Original Article

TREATMENT OF LOWER URINARY TRACT SYMPTOMS CAUSED BY DOUBLE J STENT WITH SOLIFENACIN AND COMBINATION OF TAMSULOSIN PLUS SOLIFENACIN: A COMPARATIVE STUDY

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ABSTRACT:

OBJECTIVE: To compare the mean change in international prostate symptom score (IPSS) by combination therapy of Tamsulosin and Solifenacin with Solifenacin alone in treatment of lower urinary tract symptoms (LUTS) caused by double J (DJ) stents.
STUDY DESIGN: Randomized control trial
PLACE AND DURATION OF STUDY: Urology Department, Madinah Teaching Hospital Faisalabad, from December 2015 to June 2016.
METHODOLOGY: Total 170 patients having LUTS after DJ stent insertion were selected for the study. DJ stenting was done in these patients before extra-corporeal shock wave lithotripsy (ESWL), following ureterorenoscopy (URS) and intracorporeal lithotripsy, percutaneous nephrolithotomy (PCNL), ureterolithotomy, pyelolithotomy, pyeloplasty and in patients with obstructive uropathy. All the patients were allocated two different groups. Group A received Tamsulosin 0.4 mg and Solifenacin 5 mg daily & Group B received Solifenacin 5 mg once a day every day. The IPSS questionnaire was filled on 1st post-operative day and on 6th post-operative week. Final results were made on 6th post-operative week by comparing the mean change in IPSS in both groups. Independent sample t-test and paired t-test were applied. P-value $\leq$ 0.05 was taken as significant.
RESULT: Mean age was 42.92$\pm$7.04 years in Group-A and 43.38$\pm$6.67 years in Group-B. Total number of male patients was 58 (68.24%) in Group-A and 52 (61.18%) in Group-B. Female patients in Group-A were 27 (31.76%) and 33 (38.82%) in Group-B. Mean IPSS was 9.01$\pm$1.29 in Group-A and 9.10$\pm$1.23 in Group-B at baseline (p=0.62). After 6 weeks IPSS was 4.69$\pm$0.89 in Group-A and 6.87$\pm$1.25 in Group-B (p=0.0001). The mean difference in IPSS after 6 weeks was 4.30$\pm$1.49 in Group-A and 2.23$\pm$1.13 in Group-B with p value 0.0001 reflecting a significant difference between the two groups.
CONCLUSIONS: The mean change in IPSS by combined treatment of Tamsulosin and Solifenacin was significant when compared to Solifenacin alone in treatment of DJ stents related LUTS.
KEY WORDS: LUTS, Double J stent, IPSS.

INTRODUCTION:

Double J stents are widely used in endo-urological procedures to avoid or to relieve ureteric obstruction[1]. Regardless of the extensive use of Double J stents in clinical practice, it can cause hazards, including haematuria, LUTS, sexual problems such as erectile dysfunction, pain and eventually had a negative impact on the quality of life[2,3,4].

The pathophysiology of symptoms due to DJ stent is not clearly known. However, due to the local irritation caused by stent placement, the

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lower ureter and bladder goes into spasm that results in pain and lower urinary tract symptoms[4].

The pressure transferred to the renal pelvis during micturation and irritation of bladder trigone by intra-vesicular part of stent results in stent-related symptoms. To reduce these symptoms, pharmacological management has played a vital role especially the use of selective alpha-1-blockers and anti-muscarinic agents are recommended[5].

The use of selective alpha-blocker e.g Tamsulosin has reduced stent related symptoms and improved the quality of life[6]. Alpha-blocker helps in reducing the symptoms by blocking alpha-adrenergic receptors that result in decreasing the muscle tone of the ureter, bladder trigone and prostatic urethra. This ultimately leads to decreasing bladder outflow resistance and force during urination. Anticholinergics acts on the muscarinic receptors, thereby reducing over activity of the bladder and contraction by blocking them, which assists in reducing urinary symptoms[7].

In one study by Lim KT et al, combination therapy of Tamsulosin and Solifenacin for treatment of LUTS was found effective in improving international prostate symptom score (IPSS) score by 7.16$\pm$3.37 as compared to Solifenacin alone in which improvement occurred in IPSS score by 11.04$\pm$5.29[5].

Double J stenting may cause lower urinary tract symptoms which may be settled by using antimuscarinics and alpha blockers. Antimuscarinics monotherapy has been widely used as treatment for stent related LUTS. The combination therapy of antimuscarinics and alpha blockers improves lower urinary tract symptoms better than anti muscarinic monotherapy[5].

