Effectiveness of using Solifenacin compared to Mirabegron after double-J stent installation for treatment of lower urinary tract symptoms (LUTS)

by Emmy Palinggi

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Original article

Effectiveness of using Solifenacin compared to Mirabegron after double-J stent installation for treatment of lower urinary tract symptoms (LUTS)

Emmy Palinggi[1], Muhammad Asykar Palinrungi[2], Achmad M. Palinrungi[2], Arifin Seweng[3], Khoirul Kholis[2], Syakri Syahrir[2], Syarif[2], Muhammad Faruk[1]

[1]Department of Surgery, Faculty of Medicine; [2]Division of Urology, Department of Surgery, Faculty of Medicine; [3]Department of Biostatistics, Faculty of Public Health; Hasanuddin University, Makassar, Indonesia.

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Corresponding author

Muhammad Asykar Palinrungi
Division of Urology,
Department of Surgery,
Faculty of Medicine,
Hasanuddin University,
Jalan Perintis Kemerdekaan KM 11,
Makassar-90245, South Sulawesi,
Indonesia.
Phone: +62-411587571
Email: apalinrungi@yahoo.com

Abstract

Lower urinary tract symptoms (LUTS) and ureteral-stent-related symptoms (uSRS) are similar to those of lower urinary tract symptoms caused by benign prostatic hypertrophy (BPH), and complaints about urgency and frequency of urination are the same as in patients with overactive bladder syndrome (OAB). β_3-adrenoceptor agonist (Mirabegron) and anti-muscarinic (Solifenacin) therapies used for LUTS and OAB therapy can also be used to reduce SRS complaints. This study aimed to determine the effectiveness of using Solifenacin as a treatment for uSRS as compared to Mirabegron. This study used a double-blinded experimental design. Samples were taken randomly (consecutive random sampling) from fifty patients with uSRS. Data was collected using the Ureteral Symptoms Score Questionnaire (USSQ) as a measuring instrument. Data was analyzed using the mean, t-Test, and Chi-square tests. P values of <0.05 were considered to be statistically significant. Treatment by administering 5 mg/day of Solifenacin was compared with that of 50 mg/day of Mirabegron demonstrates a fairly good result of lowering the LUTS score complaint where the average score values measured were according to urinary symptoms (5.64 vs. 6.08, p = 0.53), pain (4.48 vs. 4.52, p = 0.96), general condition (3.6 vs. 3.2, p = 0.96), work activity (2.08 vs. 2.04, p = 0.044), sexual activity (1.00 vs. 1.32, p = 0.42), and other complaints (2.48 vs. 4.00, p= 0.001). The average rate reduction of USSQ urinary symptoms, pain, general circumstances and work activity was greater in Solifenacin group. These results show insignificant differences in symptom reduction, except in the variables of work activity (AK) and other complaints (TOS).

Key words: Mirabegron, Solifenacin, Stent-related symptoms

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Placing a stent ureter is a procedure that is frequently used in endourological treatment[1]. The stent ureter becomes a simple and effective method of ureteric drainage that maintains kidney function, reduces pain due to obstruction in the ureter, and avoids the installment of medical

devices outside the body[1,2]. Several studies reported the incidence of complaints of Double J (DJ) stent side effects in patients can reach 50–80%[3,4]. Complaints related to this stent, also called as stent related syndrome (SRS), may vary across the lower urinary tract symptoms (LUTS), such as frequency of urination (60%), urgency of urination (60%) and dysuria (40%), in addition to pain complaints (80%) and hematuria (54%)[5–7].

Along with the technological advances and modifications of the stent ureters that are continuously being developed, various studies have been conducted to research the treatment of side effects associated with a DJ stent after installation, including stent design modification, medicaments, stent positions, stent coatings and intravesical therapy[8,9]. The Ureteral Stent Symptoms Questionnaire (USSQ) is a gold standard questionnaire design to assess morbidity and provide better data comparison[10,11].

Complaints of the lower urinary track as side effects after DJ stent installation are similar to the lower urinary tract symptoms caused by benign prostatic hypertrophy (BPH), and the complaints regarding urgency and frequency of urination is the same as in patients with overactive bladder syndrome (OAB). Alpha blockers and anti-muscarinic treatments used for BPH and OAB treatments are then also used to reduce the complaints related to SRS[12,13]. Complications are caused by a DJ-stent insertion, not yet widely researched and/or published about, especially in Indonesia.

