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THE ROLE OF TAMSULOSIN IN THE TREATMENT OF URETERAL STENT RELATED SYMPTOMS IN BASRAH GENERAL HOSPITAL

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Abstract

This study aimed to evaluate the efficacy of tamsulosin which is an α1-blocker as a therapeutic agent to alleviate ureteral stent related symptoms.

Seventy-two patients were included in this prospective study from August 2018 to August 2019 in Basrah Teaching Hospital. All patients underwent ureteroscopic management of ureteral stones and ureteral stent had been inserted for about one month period. Patients were divided into two groups; a tamsulosin group, and a control group. Then the International Prostatic Symptoms Scores (IPSS) & Quality of life (QoL) were compared after one-month period.

This study shows a significant decrease in the total IPSS, irritative IPSS, obstructive IPSS and the QoL scores with the administration of tamsulosin.

In conclusion: The administration of tamsulosin in patients with ureteral stent is useful in decreasing the ureteral stent related symptoms.

Keywords: Tamsulosin, ureteral stent, IPSS, QoL, α1-blocker

Introduction

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

By definition, the double J or pigtail stent is a self-retaining catheter or tube placed within the ureteral lumen in a retrograde or antegrade fashion in order to maintain its patency[2,3].

Ureteral stents play a major role in a wide range of situations where urinary drainage is needed. Urgent indications include cases of obstructive pyelo-nephritis and intolerable acute renal colic[4].

Safety indications following endoscopic procedures include; ureteral edema or perforation, steinstrasse, history of renal failure, and solitary or transplant kidney[5].

Relative indications would still include; stone burden larger than 2 cm undergoing extracorporeal shockwave lithotripsy, long-standing impacted stone, recent history of urinary tract infection or sepsis, stent to passively dilate the ureter, prolonged endoscopic operative time (over 45 minutes) and any patient with imminent post-operative plans such as a second-look ureteroscopy[6].

However, patients experience various stent-related symptoms, such as pain, frequency, and urgency, which cause a significant decrease in patient health-related quality of life (HRQoL)[7].

Several studies in literature described the symptoms related 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%), suprapubic pain (30%), incontinence and hematuria (25%) are also included[8-10].

The pathophysiology of stent-related symptoms remains unclear. However, the pain and lower urinary tract symptoms (LUTS) caused by stent placement has been attributed to lower ureter and bladder spasm due to local irritation by the stent[11].

It has been proposed that lower urinary symptoms are secondary to trigonal irritation by the distal end of the stent when it crosses the midline or forms an incomplete loop[12].

In a similar way, a recent published randomized clinical trial confirmed that urgency and dysuria were more common with longer stents and negatively impacted the patients' quality of life[13].

To solve these problems, studies have been run in several ways. First, stent material changes have been tried to reduce the symptoms. For example, double-J stents with a tapered distal end made with a hydrophilic material were introduced[14].

A hydrogel coating made of a hydrophilic polymer film attached to the stent surface allows water absorption, increasing the elasticity and decreasing friction in an attempt to ease insertion and enhance patient comfort.

Stickler and colleagues have developed a phosphoryl-choline (PC)-coated stent in an attempt to mimic cell membrane lipids and to increase biocompatibility[14].

Polyurethane shares characteristics common to both silicon and Polyethylene (PE), making a good overall stent material.

Various proprietary polymers are now available including C-flex, Silitek, Tecoflex, and Percuflex. These materials have been developed in an effort to increase biocompatibility and handling.

A further evolution in stent materials has been the design of biodegradable stents, which in theory could eliminate the need for cystoscopic stent removal. The main challenge of this technology has been the inability to reliably control the degradation rate[16].

In addition, studies about the relationship between stent length and morbidity have been reported. If a ureteral stent is needed after endoscopic surgery, ureteral length should be measured so that an appropriate stent can be used in patients, which can reduce distal migration and stent-related symptoms[17].

