### The Role of Alpha Blocker Drugs in Reducing Double J Stent Related Symptoms

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#### ABSTRACT

*Objective*: To determine the effect of alpha blocker drugs on reduction of Double J Stent related symptoms. *Study Design*: Quasi-experimental study.

*Place and Duration of Study*: Department of Urology, The Kidney Centre, Post Graduate Training Institute, Karachi Pakistan, from May 2014 to Nov 2019.

*Methodology*: Total 92 patients who had unilateral stent, inserted retrograde or antegrade, were studied. On 7<sup>th</sup> postoperative day double J stent related symptoms were documented on Ureteral Stent Symptom Questionnaire and alpha-blocker was started if score is >10. After 4 weeks, data was again collected to assess mean change in Ureteral Stent Symptom Questionnaire score.

*Results*: Of 92 patients, pre-treatment mean Ureteral Stent Symptom Questionnaire score was  $38.36\pm16.07$  and post treatment was  $14.87\pm8.62$ . Mean difference between pre and post Ureteral Stent Symptom Questionnaire score was found significant (p<0.05).

Conclusion: Administration of Tamsulosin has a positive effect on stent related urinary symptoms and quality of life.

Keywords: Alpha blockers, Double J stent, Tamsulosin, Ureteral stent, Ureteric stent symptoms questionnaire.

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#### INTRODUCTION

Double-J ureteral stents are widely used for the treatment of urinary obstructions. Pressure, bladder irritation and fever are typically symptoms of early complications linked to double-J stents; late complications are more problematic.1 Overall quality of life (QOL) is compromised in up to 80% of patients with ureteral stent.<sup>2</sup> Ureteric stents have become part of routine urological armament, but stent-related pain is documented in a high proportion of patients with detrimental effects of different amplitudes on their health-related quality of life (HRQoL).3 The need for accurate instruments to quantify the symptom complex objectively and to determine its effect on everyday activities is therefore warranted. To mitigate stent morbidity, some groups have proposed that stent position and length must be sufficient.<sup>4</sup> Others proposed that a-blockers and anticholinergics would be successful while others attempted intravenous instillation of periureteral injection or chemical agents of botulinum toxin.5 Adrenergic antagonists, calciumchannel blockers, and corticosteroids have been commonly used as a first-line treatment in clinical

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trials on the basis of their effect on the ureter, which includes the reduction of ureteric oedema and ureteric peristalsis around the stones.<sup>6</sup> However, the best effects are obtained by adrenergic antagonists, in particular Tamsulosin, which is selective in the case of  $\alpha$ 1-D receptors.<sup>6</sup>

Tamsulosin is feasible, since these receptors are also abundant in the lower third of the ureter.<sup>7</sup> The use of a-blockers to prevent stent related symptoms is based on the similarity of these symptoms to benign prostatic hyperplasia related lower urinary tract symptoms, including frequency, urgency, and suprapubic pain, induced by spontaneous contraction. It has been suggested that the use of selective ablocker, such as alfuzosin or Tamsulosin, can improve the urinary symptoms associated with stent, especially pain. Sexual function and overall wellbeing can also be best managed.8 Joshi et al.9 have created and internally validated the Ureteric Stent Symptoms Questionnaire (USSQ), a self-governing multidimensional method that examines stent-related morbidity. Subsequently, the use of the USSQ made it possible to distinguish signs related to particular stent vendors and to quantify and compare their variations as a sensitive instrument. A pair-wise meta-analysis of randomized controlled trials (RCTs) has indicated that orally

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administrated alpha-blockers reduce stent-related discomfort and storage symptoms as measured by the Ureteric Stent Symptoms Questionnaire (USSQ).<sup>10</sup> It is well documented in literature that those patients who underwent DJ stenting developed various urinary symptoms, body pain and affect quality of life. In view of the previous studies, we aimed to determine the change of before and after Tamsulosin in patient with DJ stent with related symptoms.