This study specifically discusses the efficacy comparison of treatment using Mirabegron (beta-3 adrenergic agonist) and Solifenacin (anti-muscarinic) to treat side effects in patients after the installation of a DJ stent. Solifenacin is a muscarinic receptor that blocks acetylcholine from bonding with an M-3 receptor in the bladder detrusor muscle in order to prevent bladder contraction[14,15]. Mirabegron is a selective agonist for beta-3 adrenergic receptors. A beta-3 adrenoreceptor is a beta predominant receptor that is found in the detrusor's smooth muscle cells, and its stimulation will cause detrusor muscle relaxation[3,6].

Material and methods

This study was conducted in a referral hospital in eastern Indonesia. The study used a double-blind experiment design. The sample comprised of 50 respondents selected based on the entry queue within the hospital (consecutive random sampling), which was divided into two groups: Group I (n = 25) given 5mg/day of Solifenacin and Group II (n = 25) who were given 50 mg/day of Mirabegron. Ethical approval was obtained from local Institutional Review Board (Ref. No. 1023/UN4.6.4.5.31/PP36/2019).

We distributed Ureteral Symptoms Score Questionnaires (USSQ) among patients who had recently had a DJ stent installed. The USSQ could be filled in our outpatient department or via telephone, on the seventh day after surgery. Patients who were showing symptoms of lower urinary complaint were given one of the treatments for three weeks, and the USSQ questionnaire was conducted again the fourteenth, twenty-first, and twenty-eighth days after surgery.

The inclusion criteria included male and female patients aged 18–79 years who undergone an endourology or PCNL operation followed by DJ stent insertions. We also included patients with an indication of a DJ stent with ureteric stones < 10 mm (with or without pelvic dilatation, calyx, or ureters), ureteric stenosis, and/or kidney stones who undergone shockwave lithotripsy (ESWL) with DJ stent unilateral installation for the first time. The exclusion criteria of this study was history of malignancy in the urinary track, hypertrophic prostate (prostate enlargement more than 20 cc in the ultrasonography), sexual dysfunction, stroke, alcoholism, urinary infections, or other diseases (e.g. diabetes mellitus, cardiovascular, hypertension); pregnancy; current or previous radiation hormonal therapy; surgical procedures in the minor pelvic region; ureteral reconstruction surgery; and/or Alzheimer's disease or central nervous system trauma accompanied by the comorbidities of stones in the bladder, there was a diverticula urethra in women and hypersensitivity to the Solifenacin compounds or Mirabegron.

Statistical analysis

Analysis was performed using SPSS version 21.0 for Windows (IBM SPSS Inc, Armonk, NY: IBM Corp.) to compare the effectiveness of treatment with 50 mg/day of Mirabegron and 5 mg/day of Solifenacin in treating complaints due to LUTS post-installation of a DJ stent in our institution using mean, t-test and Chi-square tests.

Results

In this study, observation and data retrieval was conducted for four weeks and evaluated six complaints of the lower urinary tract (LUTS), such as urination complaints, pain degrees, general health status, work activities, sexual activities and other complaints that cause discomfort in the patients.

Table 1 shows that as many as 33 people (66%) from the total sample are male, while 17 people (34%) are female. The most represented age group of the samples was the 46 – 60-year-old group, which amounted to 48%, while the smallest was the age group of 61–75 years amounted to 6%. A total of 52% of patients underwent URS and right DJ stent insertion, while 48% of patients underwent a URS and left DJ stent insertion.

Table 1: Patient characteristics

Variable		Solifenacin		Mirabegron		Total	
		N	%	N	%	N	%
Gender	Male	13	52.0	20	80.0	33	66.0
	Female	12	48.0	5	20.0	17	34.0
Age group (years)	Teens (18-25)	2	4.0	6	12.0	8	16.0
	Adult (26-45)	10	20.0	10	20.0	20	40.0
	Early adult (46-55)	7	14.0	9	18.0	16	32.0
	Older adult (55-65)	4	8.0	0	0.0	4	8.0
	Elderly (> 65)	2	4.0	0	0.0	2	4.0
Action	URS + Left DJ stent	11	44.0	15	60.0	26	52.0
	URS + Right DJ stent	14	56.0	10	40.0	24	48.0

Table 2: Characteristics of respondents by age, height, weight, and body mass index (BMI)

Variable	Min	Max	Mean	SD
Age (years)	18	70	42.94	13.25
Height (cm)	145	172	163.10	6.46
Weight (kg)	45	85	65.18	9.15
BMI	19.40	31.60	24.42	2.55

Table 2 shows the characteristics of respondents based on age, height, weight and BMI. The average age of respondents was 42.94 years. The average patient height was 163.10 cm. The average weight of the respondents was 65.18 kg. The average body mass index (BMI) of the respondents was 24.42, with the highest BMI being 31.60 and the lowest BMI being 19.40.

