TAMSULOSIN OR SOLIFENACIN IN LUTS PATIENTS DUE TO DJ-STENT INSERTION

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ABSTRACT

Objective: *To evaluate the efficacy of tamsulosin or solifenacin for treatment of Lower Urinary Tract Symptoms (LUTS) due to an indwelling ureteral stent.* ***Material & Method:*** *In this study, we enrolled 24 patients who had polyurethane DJ-stent inserted for urinary stone disease or ureteral stenosis. Patients were divided into 3 equal groups as follows and study medications were started on postoperative day 7. Group I received tamsulosin 0,4 mg once daily, group II received solifenacin 5 mg once daily, and group III only received placebo. LUTS were evaluated using International Prostatic Symptoms Score (IPSS) questionnaire at 7 and 14 days after the procedure and stent insertion. The evaluation of IPSS score included not only total score but also irritative and obstructive subcores.* ***Results:*** *All 24 patients fulfilled the inclusion and exclusion criteria, mean age of tamsulosin group was 54,3 years old, solifenacin group was 45,3 years old and placebo was 46,7 years old. There was significant difference in the total IPSS and irritative subscores between groups who received either tamsulosin or solifenacin (group I and II), whereas the obstructive subscore showed a difference though not statistically significant.* ***Conclusion:*** *Tamsulosin or solifenacin significantly improved irritative symptoms of LUTS in patients with an indwelling ureteral stent.*

Keywords: *Lower urinary tract symptoms, DJ-stent, tamsulosin, solifenacin.*

ABSTRAK

Tujuan penelitian: *Menilai efikasi tamsulosin atau solifenasin terhadap keluhan Lower Urinary Tract Symptoms (LUTS) yang disebabkan oleh insersi DJ-stent.* ***Bahan & Cara:*** *Pada penelitian ini, terdapat 24 pasien yang dilakukan tindakan insersi DJ-stent karena batu saluran kemih atau stenosis ureter. Pasien dibagi menjadi 3 kelompok, kelompok I diberi tamsulosin 0,4 mg satu tablet perhari, kelompok II diberikan solifenasin 5 mg satu tablet perhari, dan kelompok III diberikan plasebo selama 7 hari pada hari ke-7 pasca insersi DJ-stent. Pada hari ke-7 dan 14 dilakukan penilaian total International Prostatic Symptoms Score (IPSS), iritatif dan obstruktif, kemudian dilakukan uji perbedaan sebelum dan sesudah pemberian tamsulosin, solifenasin, dan plasebo.* ***Hasil penelitian:*** *Sebanyak 24 pasien sesuai kriteria inklusi dan eksklusi ikut serta dalam penelitian ini. Rerata umur pada kelompok tamsulosin, solifenasin, dan plasebo masing-masing adalah 54,3 tahun, 45,3 tahun dan 46,7 tahun. Terdapat perbedaan yang signifikan secara statistik untuk IPSS total dan iritatif pada kelompok yang diberi tamsulosin atau solifenasin, skor iritatif ada perbedaan tapi tidak bermakna secara statistik.* ***Simpulan:*** *Tamsulosin atau solifenasin dapat memperbaiki gejala LUTS iritatif yang disebabkan oleh insersi DJ-stent.*

Kata kunci: *Lower urinary tract symptoms, DJ-stent, tamsulosin, solifenasin.*

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INTRODUCTION

Ureteral stents has become an important part of urology for 20 years and provided benefits in the practice of urology, such as the prevention and treatment of ureteric obstruction, both primary due to obstruction in the ureter (intraluminal) such as ureteric stones, ureteral strictures, and ureteric

tumors, and secondary due to extra-ureteral pressure (extraluminal), as well as post-urological operative urine drainage to allow time for ureteral wound healing, as well as a guide to the identification of the ureters before operative procedure.[1] Insertion of ureteric stents can be carried out through open or endoscopic surgery, both antegrade and retrograde.

DJ stent insertion can cause complications and morbidity for patients, one of which is micturition complaints or Lower Urinary Tract Symptoms (LUTS).[2,3] A study by Lim et al. revealed that micturition complaint or LUTS starts in second week after of stent insertion.[4] Another study by Joshi et al. showed that the International Prostate Symptom Score (IPSS) in patients with stents inserted increased in the first week and decreased after DJ stent was removed.[5]

IPSS is a questionnaire to guide, direct and determine the presence of obstructive and irritative symptoms during micturition. IPSS 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). Joshi adopted and used IPSS to assess LUTS complaint in patients post DJ stent insertion under consideration that the complaintsare similar to the complaints in LUTS due to BPH.[6]

The idea to provide alpha blockers, particularly tamsulosin, and the antimuscarinic solifenacin, is aimed to reduce complaints due to the DJ stent insertion based on the consideration that LUTS complaints resulting from DJ stent insertion is similar to LUTS due to benign prostate enlargement, and the complaints of urgency and frequency are similar to those in patients with overactive bladder (OAB).[6]