METHODOLOGY:

Using a WHO sample size calculator, 170 patients were enrolled in the study from the outpatient department (OPD) of urology, Madinah Teaching Hospital Faisalabad. Patients between 16 to 50 years of age having LUTS after DJ stenting were selected for study after informed consent. Patients who had UTI, Pregnancy or allergy to Tamsulosin or Solifenacin were excluded from the study. The duration of study was 6 months from July 2017 to December 2017. The patients were divided into two groups by computer generated random number table. Group A (n=85 patients) received Tamsulosin 0.4 mg and Solifenacin 5 mg daily & Group B (n=85 patients) received Solifenacin 5 mg once a day every day. Each patient completed written IPSS questionnaires on 1st post-operative day and on 6th post-operative week. Final results were made on 6th post-operative week by comparing the mean change in IPSS i.e.; the difference in IPSS recorded at 1st day and 6th week post double J insertion in both groups. All the data was entered into SPSS version 16 and analyzed through its statistical package. The quantitative variables like age, IPSS score at baseline (1st post-operative day), IPSS score after 6 post-operative week and change in IPSS ware presented as mean and standard deviation. The qualitative variable like gender was presented as frequency and percentage. Independent sample t-test was used to compare the change in IPSS scores. Independent sample t-test was applied. *P*-value $\leq$ 0.05 was taken as significant.

RESULTS:

A total of 170 patients (85 in two groups) meeting the inclusion criteria were enrolled in the study. All the patients were divided into two equal groups with 85 patients in each group. Group A patients received Tamsulosin 0.4 mg and Solifenacin 5 mg daily while Group B patients received Solifenacin 5 mg once a day every day.

The age distribution of the patients showed 8.24% (n=7) patients in Group A and 5.88% (n=5) patients in Group B between 16-30 years of age while 91.76 % (n=78) patients in Group A and 94.12 % (n=80) patients in Group B were between 31-50 years of age. Mean$\pm$sd was calculated as 42.92$\pm$7.04 years in Group A and 43.38$\pm$6.67 years in Group B. (Table 1)

Gender distribution revealed 68.24 % (n=58) in Group A and 61.18% (n=52) in Group B were male while 31.76% (n=27) in Group A and 38.82% (n=33) in Group B were females. (Table No. 2)

Mean IPSS at baseline was 9.01±1.29 in Group A and 9.10±1.23 in Group B (p=0.62). IPSS after 6 weeks was 4.69±0.89 in Group A and 6.87±1.25 in Group B (p=0.0001) while the difference was calculated as 4.30±1.49 in Group A and 2.23±1.13 in Group B (p = 0.0001) showing a significant difference between the two groups. (Table No. 3)

The data was stratified for age and gender to control the effect modifiers in Table No. 4 & 5 respectively.

TABLE No. 1: AGE DISTRIBUTION (n=170)

Age (in years)	Group-A (n=85)		Group-B (n=85)	
	No. of patients	%	No. of patients	%
16-30	7	8.24	5	5.88
31-50	78	91.76	80	94.12
Total	**85**	**100**	**85**	**100**
Mean±sd	**42.92±7.04**		**43.38±6.67**	

TABLE No. 2: GENDER DISTRIBUTION (n=170)

Gender	Group-A (n=85)		Group-B (n=85)	
	No. of patients	%	No. of patients	%
Male	58	68.24	52	61.18
Female	27	31.76	33	38.82
Total	**85**	**100**	**85**	**100**

TABLE No. 3: MEAN IPSS IN BOTH GROUPS (n=170)

IPSS	Group-A (n=85)		Group-B (n=85)		P value
	Mean	SD	Mean	SD	
Baseline	9.01	1.29	9.10	1.23	0.62
After 6 weeks	4.69	0.89	6.87	1.25	0.0001
Paired test	4.30	P-value = 0.000	2.23	P-value = 1.13	

TABLE No. 4: STRATIFICATION FOR AGE OF THE PATIENTS WITH RESPECT TO IPSS (n=170) Age:16-30

IPSS	Group-A (n=85)		Group-B (n=85)		P value
	Mean	SD	Mean	SD	
Baseline	8.43	1.40	9.80	0.84	0.08
After 6 weeks	4.43	0.53	7.40	1.67	0.001
Paired test	4.00	P-value = 0.001	2.40	P-value = 0.001	

Age:31-50

IPSS	Group-A (n=85)		Group-B (n=85)		P value
	Mean	SD	Mean	SD	
Baseline	9.06	1.27	9.08	1.25	0.99
After 6 weeks	4.72	0.91	6.84	1.23	0.0001
Paired test	4.35	P-value = 0.001	2.23	P-value = 0.0001	

TABLE No. 5: STRATIFICATION FOR GENDER OF THE PATIENTS WITH RESPECT TO IPSS (n=170)

Male

IPSS	Group-A (n=85)		Group-B (n=85)		P value
	Mean	SD	Mean	SD	
Baseline	9.07	1.24	9.10	1.18	0.90
After 6 weeks	4.69	0.86	6.88	1.17	0.0001
Paired test	4.38	P-value = 0.001	2.21	P-value = 0.001	