Table 3 shows the average rate of urination complaint (US) reported in the first week when patients had not yet received treatment. Both groups have a similar average value, Mirabegron 14.00±5.87, Solifenacin 15.48±4.75. The US score decreases every week. At week IV of Mirabegron treatment an average value of 6.08±2.43 was reported, while Solifenacin patients report an average score of 5.64±2.56. The decrease in score indicates the presence of improvements in clinical symptoms after treatment. The p-value (0.093, 0.414, 0.536) > α = 0.05, indicating no significant difference between treatments.

An average score of pain complaint (N) in the first week when treatment had not yet begun, the Mirabegron group has a not much different average rate, amounting to 12.48±2.12, while Solifenacin showed 13.8±3.57. Then there is a lower score each week. In week IV the Mirabegron group has an average value of 4.52±2.43, whereas Solifenacin's values were 4.48±2.98. The p-value (0.205, 0.779, 0.959) > α = 0.05, indicating that there is no significant difference.

Regarding general condition (KU), in the first week before treatment was, the Mirabegron group has an average value of 6.56±2.0 while Solifenacin's was 9.52±3.75. Then there was a decrease in the values. In week IV, the Mirabegron group has an average value of 3.20±2.56, while the Solifenacin's values were 3.60±2.54. Although there were significant differences between the Mirabegron group and the Solifenacin group in the first week, the two groups showed relatively similar results by week IV—a decrease in the score indicating clinical improvement. The weekly p-values were 0.055, 0.468, 0.959 > α = 0.05, indicating that there is no significant difference.

In the average value of work activity (AK) in the first week before treatment was given, both groups have insignificant average values, with Mirabegron at 5.32±2.03 and Solifenacin at 6.72±3.32. Then there was a decrease in the scores in the following weeks with Solifenacin at 4.60±3.09 and Mirabegron at 3.12±1.78. In week IV the Mirabegron group had an average value of 2.04±1.27, while the Solifenacin group reported 2.08±1.89. The p-value value in the second week was 0.044 < α = 0.05, which means that the two groups tested showed a significant difference in the second week.

For the average score of sexual activity (S) in the first week before receiving treatment, the mirabegron group has a significantly different average value of 1.48±1.87 compared to

Solifenacin's 0.28±0.79. Then there was a slight decrease in the score value for the Mirabegron group, which had an average value of 1.32±1.37 at week IV. However, there was an increase in the value of the Solifenacin group score of 1.00±1.04. The p-values for each week were 0.375, 0.798, 0.416 > α = 0.05, which means that the two groups tested showed a lower score complaint each week after treatment and showed no significant differences.

The average value of complaint score (TOS) during the first week before receiving treatment should significantly different average values between the groups with Mirabegron's average value being 5.92±1.41 and Solifenacin's being 7.40±3.04. Then, after treatment, there was a decrease of scores in the second and the third weeks, with the p-value being 0.605 and 0.087 > α = 0.05, which means there is no significant difference between the treatment methods. However, there are significant differences found in week IV, namely the p-value for the variable of another complaint (TOS) was 0.001 < α = 0.05, meaning that there is a significant difference between the Mirabegron group and the Solifenacin group in week IV.

Table 3: Score value USSQ in post-installation patients' DJ stent

Variable	Observation time (Week)	Mean score		p-value
		Solifenacin	Mirabegron	
Urination complaint (US)	I	15.48±4.75	14.00±5.87	0.332
	II	11.08±3.37	9.52±3.04	0.093
	III	8.20±2.50	7.68±1.93	0.414
	IV	5.64±2.56	6.082.43	0.536
Pain complaint (N)	I	13.8±3.57	12.48±2.12	0.119
	II	9.68±3.89	8.52±2.29	0.205
	III	5.96±3.38	5.72±2.57	0.779
	IV	4.48±2.98	4.52±2.43	0.959
General condition (KU)	I	9.52±3.75	6.56±2.0	0.001
	II	6.32±3.07	4.68±2.84	0.055
	III	4.36±3.06	3.76±2.72	0.468
	IV	3.60±2.54	3.20±2.56	0.959
Work activity (AK)	I	6.72±3.32	5.32±2.03	0.079
	II	4.60±3.09	3.12±1.78	0.044
	III	3.24±1.94	2.48±1.73	0.151
	IV	2.08±1.89	2.04±1.27	0.930
Sexual activity (S)	I	0.28±0.79	1.48±1.87	0.005
	II	2.00±2.30	1.48±1.75	0.375
	III	1.44±1.66	1.56±1.63	0.798
	IV	1.00±1.04	1.32±1.37	0.416
Other complaints (TOS)	I	7.40±3.04	5.92±1.41	0.032
	II	4.92±2.46	4.64±1.07	0.605
	III	3.64±1.80	4.40±1.22	0.087
	IV	2.48±1.85	4.00±1.19	0.001

