

# Effects of Mirabegron versus Tamsulosin in Reducing Lower Urinary Tract Symptoms in patients with Indwelling Double J Stents

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## ABSTRACT

**Aim:** To compare the mean IPSS score after treatment with tamsulosin versus mirabegron in patients with double J stent related lower urinary tract symptoms.

**Study design:** Randomized controlled trial.

**Place and duration of study:** Department of Urology Shaikh Zayed Hospital, Lahore from 2<sup>nd</sup> May 2019 to 1<sup>st</sup> November 2019.

**Methodology:** One hundred patients of both genders aged between 18-60 years having DJ stent related symptoms (IPSS score  $\geq 7$ ) were enrolled. Patients were randomized into 2 groups based on treatment. Patients in Group A were given mirabegron while the one in Group B were treated with tamsulosin. Outcome variable was mean IPSS score 3 weeks after treatment which was noted and compared between the groups.

**Results:** The mean age was  $38.6 \pm 10.9$  years. There were 59 (59.0%) male and 41 (41.0%) female patients with a male to female ratio of 1.4:1. The IPSS score at baseline ranged from 14 to 23 with a mean of  $18.18 \pm 2.77$ . The follow-up IPSS score was significantly lower in patients treated by mirabegron as compared to tamsulosin ( $6.28 \pm 0.86$  vs.  $9.60 \pm 0.86$ ;  $p$ -value  $< 0.001$ ). Similar significant difference was noted between the groups across various subgroups based on patient's age, gender and baseline IPSS score.

**Conclusion:** Mirabegron was superior to conventional practice of tamsulosin in the treatment of DJ stent related symptoms in terms of significantly lower mean IPSS score after 3 weeks of treatment.

**Keywords:** DJ stent, Lower urinary tract symptoms, Mirabegron, Tamsulosin

## INTRODUCTION

Intramural application of ureteral-stents is considered as a routine procedure in various urological settings. Ureteral-stents assists in preserving the urinary flow in intrinsic and extrinsic conditions and manage the urine obstruction. Protection of the kidney from possible risks and restart of urine transport will also be the result of ureteral stent placement in patients with obvious ureteral obstruction. After an endoscopic and reconstructive procedure, the stents also prevent urinary obstruction and extravasation<sup>1</sup>.

Various comorbidities including flank pain, hematuria, encrustation as well as dysuria, infection and migration are result of stents. For an efficient stent it is important that the material of which the stent is made relieve intraluminal, biocompatible, radiopaque. In addition to this it can prevent extra-luminal obstruction, and resist the encrustation as well as infection. There might be a small discomfort involved but those stents with all aforementioned properties and economically beneficial are recommended the most. Unfortunately, the available stent materials did not meet the declared criteria<sup>2</sup>. Stents are reported to effect lower urinary-tract symptoms including urgency to urine with higher frequencies. Conditions like hematuria, pain, poor life quality and anxiety are accompanied with the Stents application.<sup>3</sup> Renal pelvis is affected by feeling of pressure and trigonal-irritation<sup>4</sup>. Length and positioning of the stent are considered as the factors which can minimize comorbidities related with stents.<sup>5</sup> For the treatment of irritative bladder symptoms, antimuscarinic agents and  $\alpha$ -blockers are routinely used.

Recently, a  $\beta$ -3 receptor agonist (Mirabegron) is currently available and approved for this purpose. As the stent-related symptoms are similar to overactive bladder symptoms, there is theoretical advantage to reduce pain or irritable symptoms due to stent placement by using Mirabegron<sup>6</sup>. Mirabegron's preclinical profile has been well described in vivo and in vitro. In animal models it increases bladder compliance, inter-voidal intervals and also reduces non-micturition contractions in the bladder thereby preserving active voiding functions. On the contrary  $\alpha$ -1a and also 1-d receptors are present on distal-ureter, bladder-trigone as well

as on the proximal part of the urethral smooth-muscles. By selective inhibition of these receptors tamsulosin causes relaxation of these smooth muscles and decreases bladder outlet resistance and hence decreases voiding pressure. As a result it decreases renal reflux and voiding symptoms<sup>7</sup>.