The complaints of urgency, frequency and suprapubic pain in patients post-DJ stent insertion are similar to those in OAB caused by involuntary bladder contractions mediated by muscarinic receptors. In this case, solifenacin serves to inhibit those receptors.[4] A study by Damiano et al. showed that the administration of 0,4 mg tamsulosin 1 tablet a day for 1 week can improve LUTS complaints and the quality of life in patients post-DJ stent insertion.[7] A study by Wang et al. also revealed similar results, where in the provision of tamsulosin, irritative subset of IPSSis lower compared to placebo.[8]

Regarding solifenacin administration, a study by Pricop et al. showed that frequency is lower compared to placebo in 254 patients with post-DJ stent insertion.[9] Another study by Park et al. on post-URS patients who underwent stent insertion compared the effect between tolterodine, alfuzosin and placebo also showed significant improvement, showing that patients receiving tolterodine and alfuzosin ureteral had Ureteral Stent Symptom Questionnaire (USSQ) lower compared to placebo.[10]

LUTS management, mainly the irritative complaints, which is one of the complications caused by the insertion of DJ stent, has not been widely researched and published, especially in Indonesia. This study was done to prove the difference in IPSS before and after the administration of 0,4 mg tamsulosin and 5 mg solifenacin in patients with LUTS post-DJ stent insertion.

OBJECTIVE

To assess the efficacy of tamsulosin or solifenacin to treat LUTS resulting from DJ stent insertion.

MATERIAL & METHOD

We performed a prospective randomized clinical trial with pre and post control design. Administration of 0,4 mg tamsulosin or 5 mg solifenacin compared to placebo, were started on day 7 post stent insertion and maintained for 1 week. Outcomes were measured by IPSS.Patients enrolled was inserted 6 Fr unilateral DJ stent.

A total of 24 patients were grouped into 3 groups, each of 8 patients. Group 1 was given 0.4 mg tamsulosin, group 2 was given 5 mg solifenacin, and group 3 received placebo.

Inclusion criteria for this study were 1) willing to participate in the study, 2) patients with an indication of unilateral DJ stent insertion endoscopically diagnosed with ureteric stones, stenosis of the ureter and or kidney stones that will undergo shockwave lithotripsy (SWL).

Data from the study were recorded, collected, and processed with SPSS program. Normality was tested by one sample Kolmogorov-Smirnov test. If normally distributed, data was testedusing parametric tests, such as paired t test and ANOVA. Other distributions used nonparametric tests, such as Wilcoxon Signed rank and Kruskal Wallis tests.

RESULT

In table 1 mean age in tamsulosin group was 54,38 ± 12,72 years, which was higher than those in placebo group (12,1 ± 46,75 years) and in solifenacin group (45,38 ± 15,47 years). The results of statistical analysis using ANOVA revealed p = 0,375, which indicated that there was no difference in mean age between the three groups. Males in tamsulosin group consisted of 5 patients or 62,5%, more than females, which comprised 3 patients or 37,5%. In solifenacin group males were 3 patients (37,5%), less than females, who were 5 patients (62,5%). In the placebo group, males comprised 6 patients (75%), more than females of only 2 (25%) patients. Fisher test results between tamsulosin and placebo groups revealed p = 1,000, between solifenacin group and placebo had p = 0,315, whereas between tamsulosin and solifenacin groups had p = 0,619. As a whole, there was no sex differences between the three groups.

Diagnosis in tamsulosin group was ureteric stones is 6 (75%) patients and ureteral stenosis in 2 (25%) patients. Diagnosis in solifenacin group was ureteric stones and stenosis, each in 4 (50%) patients, while in placebo group all had ureteric stones. Fisher test results between tamsulosin and placebo groups revealed p = 0,467, between solifenacin and placebo groups p = 0,077, and between tamsulosin and solifenacin groups p = 0,608. Overall, there was no difference in diagnosis between the three groups.

Total IPSS in each group (Table 2); tamsulosin, solifenacin and placebo was 9,88 ± 3,64; 10,13 ± 4,42; 9,5 ± 6,61. Irritative IPSS for each group; tamsulosin, solifenacin, and placebo was 8,00 ± 2,00; 7,38 ± 2,97; 6,37 ± 3,70. Obstructive IPSS in each group; tamsulosin, and placebo solifenacin was 1,88 ± 2,59; 2,75 ± 2,87; 2,87 ± 3,09. ANOVA test results showed no difference in total, irritative and obstructive IPSS among the three treatment groups on day7.

Quality of life scores on day 7 or before treatment in each group (Table 3) was 3,88 + 0,83, 4,00 + 1,41; 3,88 + 1,46. ANOVA results showed no difference in quality of life scores among the three treatment groups at H-7.

