sex respectively with the development of lower urinary tract symptoms, the statistical analysis for these data expressed by (mean \pm SE) reveal that there is no significant relationship between the

demographic characteristics of patients' (age and sex) with the need for double J stent insertion and symptoms development .

Table 1: The relation of age with lower urinary tract symptoms (mean \pm SE) .

Age Age	Frequency	Urgency	Nocturia	Urge incontinence	Small voided volume	Dysuria (pain)
25-33	1.4 ±0.18	0.6 ± 0.18	0.4 ±0.18	1.0 ±0.26	1.25 ±0.16	0.75 ±0.31
34-40	1.13 ±0.12	1.13 ±0.29	0.87 ±0.22	1.0 ±0.27	1.0 ±0.33	0.88 ±0.22
41-50	1.43 ±0.20	1.14 ±0.34	1.0 ±0.22	0.86 ±0.26	1.29 ±0.18	1.0 ±0.22

Table 2: The relation of sex with lower urinary tract symptoms (mean \pm SE).

Sympto m Sex	Frequency	Urgency	Nocturia	Urge incontinenc e	Small voided volume	Dysuria (pain)
Male	1.23 ±0.12	1.15 ±0.25	0.62±0.18	0.69±0.17	1.30 ±0.17	0.84 ±0.19
Female	1.4 ±0.16	0.7 ±0.15	0.9 ±0.18	1.30 ±0.21	1.0 ±0.2	0.9 ±0.23

Table (3) show the changes in LUTS in patients groups, control group without tamsulosin and tamsulosin group. The results showed that the larger decrease in LUTS occur with tamsulosin treated group which was significantly reduced in tamsulosin treated group with p value <0.01.

Table 3: Changes in lower urinary tract symptoms (LUTS) in patients' groups (mean \pm SE) .

Symptoms Groups	Frequency	Urgency	Nocturia	Urge incontinence	Small voided volume	Dysuria (pain)
Control (days)	4.5 ±0.16	4.04±0.15	3.8±0.17	3.54±0.18	4.33±0.21	5.41±02
Tamsulosin group (days)	1.29*±0.09	0.91*±0.16	0.75*±0.12	0.95*±0.14	1.20*±0.13	0.83*±0.14

P value <0.01 (*)Mean significant difference.

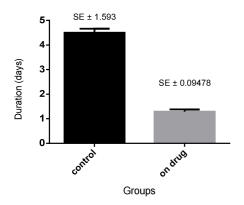


Figure (1): Changes in lower urinary tract symptom (ferquency) in patients' groups.

Figure (2):Changes in lower urinary tract Symptoms (urgency) in patients groups.

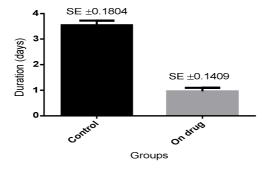
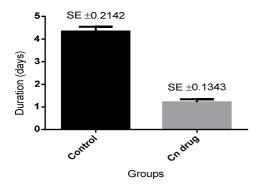


Figure (3): Changes in lower urinary tract symptom (urge incontenance) in patients' groups.



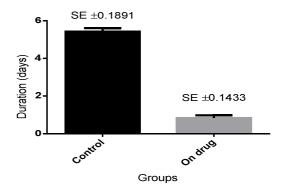


Figure (4):Changes in lower urinary tract symptom (small voided volume) in patients' groups.

Figure (5):Changes in lower urinary tract symptom (dysuria) in patients' groups.

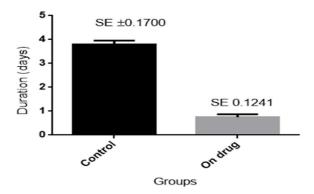


Figure (6): Changes in lower urinary tract symptom (nocturia) in patients' groups.

DISCUSSION:

Ureteric insertion of double J stents are considered an integral part of endoscopic procedures, but the symptoms that result from this procedure such as discomfort and pain impair quality of life (QoL), and many patients consider that this to be the worst part of the procedure. The most commonly occurring symptoms that are flank pain, haematuria, dysuria, frequency, and urgency. The pain and LUTS caused by stent placement have been result from local irritation of the bladder and ureteric mucosa causing smooth muscle spasm and pain also occur due to high pressure ureteric reflux. A unified instrument merging these symptoms was developed to evaluate stent symptoms; the ureteric stent symptoms questionnaire (USSQ) evaluates urinary symptoms, body pain, general health, work performance, sexual matters and additional problems, The Arabic version of the USSQ was previously validated and considered a reliable tool in order to evaluating these symptoms and health-related quality of life in patients with ureteric stents insertion [18]. So, it is used in the present study. It allows for meaningful comparison between the case control without tamsulosin and the case on drug in the ongoing effort to improve stent tolerance. This study focused on some important clinical factors like (demographic data of patients like age and sex in addition to LUTS).

In this study we choose monotherapy selective α_1 blockers (tamsulosin) and compare the efficacy of this drug by measuring the change in LUTS (like frequency ,urgency ,nocturia ,urge incontinence, voided volume, flank pain and pain during voiding) before and after drug administration

The results were as followed:

The Relationship between the Demographic Parameters of the Patients (age and sex) and the Incidence of Lower Urinary Tract Symptoms after double J stent insertion:

The results of this study showed that there is no significant relationship between demographic parameters of patients (age and sex) and the occurrence of LUTS as comparing the results of control group with the result of (tamsulosin) group . Using T-test and P value <0.01

There is no such study that compare the demographic parameters (age and sex) of the patients with the incidence of LUTS

Comparing The effect of selective α_1 blockers (tamsulosin) on lower urinary tracts symptoms with the control group:

The results of this study showed that tamsulosin (0.4 mg/day) oral administration for two weeks post operative reduces the incidence of frequency, urgency, urge incontinence, small voided volume, dysuria and nocturia significantly when comparing the results of control group with the results of second group (on tamsulosin) after drug administration.