In one study mean IPSS score before treatment with mirabegron was  $14.37 \pm 8.47$  and after treatment with mirabegron it was  $5.02 \pm 9.387$ . In other study IPSS score before treatment with tamsulosin was  $3.55 \pm 0.63$  and  $5.90 \pm 0.69$  after treatment.<sup>1</sup> According to another study IPSS score before treatment with tamsulosin was  $12.77 \pm 4.79$  while after treatment with tamsulosin it was  $12.77 \pm 5.24$ <sup>4</sup>.

The rationale of this study is determining the effects of mirabegron on comparison to tamsulosin for decreasing double-J stent associated lower-urinary tract symptoms in terms of change in mean IPSS Score, leading to increase patient comfort and reduce hospital stay.

## MATERIALS AND METHODS

This prospective randomized controlled trial was conducted at Department of Urology, Shaikh Zayed Hospital Lahore from 2<sup>nd</sup> May 2019 to 1<sup>st</sup> November 2019. A total of 100 cases (50 cases in each group) were calculated with 95% confidence interval and 80% power of test while taking expected mean IPSS score after treatment to be  $12.77 \pm 5.24$ <sup>4</sup> in tamsulosin group and  $5.02 \pm 9.387$ <sup>1</sup> in mirabegron group. All patients who were 18 to 60 years of age, both sexes and double-J stent placement during last 2 weeks having lower urinary tract symptoms were included. All patients who were known allergic to mirabegron or tamsulosin, undergone ureteral stent placement previously which might cause false perception of symptoms, benign prostatic enlargement diagnosed on clinical evaluation which was causing persistence of lower urinary tract symptoms, any bladder pathology for example diagnosed bladder cancer, overactive bladder that had already been diagnosed by urodynamics might cause false perception of symptoms, overactive bladder (already diagnosed by urodynamics) due to false perception of symptoms, urinary tract infection diagnosed on urine culture (10<sup>5</sup> or high growth/HPF) and neurogenic bladder or any psychiatric disease were excluded.

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The drugs were packed by pharmacologist in boxes and each box was labelled with number of the group members such as 1 and 2. There was no change in box size or shape. Each patient was administered randomly an un-named drug from a numbered box. Each patient was already intimated about drug side effects and not of the group number. Mirabegron was administered randomly as group 1 in a 50 milligram OD dosage while in group 2 the 400 micrograms tamsulosin in OD was given in accordance to British National Formulary 67. A single injection of NSAID (Ketorolac 30 mg) with a acetaminophen tab prescription was given in case of acute unbearable pain. Patients were further requested for completing the IPSS based questionnaire post 3 weeks' time and the score was recorded. All the collected data was entered and analyzed through SPSS-21. Independent sample t-test has been applied to compare the mean IPSS score after 3 weeks of treatment between the study groups taking p-value  $\leq 0.05$  as significant.

## RESULTS

The age of the patients ranged from 20 years to 60 years with a mean of  $38.6 \pm 10.9$  years. Most of the patients were aged between 40-60 years (53%) followed by 20-39 years (47%). There were 59(59%) male and 41(41%) female patients and male female ratio of 1.4:1. The IPSS score at baseline ranged from 14 to 23 with a mean of  $18.18 \pm 2.77$  (Table 1). The follow-up IPSS score was significantly lower in patients treated by mirabegron as compared to tamsulosin ( $6.28 \pm 0.86$  vs.  $9.60 \pm 0.86$ ; p-value  $< 0.001$ ) [Table 2].

Table 1: Demographic information of the patients (n=100)

Characteristics	No.	%
<b>Age (years)</b>		
20-39	47	47.0
40-60	53	53.0%
<b>Gender</b>		
Male	59	59.0
Female	41	41.0
<b>IPSS Score at Baseline</b>		
14-18	55	55.0
19-23	45	45.0

Table 2: Comparison of mean IPSS score follow-up IPSS score in both groups

IPSS score after 3 Weeks	Mirabegron	Tamsulosin	P value
	$6.28 \pm 0.86$	$9.60 \pm 0.86$	$< 0.001$

## DISCUSSION

Ureteral-Stents is an efficient application of indwelling and endoluminal splint. It was earlier described in the work of Zimskind et al.<sup>1</sup> Previously the intention in its application was for treating urinary obstruction or for fistula treatment.<sup>1,8</sup> With advancement of research the application of the stents enhanced parallel to the development of techniques like extracorporeal shockwave-lithotripsy (ESWL) and permitted the endo-luminal based investigation in various urinary tract ailments<sup>9</sup>. In advanced years there are number of indication for placement of ureteral-stent.<sup>8-10</sup> However with the proper understanding of these stents there has been a high level knowledge about the complication and unfavorable consequence involved<sup>11-13</sup>.