Female

IPSS	Group-A (n=85)		Group-B (n=85)		P value
	Mean	SD	Mean	SD	
Baseline	8.89	1.40	9.12	1.34	0.51
After 6 weeks	4.70	0.95	6.85	1.39	0.0001
Paired test	4.19	P-value = 0.001	2.27	P-value = 0.0001	

DISCUSSION:

The management of benign prostatic obstruction has traditionally been the main focus of treatment for male LUTS, but recently the role of bladder dysfunction has been documented[8,9]. Thus, it is understood that lower urinary tract symptoms have multifactorial etiology and every so often occur in clusters[10]. The safety & efficacy of combination therapy of Tamsulosin and Solifenacin for the treatment of lower urinary tract symptoms in men have been evaluated in several studies[11,12].

This study was planned to compare the mean change in IPSS by combining treatment with Tamsulosin and Solifenacin with Solifenacin alone in treatment of LUTS caused by double J stents. Combination therapy proved to be more effective then Solifenacin alone[13,14,15].

These results were compared with the study of Lim KT et al, combination therapy of Tamsulosin and Solifenacin was found effective in improving international prostate symptoms score (IPSS) total score by 7.16±3.37, for treatment of LUTS as compared to Solifenacin alone in which improvement occurred by IPSS total score by 11.04±5.29[5]. The findings of this study are in agreement with our findings.

In another study Yun et al[6]. assessed that tamsulosin monotherapy against tamsulosin and solifenacin combination therapy in initial treatment of men. Patients were divided into storage (60%) and voiding (40%) groups. The storage group benefited more from combination therapy in terms of IPSS and QOL improvement, while voiding group benefited from monotherapy with Tamsulosin.

Non-adherence is an important problem in patients undergoing medical treatment for LUTS[17,18]. Combination therapies have better compliance rate compared to monotherapies[19,20]. Less frequent dosage improves adherence to medical management[21]. Therefore, a potential advantage of the fixed dose combination of Solifenacin/Tamsulosin is improvement of patients' adherence.

LUTS caused by bladder and urethral outflow resistance and bladder instability are similar to the stent related symptoms[22]. Hence, many studies have reported that selective alpha-1-blockers improve stent-related symptoms. In a study, Beddingfield et al reported that there is improvement in frequency and flank pain in patients taking alfuzosin 10 mg daily[23]. Deliveliotis et al reported that there is improvement in stent related symptoms and pain along with sexual function and general health by using alfuzosin[24].Wang et al suggested that there is improvement in urinary symptoms, flank pain and pain during voiding using selective alpha-1-blocker tamsulosin[25].

In another study, Valiere Vialeix et al. compared Tamsulosin with placebo for treatment of stent related discomfort which did not show the superiority of one over other[26].

Mokhtari et al. compared patients having DJ

stent with placebo to evaluate the effect of Terazosin for relief of flank pain and urinary tract symptoms. By using IPSS questionnaire and VAS for evaluation they concluded that there is improvement of urinary tract symptoms and pain with administration of Terazosin but has no effect on hematuria[27].

The findings of our study are justifying the hypothesis that "the combination therapy of Tamsulosin and Solifenacin improves stent related LUTS better than Solifenacin monotherapy".

CONCLUSION:

The mean change in IPSS by combination therapy of Tamsulosin and Solifenacin was significantly improved when compared to Solifenacin alone in treatment of LUTS caused by double J stents.

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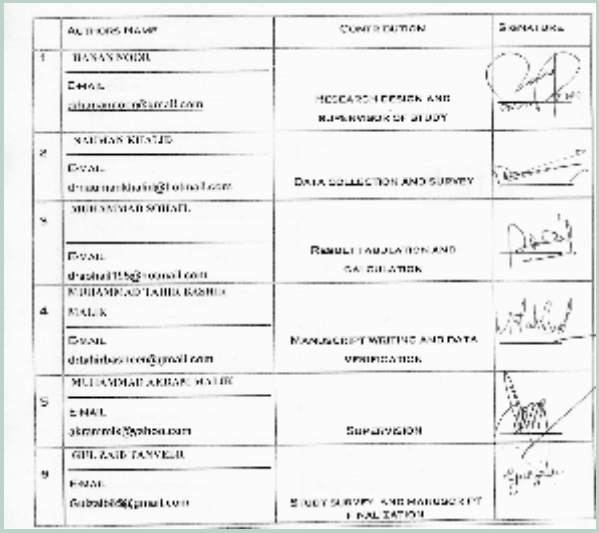

Submitted for publication: 11.06.2018

Accepted for publication: 15.10.2018
After Revision