

Endourology

Effects of Tamsulosin, Solifenacin, and Combination Therapy for the Treatment of Ureteral Stent Related Discomforts

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Purpose: To evaluate the effect of tamsulosin, solifenacin, and combination therapy of two agents in improving the lower urinary tract symptoms of patients with indwelling double-J ureteral stents.

Materials and Methods: A total of 168 patients underwent placement of a double-J ureteral stent after retrograde ureteroscopy for urinary stone disease. All patients received polyurethane double-J ureteral stents (6 Fr, 24 or 26 cm), which were removed a mean of 14 days postoperatively. A total of 48 patients were given no medication (Group 1), 43 patients were given tamsulosin 0.2 mg once daily (Group 2), 45 patients were given solifenacin 5 mg once daily (Group 3), and 32 patients were given a combination of two agents postoperatively (Group 4). International Prostate Symptom Score/quality of life (IPSS/QoL) and visual analogue pain scale (VAPS) questionnaires were completed by each patient at 1 day postoperatively and on the day of stent removal.

Results: In the total group of patients, the mean age was 50.24 ± 12.90 years. There was a significant difference in the IPSS total score between group 1 and groups 3 and 4. Group 4 also differed significantly from group 1 in the irritative subscore. The obstructive subscore differed between groups 2 and 4 and group 1. There was a statistically significant difference between group 1 and group 4 in the QoL score. There were no significant differences in the VAPS.

Conclusions: Combination therapy with tamsulosin and solifenacin improved both irritative and obstructive symptoms more than in the other groups. Combination therapy should be strongly considered for patients who complain of stent-related symptoms.

Key Words: Pain; Stents; Ureter

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INTRODUCTION

Ureteral stents, which were introduced by Zimskind et al in 1967, are widely used for urinary tract disease [1]. The double-J stent, which is the most common form of ureteral stent, is used in obstructive pyelonephritis, intolerable acute renal colic, ureteral edema, ureter perforation following endoscopic procedures, and diseases such as steinstrasse [2,3].

Despite the usefulness of stents, however, patients experience various stent-related symptoms, such as pain, frequency, and urgency, which cause a significant decrease in patient health-related quality of life (HRQoL) [4]. The etiol-

ogy of these symptoms is unknown. Thomas reported that an important factor of stent-related symptoms is the pressure transmitted to the renal pelvis during urination and trigonal irritation by the intravesicular part of the stent [5]. For this reason, several attempts to minimize stent-related symptoms have recently been reported. Pharmacologic management is one such trial, especially the prescription of selective alpha-1-blockers and antimuscarinic agents. We believe that pharmacologic management is simpler and less invasive than other ways. The purpose of this article was therefore to analyze and assess the effectiveness of a selective alpha-1-blocker (tamsulosin) and antimuscarinic (solifenacin) in improving the lower urinary tract symp-

toms of patients with indwelling double-J ureteral stents.

MATERIALS AND METHODS

1. Materials

Between January 2010 and December 2010, 168 patients (108 men and 60 women) underwent double-J stenting retrogradely after retrograde ureteroscopy for urinary stones by a single surgeon. Patient data were obtained retrospectively through chart review. Patients who were previously diagnosed with benign prostatic hyperplasia or overactive bladder and who were prescribed a selective alpha-1-blocker or antimuscarinic agent were excluded from this study. In addition, patients who were using analgesics before surgery were also excluded. The ureteral stent was composed of polyurethane material and its diameter was 6 Fr; the lengths were 24 cm and 26 cm. The length of ureteral stent was dependent on the patient's height.

