Original Article

Role of Solifenacin in Unilateral Double-J Stent Related Irritative Lower Urinary Tract Symptoms

Hamza Ashraf[1], Muhammad Shahab[2], Noor ul Hayat[3], and Kafeel Azhar[4]

ABSTRACT

Objective: To evaluate the efficacy of Solifenacin 5mg daily compared to placebo in patients with Irritative LUTS secondary to DJ stent in situ assessed by storage IPSS.

Study Design: Randomized Controlled study

Place and Duration of Study: This study was conducted at the Urology Unit, Benazir Bhutto Shaheed Teaching Hospital, Abbottabad from Nov 2019 May-2020.

Materials and Methods: Sample size is 76 in each group, using WHO software for sample size determination in healthy studies, applying the formula of hypothesis test, for two population proportions (one- sided) with the following assumption:[9]

Significance level = 5%

Statistical power = 80%

Proportion of patients with LUTS associated with unilateral double-J stent (DJ Stent) Stenting (Group A- Mean Irritative IPSS pre and post Solifenacin treatment 7.38 vs 2.75) = 31%

Proportion of patients with Lower Urinary Tract Symptoms (LUTS) associated with unilateral DJ stenting (Group B- Mean Irritative International Prostate Symptom Score (IPSS) pre and post Placebo treatment 6.38 vs 5.13) = 8%

Sampling technique: Consecutive non probability sampling.

Results: There was a 30.8% mean improvement of storage IPSS compared to placebo, 9.97%. This difference in efficacy between Solifenacin vs placebo was also found statistically significant (p=0.000).

Conclusion: Solifenacin 5mg daily significantly improved the storage symptoms compared with placebo, in men with moderate to severe lower urinary tract symptoms due to A double-J stent (DJ Stent) stent placed in situ.

Key Words: Irritative Lower urinary tract symptoms, Solifenacin, double-J stent (DJ Stent)

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INTRODUCTION

Ureteric stents introduced in 1967, have been widely used for urinary tract diseases. The double-J (DJ) stents are common tools and essential part used in end urologic procedures.

They play a major role in a wide range of situations to prevent or to relieve ureteral obstruction; both primary due to obstruction in the ureter (intraluminal) such as Ureteric strictures, Ureteric stones, and ureteric tumors; and secondary due to extra-ureteric pressure (extra luminal), as well as after the urological procedures as urine drainage to allow adequate time for ureteric wound healing, as well as a guide to the identification of the ureter before operative procedure.[1, 2]

Despite the usefulness of double-J stent, some of the patients might encounter stent-related morbidities such as urinary tract infection (UTI), hematuria in 40-52% patients, flank pain in 48-58%, lower urinary tract symptoms (LUTS); urinary frequency in 66 - 78%, Dysuria in 72-80%, urgency in 60-72% and suprapubic pain in 42-50% of cases respectively.[1] These symptoms represent a prevalent problem with considerable effects on the quality of life, substantial general health, work performance, and sexual matters in both genders.[2] A study revealed that micturation complaints or LUTS starts in second week after of stent insertion.[3] The Pathophysiologoy of stent-related symptoms remains unclear. However, the pain and LUTS caused by stent placement has been attributed to lower ureter and bladder spasm due to local irritation of the stent and an important factor of stent-related symptoms is the pressure transmitted to the renal pelvis during micturation and trigonal irritation by the intravesicular part of the stent.[4]

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International Prostate Symptom Score (IPSS) in patients with stents inserted increases in the first week and decreases after DJ stent removal.[5] IPSS is a questionnaire to guide, direct and determine the presence of obstructive and irritative symptoms during micturation, and has been used routinely in patients with prostate enlargement. This score is useful for assessing and monitoring the condition of patients with benign prostate hyperplasia (BPH). IPSS can be used to assess LUTS complaint in patients post DJ stent insertion on the assumption that the complaints are similar to the complaints in LUTS due to BPH.[5,6,7,8,9].