# METHODOLOGY

The quasi-experimental study was conducted at the Department of Urology, The Kidney Centre, Post Graduate Training Institute, Karachi Pakistan, from May 2014 to November 2019. Sample size was estimated using proportion of effect of Ultrasound insertion on QOL as 80%2. The consecutive sampling technique was employed. Ethical committee approval was taken before commencement of work (Reference No. 06-URO-082013). Informed consent was taken from all study participants.

**Inclusion Criteria:** Patients of either gender, aged 18– 50 years, who had unilateral double J stent related Lower urinary tract symptoms (LUTS) such as frequency, urgency, nocturia, weak stream, intermittency, sense of incomplete bladder emptying, hesitancy and dysurea, irrespective of indication of JJ stenting, and USSQ Score >10 were included in the study.

**Exclusion Criteria**: Patients with bilateral JJ stent placement, prior history of JJ stent placement, with urinary tract infection or any other bladder pathology like (bladder tumor, bladder stone, neurogenic bladder etc.), already taking alpha blockers or analgesics (pain killers), and with prior LUTS of International Prostate scoring system (IPSS) >8 were not included in the study.

The same double J ureteral stent design, consisting of biocompatible aliphatic polyurethance (Urotech, Achenmuhle), was administrated and confirmed on next day of insertion by X-ray to all enrolled patients in the study. All patients were discharged as per routine protocol, on regular pain killer of same group. Postoperatively, on 7<sup>th</sup> day double J stent related symptoms were documented on USSQ and alpha-blocker was started if USSQ score was >10. After 4 weeks with treatment by alpha-blockers, all patients were reviewed and data was again collected on USSQ proforma to assess mean change in USSQ score. Mean change was determined by experienced consultant surgeon or principal investigator under the supervision of consultant by

comparing pre and post use of alpha blockers on the basis of USSQ score.

The data was analyzed using Statistical Packages of Social sciences (SPSS) version 23. Mean and SD were calculated for age and USSQ score at baseline and post use of alpha blocker drug. Frequency and percentage were calculated for gender. Paired t-test was applied to compare the USSQ score pre and post used of alpha blocker. Pre and post treatment USSQ score was compared using paired t-test. The *p*-value of  $\leq$ 0.05 was taken as significant.

# RESULTS

Of 92 patients, 59(64.1%) were males and 33(35.9%) were females. The overall mean age of study subjects was 35.57±10.73 years. Thirty seven patients (40.2%) were ≤30 years of age, 27 patients were 31–40 years of age (29.3%), and 28 patients were >40 years of age (30.4%), respectively. The mean age of male patients was 35.47±10.64 years and mean age of female patients was 35.73±11.05 years. Pre and post treatment with  $\alpha$ -blocker (Tamsulosin) USSQ Score was evaluated. Pretreatment, it was observed that mean USSQ score was 38.36±16.07 (Range: 12-77). Post treatment it was observed that mean USSQ score was 14.87±8.62 (Range: 3-32). The USSQ score significantly reduced after treatment with  $\alpha$ -blocker (Tamsulosin) (*p*=0.001) as shown in Table-I.

Table-I: Comparison of Baseline and Post Treatment Ureteric
Stent Symptoms Questionnaire Score (n=92)

USSQ score	Pre Treatment	Post Treatment	<i>p</i> -value
	38.36±16.07	14.87±8.62	0.001*

USSQ Score was also evaluated according to gender and age groups. In male (p=0.001) and female (p=0.001) patients, mean USSQ score was significantly decreased after treatment. In all age groups, mean USSQ score was significantly decreased after treatment (p<0.05) as listed in Table-II.