These results agree with Wang *et al.*, [19] reported a prospective, randomized study comparing tamsulosin with placebo in 79 patients with double-J stents and found that tamsulosin improved stent-related symptoms and quality of life, and could be applied in routine clinical practice. Also Damiano *et al.*, [20] demonstrated the positive effect of tamsulosin 0.4 mg once daily in improving stent-related urinary symptoms and pain after 1 week of drug use.

Previous studies by Joshi et al., [21]. Coyne et al., [22]. had found an association between the ureteric stent symptoms (USSs) and patients' quality of life and this study also indicated the association, as the improved quality of life may be mainly contributed by the improved urinary symptom and pain index.

CONCLUSION:

In conclusion, the use of tamsulosin 0.4 mg (oral rout) daily for 14 days is a safe and well tolerated for stent-related symptoms improvement after double J stent insertion.

AKNOWLEDGMENTS

Author is thankful to Assist. Prof. Dr. Muhammad R. Judi and Dr. Abbas F. Alhussaini for sharing their knowledge ,and all who participates in this work.

REFERNCES

- [1] Raymond KO.,(2009):complex stone and laser Endourologist laparo endoscopic surgeon. J Endourol .26:25–31.
- [2] Singh I.,(2003): Indwelling JJ ureteral stents-a current perspective and review of literature. Indian J of Surgery; 65: 405-12
- [3] Chew BH, Knudsen BH, Denstedt D.,(2004):The use of stents in contemporary urology. CurrOpinUrol;14:111–5.
- [4] Haleblian G, Kijvikain K, de la Rosette J, Preminger G.,(2008):Ureteral stenting and urinary stone management: a systematic review. J Urol;179:424–30.
- [5] Smedley FH, Rimmer J, Taube M. (1988):168 Double J (pigtail) ureteric catheter insertions: A retrospective review. Ann R. Coll.Surg.Engl;70:377–9.
- [6] Singh I, Gupta NP, Hemal AK. (2001):Severely encrusted polyurethane ureteral stents: management and an analysis of potential risk factors. Urology; 58:526-531.
- [7] Joshi HB, Okeke A, Newns N, Keeley Jr, Timoney AG.,(2002):Characterization of urinary symptoms in patients with ureteral stents. Urology.59:511–9
- [8] Byrne RR, Auge BK, Kourambas J. (2002): Routine ureteral stenting is not necessary after ureteroscopy and uretero pyeloscopy: a randomized trial. J Endourol. 16:9–13.
- [9] Ho CH, Chen SC, Chung SD, Lee YJ, Chen J, Yu HJ. (2008): Determining the Apropriate Length of a Double-Pigtail Ureteral Stent by Both Stent Configurations and Related Symptoms. ccc
- [10] Rane A, Saleemi A, Cahill D, Sriprasad S, Shrotri N, Tiptaft R.,(2001): Have stent-related symptoms anything to do with placement technique? JEndourol. 15:741–4.
- [11] Ramsay JW, Payne SR, Gosling PT, Whitfield HN, Wickham JE, Levison DA.,(1985):Effects of double-J stenting on unobstructed ureter: an experimental and clinical study. Br J Urol. 57:630–4.
- [12] Mosli H, Farsi H, Al-Zemaity MF, Saleh TR, Al-Zamzami MM.,(1991): Vesico-ureteral reflux in patients with double pigtail stents. J Urol. 146:966–9.
- [13] Saltzman B.,(1988): Ureteral stents: indications, variations and complications. UrolClin N Am. 15:481–91.]
- [14] Breau RH, Norman RW.,(2001): Optimal prevention and management of proximal ureteral migration and remigration. J Urol. 166:890–3.
- [15] Lyseng-Williamson KA, Jarvis B, Wagstaff AJ.,(2002):Tamsulosin: an update of its role in the management of lower urinary tract symptoms. Drugs .62:135-167.
- [16] Schwinn DA, Michelotti GA.,(2000): α1-adrenergic receptors in the lower urinary tract and vascular bed: potential role for the α1d subtype in filling symptoms and effects of ageing on vascular expression. BJU Int .85(Suppl2):6-11.
- [17] Jody A.Charnow.,(2011):"Tamsulosin Aids Stone Expulsion". Renal and Urology News.44:425-432.

- [18] El-Nahas A.R., Elsaadany M.M., Tharwat M., Mosbah A., Metwally A., Keeley F.X., Jr.(2014) Validation of the Arabic linguistic version of the ureteral stent symptoms questionnaire. Arab J Urol;12:290–293.
- [19] Wang CJ, Huang SW, Chang CH., (2009): Effects of specific α -1A/1D blocker on lower urinary tract symptoms due to double-J stent: a prospectively randomized study. Urol Res. 37: 147 152.
- [20] Damiano R, Autorino R, De Sio M .(2008): Effect of tamsulosin in preventing ureteral stentrelated morbidity: a prospective study. JEndourol. 22:651-656.
- [21] 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(3):1060–1064.
- [22] Coyne KS, Wein AJ, Tubaro A. (2009):The burden of lower urinary tract symptoms: evaluating the effect of LUTS on health-related quality of life, anxiety and depression:BJU Int.103(s3):4–11.