MATERIALS AND METHODS

Settings: Benazir Bhutto Shaheed teaching hospital, Abbottabad

Duration: (from 01-11-2019 to 01-05-2020).

Study Design: Randomized Controlled Trial.

Sample Size: Sample size is 76 in each group, using WHO software for sample size determination in healthy studies, applying the formula of hypothesis test, for two population proportions (one- sided) with the following assumption:[9]

Significance level = 5%

Statistical power = 80%

Proportion of patients with LUTS associated with unilateral DJ Stenting (Group A- Mean Irritative IPSS pre and post Solifenacin treatment 7.38 vs 2.75) = 31%

Proportion of patients with LUTS associated with unilateral DJ Stenting (Group B- Mean Irritative IPSS pre and post Placebo treatment 6.38 vs 5.13) = 8%

Sampling technique: Consecutive non probability sampling.

RESULTS

An independent sample t-test (Student's t- test) was conducted to compare the storage IPSS scores in the two treatment arms. There was a significant difference in storage IPSS for Solifenacin group (M=2.59, SD=0.880, 30.8%) vs Non Solifenacin (M=0.79, SD=1.075, 9.97%) p = 0.000.

Table No.1: Baseline characteristics; age, gender and side of DJ stent, along with statistical difference between the study groups

	Age (mean)	Gender		Side of DJ stent	
		Male	Female	Left	Right
Solifenacin	28.83 ± 8.019	45	31	35	41
Non solifenacin	27.39 ± 8.568	47	29	39	37
p - value	**0.858**	**0.740**		**0.516**	

These results suggest Solifenacin therapy really does have an effect in improving the storage sub score of IPSS. Specifically, these results suggest that Solifenacin 5 mg daily significantly improves the Irritative/storage lower urinary tract symptoms due to a double J stent in situ. Baseline mean storage IPSS in group I was 8.39 ± 1.212 and 7.92 ± 1.197 in patients of group II (p=0.01). Post Treatment mean storage IPSS in group I patients improved to 5.80 ± 0.880 [a mean difference of -2.59(30.8%) (p=0.000)]] And up to 7.13 ± 1.075 in group II patients [a mean difference of 0.79(9.97%) (p=0.009)].

Table No.2: Means of Pre-treatment storage IPSS of patients in both study groups

Mean	Storage IPSS	p - value
Solifenacin	8.39 ± 1.212	0.015
Non Solifenacin	7.92 ± 1.197	

Table No.3: Percentile improvement in Means of Post treatment storage IPSS and its individual components of patients in both study groups

Variables	Solifenacin	Non Solifenacin
Frequency	32%	9.92%
Urgency	32.8%	12.3%
Nocturia	26.7%	6.58%
Total storage score	30.8%	9.97%

Table No.4: Means of Post treatment storage IPSS of patients in both study groups

Mean	Storage IPSS	p - value
Solifenacin	5.80 ± 0.880	0.000
Non Solifenacin	7.13 ± 1.075	

DISCUSSION

Ureteral stents play a major role in a wide range of situations where urinary drainage is needed.

Different strategies have been studied to prevent as well as manage these stent related problems. Many improvements have been known recently that may improve the quality of stent and reduce the side effects of theses stents keeping the role of its indication intact. Apart from this many different medical options have been introduced in the market that may help relief the symptoms due to a stent. They can be directly instilled inside the bladder or taken orally. This list includes anti cholinergic, alpha blockers, urinary bladder sedatives, calcium channel blockers and much more. But the most well suited group of medicines that help in alleviating the side effects of a Ureteric stent are anti cholinergic.[10] Beiko, et al No side effects were reported and ketorolac was associated to a significant decrease in Irritative symptoms at 1-hour after intervention.11 Subsequent studies failed to demonstrate differences between intravesical agents for relief of stent-related symptoms.