Table-II: Comparison of Baseline and Post Treatment Ureteric Stent Symptoms Questionnaire Score with Respect to Age and Gender (n=92)

Age groups	Pre-treatment USSQ	Post-treatment USSQ	<i>p</i> -value
≤30 years	38.73±15.73	14.08±9.01	0.001*
31-40 years	37.44±18.43	15.63±8.43	0.001*
>40 years	38.75±14.57	15.18±8.52	0.001*
Gender	Pre-treatment USSQ	Post-treatment USSQ	<i>p</i> -value
Male	42.29±14.91	16.03±8.30	0.001*
Female	31.33±15.88	12.79±8.92	0.001*

# DISCUSSION

Double-J stents have been commonly used for numerous purposes for more than two decades. Complications related to the use of ureteral stents are mainly mechanical. Stent occlusion can be frequent and involves a quick swap of catheters. Notwithstanding of the initial sign for stent placement, transurethral cystoscopic exchange is typically an easy and successful procedure for occlusion.<sup>11-12</sup> Up to 80% of patients with ureteral stents have a full variety of urinary tract complications shortly after insertion, as determined by validated questionnaires.<sup>13</sup>

Literature reported the symptoms related to ureteric stents, including frequency (50-60%), urgency (57-60%), dysuria (40%), incomplete emptying (76%), flank (19-32%) and suprapubic pain (30%), incontinence and hematuria (25%).14 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 Urinary Symptom Score Questionnaire (USSQ) QoL questionnaire. The authors reported that Tamsulosin had positive effects on stent-related urinary symptoms and QoL.15 In our study, all patients tolerated the ureteric stents for the 4 weeks postoperative period. The USSQ scores were significantly lower and the QoL scores were significantly better in patients who received Tamsulosin.

In this study, Tamsulosin was chosen from among the available a-blockers because it is a combined a1A and a1-D selective adrenergic antagonist, taking into account studies that have demonstrated the existence of a1A and a1-D adrenoceptor sub types in the smooth muscle cells of the human ureter. Tamsulosin increases the urine bolus and intraureteral pressure above the stone. It also decreases peristalsis below the ureter, which consequently lowers intraureteral pressure in association with the decrease in basal and micturition pressure, even at the bladder neck; thus, it increases the chance of stone expulsion. Furthermore, the phasic peristaltic contractions also decrease in the obstructed ureter, which leads to an eventual decrease in the painful stimulus. Several studies in the past decade investigated the issue.<sup>16</sup>

In a meta-analysis of five studies by Lamb *et al.*<sup>17</sup>, there was a substantial decrease in USSQ concerning body pain and urinary symptoms, although there was a significant increase in sexual activity and general health. Thus,  $\alpha$ -blockers are related with betterment in ureteral stent symptoms and encourage their use in

normal clinical practice. Whereas, another metaanalysis by Yakoubi *et al.*<sup>18</sup>, twelve trials which found somewhat different findings, found reduction in urinary symptoms and pain while also betterment in general health in patients treated with  $\alpha$ -blockers. In current study pre and post treatment [ $\alpha$ -blocker (Tamsulosin)] the USSQ Score was evaluated and score significantly decreased after treatment (p<0.05). Furthermore, with respect to age and gender, change in USSQ score showed significant decrease after treatment (p<0.05).

### LIMITATION OF STUDY

There were many drawbacks to our analysis. First, our sample size, second, just for Tamsulosin, not for novel agents or drug formulations, we measured the effect on the lives of patients. Finally, no adverse effects caused by the use of a-blockers were formally assessed, and no patients stopped the drug because of side effects. Provided that new agents have already emerged in the family of alpha-blockers, it remains to be answered if they could provide more in the treatment of stent-related symptoms as well as other drugs or drug combinations of current or potential drugs. We applied stents of the same size and length, while we were also able to use various stent sizes proportionate to the length of the patient. The stenting period was different and revealed that the conditions associated with the stent remained constant for a few days.

### CONCLUSION

While several advancements in stent innovation have been made, in most patients, stent-related morbidity is a reality. It has been shown that oral administration of alphablockers alleviates stent morbidity. This study suggests the use of a selective alpha1-blocker, such as Tamsulosin, to enhance urinary symptoms associated with ureteric stenting following ureteroscopy and ureteric stone removal. The latest USSQ is a legitimate and accurate technique that is intended to become a common outcome test for stent impact evaluation. Our results suggest that Tamsulosin administration has a beneficial effect on urinary symptoms and QoL associated with stenting.

### Conflict of Interest: None.

### Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

WAM & AHK: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

SEK & A: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SS, JS & KA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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