Table 1. Characteristics of treatment samples.

Variables	Treatment Groups		
	Tamsulosin	Solifenacin	Placebo
Age	54,38 ± 12,72	45,38 ± 15,47	46,75 ± 12,17
Sex			
Male	5 (62,5)	3 (37,5)	6 (75,0)
Female	3 (37,5)	5 (62,5)	2 (25,0)
Diagnosis			
Ureteral Stone	6 (75,5)	4 (50,0)	8 (100,0)
Ureteral Stenosis	2 (25,0)	4 (50,0)	0 (0,0)

Table 2. IPSS on day 7 between groups.

	Treatment Groups			p
	Tamsulosin	Solifenacin	Placebo	
Total IPSS	9,88 ± 3,64	10,13 ± 4,42	9,50 ± 6,61	0,969
Irritative IPSS	8,00 ± 2,00	7,38 ± 2,97	6,37 ± 3,70	0,554
Obstructive IPSS	1,88 ± 2,59	2,75 ± 2,87	2,87 ± 3,09	0,75

Table 3. Quality of life scores on day 7 between groups.

Observation Time	Treatment Groups			p
	Tamsulosin	Solifenacin	Placebo	
Day 7	3,88 ± 0,83	4,00 ± 1,41	3,88 ± 1,46	> 0,05

Table 4. The difference in IPSS between observations on day 7 and 14.

Groups	Observation Time		p
	H7	H14	
Tamsulosin			
Total IPSS	9,88 + 3,64	2,75 + 1,98	< 0,0001
Irritative IPSS	8,00 ± 2,00	1,75 ± 1,49	< 0,0001
Obstructive IPSS	1,88 + 2,59	0,87 + 0,99	0,155
Solifenacin			
Total IPSS	10,13 + 1,56	3,00 + 1,32	< 0,0001
Irritative IPSS	7,38 ± 1,05	2,75 ± 1,18	< 0,0001
Obstructive IPSS	2,75 + 1,01	0,25 + 0,16	0,46
Placebo			
Total IPSS	9,50 + 6,61	8,25 + 6,76	0,250
Irritative IPSS	6,38 ± 3,70	5,13 ± 3,27	0,095
Obstructive IPSS	2,88 + 3,09	2,38 + 3,02	0,227

Note: Significant (p <0,05).

Table 5. Differences of IPSS change on day 7 and 14 between groups.

Variables	Treatment Groups			p
	Tamsulosin	Solifenacin	Placebo	
Irritative	-6,25 ± 1,67[a]	-4,63 ± 1,92[a]	-1,25 ± 1,83[b]	< 0,0001
Obstructive	-1,00 ± 1,78	-2,50 ± 2,93	-0,50 ± 1,07	0,157
Total	-7,13 ± 2,23[a]	-7,15 ± 3,23[a]	-3,00 ± 3,02[b]	< 0,0001

Note: Different superscript letters indicates significant differences (p < 0,05) using LSD test.

Table 6. The difference in quality of life scores between the observations on day 7 and 14.

Groups	Observation Time		p
	H7	H14	
Tamsulosin	3,88 ± 0,83	0,87 ± 0,64	< 0,001
Solifenacin	3,88 ± 1,46	1,50 ± 0,53	0,001
Placebo	4,00 ± 1,41	4,25 ± 1,67	0,685

Table 7. Difference in the change of quality of life scores between groups.

	Treatment Groups			p
	Tamsulosin	Solifenacin	Placebo	
Quality of Life	-2,38 ± 1,19[a]	-3,00 ± 1,06[a]	0,25 ± 1,66[b]	< 0,0001

Table 4 shows no significant difference in total and irritative IPSS in treatment group receiving solifenacin and tamsulosin in observation days 7 and 14. There was no difference in obstructive IPSS, while in placebo group there was no difference between observations on day 7 and 14.

There were significant differences in total and irritating IPSS (table 5) in tamsulosin and solifenacin groups compared to placebo on the day 14 observation after treatment, while no significant difference was found in obstructive IPSS in those three groups. The table above also shows no difference in total, irritative and obstructive IPSS scores between tamsulosin and solifenacin groups.

There are significant differences in quality of life scores (Table 6) in tamsulosin and solifenacin group and there was no difference in placebo group on observation day 14 after treatment.

Table 7 shows significant decline in quality of life scores in tamsulosin and solifenacin groups compared to placebo (p < 0,0001).