Table 4: Decreased average value of USSQ in post-installation patients DJ stent

Average decline in USSQ variable	Intervention		p-value
	Solifenacin	Mirabegron	
Urination complaint (US) Pre-H + 21	9.84	7.92	0.99
Pain (N) Pre-H+21	9.32	7.96	0.38
General condition (KU) Pre-H + 21	5.92	3.36	0.68
Work activity (AK) Pre-H + 21	4.64	3.28	0.05
Sexual activity (S) Pre-H + 21	1.00	0.16	0.18
Other complaints (TOS) Pre-H + 21	4.92	1.92	0.01

Table 4 above shows that variables US, N, KU, and S indicate the decreased scores for both groups, but it does not indicate a significant difference between the two groups with p-value respectively being 0.99, 0.38, 0.68 and 0.184. However, in the variables AK and TOS, this study suggests a significant difference between the two treatment options, with respective p-values of 0.05 and 0.01.

Discussion

Our study reveals that male subjects dominated the incidence of LUTS as they represented 66% of our subjects. The age groups with the highest numbers of participants were in the adult category (26–45 years), being 40% and the elderly category (46–55 years) being 32%, with an average age of 43 years. Meanwhile, URS DJ stent installation is slightly more dominant on the right side with an occurrence of 52%. This result is similar to the research by Pansota et al (2015), who examined the indications and complications of DJ stent installation in Pakistan and included eighty patients with a stent[16]. The results showed that the majority of patients (40.0%) were aged between 36 and 50 years with male and female ratios of 2.6:1. Out of eighty patients who had a DJ Stent installed because of the obstructive uropathy of the upper region, most received a DJ Stent after surgery. Additionally, it is reported that the most common cause of obstructive uropathy is kidney stone disease, whether ureteric or combined (87.5%). Meanwhile, 12.5% of other patients fall among PUJ's obstruction, carcinoma and pregnancy[16].

Our results showed that the score of all variables examined in this study showed a decrease from week to week, including urination/urinary symptoms (US), pain in the body (N), general status (KU), work activity (AK), sexual problems (S), and other discomfort (TOS). However, the variables US, N, KU and S did not indicate any significant difference between the Solifenacin group and the Mirabegron group. While the AK and TOS variables indicate a significant difference between the two treatment options with respective p-values of 0.044 and 0.001. These results suggest that treatment with Mirabegron has a greater effectiveness in improving the general situation and score of other complaints as expressed by the subjects through research questionnaires.

This study shows that Solifenacin and Mirabegron can be effective in decreasing patient LUTS complaints, but Solifenacin treatment has a larger though insignificant overall decrease than that of Mirabegron. Mirabegron treatment has a larger and significant influence on the effectiveness score in general condition and other complaints as reported by subjects. The results of this study could be influenced by the fact that both treatment options were prepared in the same workspace as an inhibitor of M3 receptors, which would clearly indicate similar results to those reported[14]. For the significant result in general condition and other complaints, it is very likely to have been influenced by the characteristics of the respondents who received the drug in the Mirabegron group. The oldest age group involved in the Mirabegron group was only in the 51–60-year-old range while the Solifenacin group patients in the 61–70 range. The high age difference is very likely to affect the external therapeutic outcome. These results are in keeping with the research of Maharajh et al (2015), which states that age is definitely a factor in relation to LUTS, due to the hormonal and mitogenesis differences that are connected with the risk of urological diseases[17].

Conclusion

Patients using 5 mg/day of Solifenacin were compared patients using 50 mg/day of Mirabegron to cure complaints of LUTS after double-J stent installation. These results show insignificant differences in symptom reduction, except in the variables of work activity (AK) and other complaints (TOS).

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Conflict of interest: None

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