In 2006, a study by Deliveliotis, et al. Found the position of alpha1-blockers for treating these symptoms. They performed a prospective, randomized, placebo-controlled study to compare the impact of stent symptoms on patients. Standard of health using a prove question sheet. Patients who undergone examination by

cyst scope placed a splint placed temporarily inside a duct, canal, or blood vessel to aid healing or relieve an obstruction to treat stone linked when a kidney has an excess of fluid due to a backup of urine were given ten mg alfuzosin once daily for four weeks. Results showed a decrease in mean relating to urinary system symptom index ($p<0.001$), frequency of stent-related pain ($p=0.027$), and an improvement in the general health index score ($p<0.001$) for patients in the alfuzosin group.[12]

In a recently published study, Bedding field et al. also evaluated alfuzosin as an adjunct to the improvement of stent related symptoms. A total of 55 patients were randomized to receive either 10 mg alfuzosin hydrochloride or placebo once a day for 10 days following post ureteroscopy stent placement. USSQ and narcotic use diary were assessed. Results showed a significant improvement for the alfuzosin group regarding sleep interrupted by pain, frequency of painkiller, pain interfering with life, and flank pain associated with micturation ($p<0.005$). The placebo group showed worsening for these same symptoms. Although alfuzosin led to a decrease in the frequency of narcotic use, the total amount was not changed.[13]

Another study compared alfuzosin with tolterodine ER and placebo. A total of 52 patients were randomized after different end urological procedures and stent placement to receive one of the following three doses: 10 mg alfuzosin, 4 mg tolterodine ER, or placebo for a 6-week period. Both alfuzosin and tolterodine were able to improve pain and urinary symptom index scores when compared with placebo ($p=0.02$ and $p=0.008$, respectively). Tamsulosin also proved to be efficacious in improving stent related morbidity.[14] in a study by Damiano, et al. it was shown to decrease flank pain and urinary symptoms at 1 week and increase the general health index score, although this study was not double-blinded or placebo controlled.[15]

In contrast to this data, Norris, et al. recently published their experience with a small but well conducted double blind, placebo-controlled study comparing ER oxybutynin, phenazopyridine, and placebo in patients who had a stent place after ureteroscopy.[16] Assessment tools included a questionnaire for stent symptoms, visual analog scale scores, and requirement of narcotic medications. Results did not show differences for flank pain, suprapubic pain, urinary frequency, urgency, Dysuria, narcotic usage, or hematuria (except for phenazopyridine versus placebo on Day 2).

Solifenacin is one of the recently found anti cholinergic agent with maximal urinary tract and minimal systemic effects. Different studies have been conducted in past to study the effect of various anti cholinergic including Solifenacin in relieving Ureteric stent related symptoms. Regarding Solifenacin administration, a study by Pricop et al in 2009 showed that urinary frequency is lower compared to placebo with post-DJ stent insertion.[17] This study showed an improvement of about 32% vs. 9.97% in urinary frequency, 32.8% vs. 12.3% improved urgency, 26.7% vs 6.58% improvement of Nocturia and 30.8% vs 9.97% improvement in total storage symptoms in patients fulfilling the selection criteria, treated with Solifenacin and placebo respectively, calculated by IPSS. Also previous studies show about 31% improvement in IPSS Irritative score among Solifenacin group compared to placebo 8%.[9] which is quite in concordance with this study. A student's t test was applied to see the statistical difference between the outcomes of two treatment groups. With a p-value of 0.000, null hypothesis is rejected and Solifenacin treatment was found statistically significant over the placebo, suggesting its effectiveness in relieving the LUTS secondary to DJ stent in situ. Also Solifenacin offered minimal side effects of an anti-cholinergic and hence can be prescribed as a safe medicine.

CONCLUSION

This study proves the efficacy and suggests the use of Solifenacin 5mg daily to alleviate the Irritative lower urinary tract symptoms due to a double J/Ureteric stent.

Author's Contribution:

Concept & Design of Study:	Hamza Ashraf
Drafting:	Muhammad Shahab
Data Analysis:	Noor ul Hayat, Kafeel Azhar
Revisiting Critically:	Hamza Ashraf, Muhammad Shahab
Final Approval of version:	Hamza Ashraf

Conflict of Interest: The study has no conflict of interest to declare by any author.

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