DISCUSSION

The mean age in tamsulosin group was 54 years, which was higher than that in solifenacin group (45 years) and placebo (45 years). The mean age was similar to previous studies by Lim KT, in which mean age in tamsulosin, solifenacin and placebo groups were 49 years, 49 years and 50 years.4 In a study by Navanimitkul and Lojanapiwat showed that the mean age in tamsulosin and placebo groups were 46 and 51 years old.[11]

Males in tamsulosin group were 5 patients or 62.5%, more than females that comprised 3 patients or 37,5%. In solifenacin group males were 3 people or 37,5% less than women 5 people or 62,5%. In the placebo group males comprised 6 patients (75%) more than females of 2 (25%) patients. In a study by KT Lim et al. males were more than 50% in all groups, and this was in contrast to that of this study, in which males in solifenacin group were less than the females (37,5% and 62,5%).[4]

DJ stent insertion in this study was done to ureteric stone patients as many as 18 or 75% and ureteral stenosis in as many as 6 patients or 25%. This was contrasts to the study by KT Lim et al. where all (100%) DJ stent insertions were done on patients with ureteric stones.[4] In the literature, some indications of DJ stent insertion are ureteric stones in post-URS patients who experienced complication of ureteral edema, ureteral perforation, impacted stones or ureter stenosis. In this study, endoscopic DJ stent insertion was limited only to patients with ureteric stones, kidney stones and those who would undergo ESWL and ureteral stenosis.

Mean total IPSS on day 7 after DJ stent insertion before treatment in the tamsulosin group was 9,8, solifenacin 10,1 and placebo 9,5. These total IPSS were similar to data from Lim KT, which were 12,5 in tamsulosin group, 11,1 in solifenacin and 11,6 in placebo.[4]

Irritative IPSS on day 7 after DJ stent insertion in tamsulosin group was 8,0, solifenacin 7,3, and placebo group 6,3. Irritative IPSS in this study were also similar to those in a study by Lim KT et al., where tamsulosin group was 7,7, solifenacin 6,2 and placebo 6,4.[4] Obstructive IPSS on day 7 post-DJ stent insertion in tamsulosin group was 1,8, solifenacin 2,7 and placebo 2,8.

A study by Leibovici et al. showed that irritative LUTS was the most predominant complaints experienced by the patients after DJ stent insertion. The complaints were frequency, urgency, dysuria and nocturia.[12]

In this study, the first hypothesis stating that there was a difference in IPSS before and after 0.4 mg tamsulosin on LUTS complaints in patients with post-DJ stent insertion. This study has proved that there was difference in the form of a decrease in total and irritative IPSS. This decrease was statistically significant compared to placebo ($p < 0,0001$). As for obstructive IPSS, the decrease was also found, but was statistically significant (p, 155).

This result was slightly different from the results obtained by Navanimitkul N & Lojanapiwat B showing that not only total and irritative IPSS that decreased, but also obstructive IPSS. The difference was that in this study tamsulosin was given for 4 weeks.[11] Further study is necessary, whether administration of tamsulosin for more than one week significantly affects symptoms.

In this study, the causes of statistically significant decline in irritative IPSS could be caused by LUTS complaints, which was most predominant on day 7 post-DJ stent insertion. The complaints were irritating symptoms (frequency, urgency, and nocturia). Some literatures and some previous studies also mentioned that irritative LUTS complaints were more predominant than obstructive one in patients with post-DJ stent insertion.[4,11] Since irritative IPSS in LUTS was the most predominant, the provision of tamsulosin, the irritative IPSS would decrease significantly compared to obstructive IPSS.

The second hypothesis stated that there was a difference in IPSS before and after the administration of 5 mg solifenacin in LUTS complaints in patients with post-DJ stent insertion. From this research, there were differences in total, irritative and obstructive IPSS. However, only total and irritative IPSS were statistically significantly different.

The results were consistent with those obtained by KT Lim et al, in which the administration of 5 mg solifenacin daily for 2 weeks has decreased total, irritative, and obstructive IPSS. However, significant decrease occurred in total and irritative IPSS.[4]

In the second hypothesis, statistically significant decrease in irritative IPSS could result from predominant LUTS complaint on day 7 after DJ stent the insertion, which consisted of irritative symptoms (frequency, urgency), and according to Lim JS these symptoms were similar to the symptoms of overactive bladder (OAB).

Park SJ et al. also wrote that micturition complaints of post DJ stent insertion with OAB complaints, which were frequency and urgency, were caused by involuntary contraction of the bladder mediated by muscarinic receptors. In this case, the provision of anti-muscarinic would improve OAB symptoms by reducing frequency and urgency.[10]

In the third hypothesis there was a difference in IPSS between after 0.4 mg tamsulosin and to 5 mg solifenacin delivery for 1 week in patients with post DJ stent insertion. This was not proved in this study. There was no difference in the reduction of total, irritative, and obstructive IPSS between tamsulosin and solifenacin groups.

CONCLUSION

Tamsulosin or solifenacin can improve irritative LUTS symptoms caused by the insertion of DJ stent.

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