Mathematic formulas have also been proposed to calculate stent length. Hao, et al. used the following: (length = 0.125x body height + 0.5 cm) or the vertical distance from the second lumbar vertebra to the pubic symphysis minus 2 cm[18].

Hruby, et al. calculated that the xyphoid process to pubic symphysis distance as well as acromium process to the head of the ulna distance could both be used to predict double J length[19].

In the pediatric population, a rule of thumb has been proposed to determine the suitable JJ stent regardless of gender or size, which is simply to add 10 to the age of the patient (stent length = patient age [years] + 10)[20] .

Periureteral injection of botulinum toxin type A after stent insertion has been shown to decrease pain and narcotic requirement[21].

Currently, there is a wide variety of medical treatments to relieve irritative bladder symptoms. They can be directly instilled inside the bladder or taken orally. Intravesical instillation of chemical agents aiming to improve stent discomfort is a relatively recent approach.

Beiko, et al. conducted a double-blind prospective trial on intravesical instillation of one of three chemicals (ketorolac, alkalinized lidocaine, or oxybutynin) versus saline, as control, immediately after stent placement[22].

These stent-related symptoms are similar to the benign prostatic hyperplasia symptoms caused by urethral and bladder

resistance and bladder instability, for this reason, some studies have reported that selective alpha-1-blockers may improve stent-related symptoms[23].

Tamsulosin is a competitive blocker of Alfa-1a/1d receptors that mediated contraction of the smooth muscles in distal ureter, bladder trigone, bladder neck and prostatic smooth muscles , its used to treat LUTS caused by benign prostatic hyperplasia , it is thought that relaxing these smooth muscles decreases bladder outlet resistance and voiding pressure, with beneficial effect on stent symptoms[24,25].

There is a controversy about the usefulness of selective Alfa blockers in relieving ureteral stent related symptoms.

Our aim in this study is to further evaluate the effect of tamsulosin in relieving these symptoms.

Patients and methods

This study was conducted between August 2018 and August 2019, in Basrah Teaching Hospital urology department. For all patients, history taking and clinical examination were done. Laboratory investigations and radiological imaging including intravenous urography (IVU) or Computed Tomography (CT) were used in evaluation of the patients who were presenting with ureteral stone.

The exclusion criteria were benign prostatic hyperplasia, pregnancy, patient with comorbidities (diabetes mellitus, chronic kidney disease CKD, cerebrovascular accident (CVA).

The study included 79 patients who underwent double J (DJ) stenting after ureteroscopic management for ureteral stones without ureteral orifice meatotomy, dilatation or residual stones. An 8 French semi-rigid Storz ureteroscope is used in all cases. The ureteral stent was 4.8 French, 28 centimeter in length and of polyurethane (Coloplast).

Under general anesthesia a ureteroscopic lithotripsy was done using semi-rigid 8 French 6 degree lens angle 43 cm Storz ureteroscope and Calculase II 20W Holmium:YAG laser lithotripsy .

Complete stone fragmentation was performed in all patients and a DJ ureteric stent was inserted by passing a stent that is open at both ends through the working channel of a 22 French Storz rigid cystoscope over an initially placed guide wire which has been passed and advanced up the ureter to the renal pelvis by the ureteroscope then the stent is advanced with a pusher while visually observing the ureteral orifice through the cystoscope. The operative procedure was nearly the same in all patients.

The position of the stent was confirmed by plain X-ray at first postoperative day. The mean of postoperative stent duration was 4 weeks.

At day of discharge from the hospital, we explained the study to the selected patients and took their consent about enrolling in this trial.

These 79 patients were divided by random digit table into two groups, group 1 (tamsulosin group) was 42 and group 2 (control group) was 37 in number, and this information was kept hidden till the time of data analysis.

Both groups were given ciprofloxacin 500 mg twice a day plus Paracetamol 500 mg three times a day for 5 days, Only Group 1 received in addition Tamsulosin 0.4mg (Omnic®) orally once per day till the day of stent removal[15].