Many patients with ureteral stents develop lower urinary tract symptoms which adversely affect the patient's quality of life.<sup>11</sup> Lower urinary-tract symptoms (LUTS) incidence following the placement of D-J stent is 50%–70%.<sup>1,3,11</sup> Tamsulosin is routinely used drug for the treatment of LUTS in such cases<sup>4</sup>. Mirabegron is a novel, once-daily, orally active, first-in-class and potent  $\beta_3$ -adrenoceptor agonist recently approved by Food and Drug Administration for overactive bladder therapy. The mirabegron was superior to the conventional practice of tamsulosin for the management of DJ stent related LUTS in terms of significantly lower mean IPSS score among such cases after 3 weeks of treatment<sup>6,7</sup>.

The current study results interpret mean patient age undergoing double J stent insertion was  $38.6 \pm 10.9$  years. Ahmad et al<sup>14</sup> has reported DJ Stent placement patients mean age as  $40 \pm 10.4$  years, which is similar to current research data among aforementioned patients at Bahawal Victoria Hospital Bahawalpur. Khan et al<sup>15</sup> reported slightly lower mean age of  $34.5 \pm 8.9$  years among patients undergoing ureteral stenting at PNS Shifa Karachi. A similar mean age of  $38.35 \pm 9.23$  years was observed by Tehranchi et al<sup>16</sup> in Iranian patients undergoing DJ stenting. However, higher mean age has been reported by Shabeena et al<sup>17</sup> in 2018 ( $42.5 \pm 12.6$  years) in Indian population, Kuyumcuoglu et al<sup>1</sup> in 2012 ( $45.21 \pm 3.05$  years) in Turkish population, Lim et al<sup>4</sup> in 2011 ( $49.87 \pm 13.29$  years) and Park et al<sup>18</sup> in 2009 (47.7 years) in Korean Population.

The gender ratio observation was 1:4:1 and presented results where 59% males and 41% females were included in the research. Scarneci et al<sup>19</sup> also reported similar gender ratio in their study. Ahmad et al<sup>14</sup> stated male to female ratio as 1.6:1 within DJ stent patients at Bahawal Victoria Hospital Bahawalpur. Male are reported to be predominant in various studies such as of Kuyumcuoglu et al<sup>1</sup> reported that male to female ratio was 1.3:1. Similarly in similar patient groups Lim et al<sup>4</sup> (1.3:1) and Park et al<sup>18</sup> (1.5:1) as well as Tehranchi et al<sup>16</sup> (2.2:1) in reported similar ratio gender ratio finding in their researches. Khan et al<sup>15</sup> found 5:1 male to female ratio while Shabeena et al<sup>17</sup> from India also reported in 2018 a higher male cases undergoing DJ stent placement than female cases with a gender ratio as 5.5:1.

In the present study, the follow-up IPSS score was significantly lower in patients treated by mirabegron as compared to tamsulosin ( $6.28 \pm 0.86$  vs.  $9.60 \pm 0.86$ ; p  $< 0.001$ ). Similar significant variance was noted between the groups across various subgroups based on patient's age, gender and baseline IPSS score. Our observation is in line with that of Tae et al<sup>6</sup> also reported similar significantly lower mean IPSS score after mirabegron treatment in Korean patients with LUTS related to ureteral stents ( $5.0 \pm 9.4$  vs.  $8.4 \pm 8.3$ ; p  $< 0.05$ ). Sahin et al<sup>20</sup> observed similar significantly lower mean IPSS score following treatment with mirabegron compared to combination therapy consisting of tamsulosin and solifenacin ( $13.7 \pm 4.9$  vs.  $15.6 \pm 4.4$ ; p = 0.001) in Turkish patients with DJ stent related low urinary tract symptoms.

## CONCLUSION

Mirabegron was identified as dominant/superior to the conventional practice of usage of tamsulosin in DJ stent related symptoms in terms of significantly lower mean IPSS score after 3 weeks of treatment which advocates its preferred use in the management of such patient's in future urological practice.

**Conflict of interest:** Nil

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