At preoperative day of the ureteral stent removal, the stent position for each patient was checked again by plain X-ray.

Seven patients were excluded in this study as the following: one patient from group 1 has slipped DJ stent, three of group1 and three of group 2 were not compliant.

The International Prostate Symptom Score/quality of life (IPSS/QoL) was completed for the remaining patients.

The scores were divided into the total seven IPSS, four obstructive IPSS (Incomplete emptying, Intermittency, Weak stream, Straining), and three irritative IPSS (Frequency, Urgency, Nocturia).

This division is to evaluate each sub-score alone to determine which part of IPSS is the most affected in this trial.

These scores and QoL score were compared for both groups (tamsolusin and control group).

Statistical analysis done using Statistical Package for the Social Sciences (SPSS) v20.0, chi-square test, and the $p<0.05$ was considered statistically significant.

Results

Although the total number of the patient enrolled in this study was 79, 7 patients were excluded from this study because of poor follow-up and the remaining number was 72 and all statistical analysis was related to this number.

The general characteristics of the two groups are shown in table I which include patients age, gender, and ureteric stone location.

The mean age of all patients was 42.79±15.29 years. There were no significant differences between the two groups regarding age, gender, and stone location ($p>0.05$). A total of 72 patients has ureteral stones, 22(30%) had upper, 18(25%) had middle and 32(45%) of them had lower ureteral stones.

The main symptoms were frequency, urgency, nocturia, intermittency and incomplete empting.

The highest score was for frequency and urgency, the mean score was 2.53 for frequency and 2.06 for urgency. The lowest score was for straining and weak stream, the mean score was 0.97 for straining and 1.0 for weak stream.

After comparison of the total IPSS, irritative IPSS, obstructive IPSS and the quality of life score, it was found that these scores were statistically significantly lower in group 1 than in group 2.

In addition the irritative IPSS appeared statistically more significantly decreased than the obstructive IPSS which was the least affected score, as shown in table II.

The side effects of tamsulosin were minimal. No patient discontinued the medication because of the side effects. Seven patients (10%) who were treated with tamsulosin had side effects in form of mild headache and dizziness and the rest of the patients had no side effects related to tamsulosin.

Table I: Basic characteristics of studied patients

Variable	Group 1 (Tamsulosin)	Group 2 (Control)	Total	P Value
No. of patients	38	34	72	>0.05
Mean age±SD (years)	40.03±15.24	45.88±14.97	24.79±15.29	
Gender				
Males	24	21	45	
Females	14	13	27	
Site of stone				
Upper stone	12	10	22	
Middle stone	7	11	18	
Lower stone	19	13	32	

Table II: Comparisons of IPSS, irritative, obstructive and Quality of life in the two groups

Score	Group 1 (Tamsulosin)	Group 2 (Control)	P Value
IPSS (irritative)	4.47±1.92	6.15±1.15	<0.001
frequency	1.63±0.589	2.53±0.710	<0.001
Urgency	1.82±1.625	2.06±0.547	<0.001
Nocturia	1.03±0.677	1.56±0.561	<0.001
IPSS (obstructive)	3.13±1.83	5.09±1.83	0.011
Intermitancy	1.05±0.462	1.56±0.660	<0.001
Weak stream	0.50±0.688	1.00±0.739	0.01
Straining	0.55±0.645	0.97±0.674	0.03
Incomplete empting	1.03±0.592	1.56±0.561	<0.001
IPSS (total)	7.61±2.48	11.24±2.70	0.06
QoL	2.92±0.53	3.55±0.61	0.001

Discussion

Ureteral stents can be used variously in the management of urinary tract diseases. For example, for the prevention of ureteral obstruction and recovery of damaged ureteral tissue[26]. Ureteroscopy, especially after ureteroscopic lithotripsy, routinely necessitate use of ureteral stents[27]. The use of ureteral stents aids in the improvement of urinary tract disease, whereas patients with indwelling stents have been known to complain of a variety of stent-related symptoms Joshi et al reported that, 80% of patients have a reduced Health Related Quality of Life (HRQoL) due to stent-related symptoms[28].

Many methods were used to decrease the ureteral stent related symptoms including the intravesical medication, periureteral orifice injection of botulinum toxin, biodegradable stents[21].

Medications to decrease morbidity should be regarded as a palliative adjunctive approach, but seem to be a more reachable solution in the short-term. In this study we used the tamsulosin because of its availability, simple rout of administration (oral) minimal side effects.

Since I-PSS introduction in 1992, the American Urological Association (AUA) symptom index has been widely used and validated as an important means of assessing men with lower urinary tract symptoms. The original AUA symptom score is based on the answers to seven questions concerning frequency, nocturia, weak urinary stream, hesitancy, intermittency, incomplete bladder emptying, and urgency. The International Prostate Symptom Score (I-PSS) includes these seven questions, as well as a global quality-of-life question.

The I-PSS is a helpful tool both in the clinical management of men with lower urinary tract symptoms and in research studies regarding the medical and surgical treatment of men with voiding dysfunction. In addition, the symptom score and obstructive and irritative voiding symptoms are nonspecific, and the symptoms may be caused by a variety of conditions other than BPH. the I-PSS is a simple adjunct in assessing men with lower urinary tract symptoms and may be used in the initial evaluation of those with lower urinary tract symptoms, as well as in the assessment of treatment response[29].

In this study, the patients were prospectively assessed for lower urinary tract symptoms including the IPSS/QoL, which was chosen because of its validity and reproducibility.

Also the IPSS score was subdivided into: Irritative score include the summation of the scores of frequency, urgency and nocturia. Obstructive score includes the summation of the scores of incomplete empting, intermittency, week stream and straining.

This division was to find which symptom category was more affected by tamsulosin.

These symptoms were compared between tamsulosin and control groups just before the stent removal (preoperative day) to eliminate the patients incompliance and the difficulties of patients follow up before the date of stent removal.

The result of this prospective randomized control trial shows that ureteral stent related symptoms including irritative, obstructive and the Quality of life are significantly reduced with the use of tamsulosin.

This result goes with that of Deliveliotis et al. who concluded that selective alpha-blockers such as alfuzosin improve stent-related symptoms, sexual function and general health[30].

Also Damiano et al performed a prospective randomized study comparing the efficacy of tamsulosin versus placebo for stent-related symptoms. The stent-related morbidity was evaluated with IPSS/QoL questionnaire; they reported that tamsulosin had positive effects on stent-related urinary symptoms and QoL[23].

Shelbaia et al, showed similar results and concluded that the IPSS scores were significantly lower and the QoL scores were significantly better in patients who received tamsulosin[31].

Wang et al, in prospective randomized study comparing tamsulosin to placebo also reported that tamsulosin improved the stent related urinary symptoms, QoL, and they recommended its routine use[32].

While Kyoung Taek Lim et al, reported that the IPSS total score, irritative subscore, QoL, and visual analog pain scale (VAPS) had show no statistically significant differences. However, the difference in the obstructive subscore was statistically significant[33].

On the other hand, Kuyumcuoglu et al reported in a prospective randomized study that tamsulosin was not different than placebo in controlling stent-related symptoms[34].

The limitations of this study were; small patient sample, the IPSS completed only at the day of stent removal.

Conclusion:

The administration of tamsulosin which is a selective α1-blocker is useful in decreasing lower urinary tract symptoms that follow the insertion of ureteral stent after ureteroscopical stone managements.

Recommendations :

Tamsulosin could be considered for patients who complain of stent-related symptoms.

However, there is a need for further studies to compare the effectiveness of combination of different alpha blockers and antimuscrinic agents in order to optimize medical therapy for treatment of symptoms related to stent placement.

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