2. Methods

Surgery was performed under general anesthesia and the position of the stent was confirmed by plain X-ray. The stents were removed 14 days after surgery. The patients were divided into four groups. Group 1 (n=48) was the control group and did not take any drugs. Group 2 (n=43) received tamsulosin 0.2 mg once a day every day. Group 3 (n=45) received solifenacin 5 mg once a day every day. Group 4 (n=32) received tamsulosin 0.2 mg and solifenacin 5 mg daily. The day before surgery, on postoperative day 1, and on the day of stent removal, each patient completed written International Prostate Symptom Score/quality of life (IPSS/QoL) and visual analogue pain scale (VAPS) questionnaires. The IPSS was divided into the total score, obstructive symptom score, and irritative symptom score, and each was compared. Each group's preoperative day, postoperative day, and stent removal day scores were compared. Chi-square test, one-way ANOVA, and one-way repeated-measures ANOVA were used for comparisons between each of four groups. Values of $p < 0.05$ were considered statistically significant. Statistical analyses were performed with SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The mean age of the patients was 50.24 ± 12.90 years, and there were no significant differences between the groups. A total of 103 patients has lower ureter stones, whereas 18 patients had mid ureter stones. The stone distribution was significantly different in each group ($p < 0.001$) (Table 1). There were statistically significant differences in the IPSS total score and the obstructive subscore by one-way repeated-measures ANOVA ($p=0.013$, 0.006). There were significant differences between group 1 and group 4 ($p=0.015$), and between group 2 and group 4 ($p=0.031$), in the IPSS total score. For the obstructive subscore, group 4 differed significantly from group 1 ($p=0.003$). There were no statistically significant differences in the irritative subscore, QoL, or VAPS ($p=0.075$, 0.068 , and 0.088 , respectively). However, the p-value of interaction was statistically significant for the IPSS total score, irritative subscore, obstructive subscore, and QoL ($p < 0.001$, < 0.001 , 0.015 , and 0.012 , respectively).

We therefore compared each group by one-way ANOVA at each time point. On the day of stent removal, all scores were significantly different in each group except the VAPS ($p < 0.001$, < 0.001 , < 0.001 , < 0.001). In particular, all scores were significantly lower in group 4 except for VAPS. In group 2, only the obstructive score was significantly lower. The total and irritative subscore were significantly lower in group 3. Preoperatively and 1 day postoperatively, there were no significant differences in any group. The VAPS did not appear to significantly change in any groups (Table 2). According to the multiple comparison test on the day of stent removal, there was a significant decrease only in group 4. This suggests that that stent-related symptoms improved more in group 4 than in group 1. Symptoms did not significantly improve in the other groups.

The side effects of tamsulosin and solifenacin were minimal. No patients discontinued the medication because of side effects.

DISCUSSION

Ureteral stents can be used variously in the management

TABLE 1. The characteristics of 168 patients

	Group 1	Group 2	Group 3	Group 4	p-value ^a
Patient (n)	48	43	45	32	
Age ^b (yr)	50.08 ± 11.47	49.91 ± 15.23	49.87 ± 13.29	50.72 ± 11.46	0.986
Gender					0.564
Male	31	24	31	22	
Female	17	19	14	10	
Stone location					< 0.001
Upper ureter	7	12	14	14	
Mid ureter	5	0	3	10	
Lower ureter	36	31	28	8	

^a: chi-square test, ^b: Mean \pm SD

TABLE 2. Comparisons of IPSS/QoL and VAPS in group 1, 2, 3 and 4

		Group 1	Group 2	Group 3	Group 4	p-value ^a	p-value ^b
IPSS total score	Preoperative	8.94±4.13	8.60±4.12	9.04±3.94	8.72±4.16	0.013 (<0.001) ^c	0.958
	On one day postoperatively	11.65±4.38	12.53±4.79	11.16±5.13	11.47±3.98		
	On the day of stent removal	13.77±4.50	12.77±5.24	11.04±5.29	7.16±3.37		
	T ^d	1	1, 2	2	3		
IPSS irritative subscore	Preoperative	4.15±2.59	4.30±2.84	4.49±3.09	4.84±2.71	0.075 (<0.001) ^c	0.735
	On one day postoperatively	6.44±3.46	7.79±3.69	6.27±4.00	7.09±3.52		
	On the day of stent removal	7.48±3.50	8.05±3.88	5.73±4.00	4.22±2.70		
	T ^d	1, 2	1	2, 3	3		
IPSS obstructive subscore	Preoperative	4.79±3.16	4.30±2.95	4.56±2.78	3.88±2.88	0.006 (0.015) ^c	0.572
	On one day postoperatively	5.21±2.57	4.74±2.91	4.89±2.73	4.38±2.54		
	On the day of stent removal	6.29±2.63	4.72±3.24	5.31±2.91	2.94±2.06		
	T ^d	1	2	1, 2	3		
QoL	Preoperative	2.52±1.79	2.19±1.80	2.42±1.62	1.88±1.77	0.068 (0.012) ^c	0.385
	On one day postoperatively	2.21±1.76	2.44±1.71	2.51±1.74	2.34±1.56		
	On the day of stent removal	2.83±1.72	3.07±1.67	2.87±1.77	1.47±1.44		
	T ^d	1	1	1	2		
VAPS	Preoperative	6.42±1.71	6.60±1.59	6.18±1.70	6.28±1.65	0.088 (0.634) ^c	
	On one day postoperatively	2.56±1.47	2.88±1.50	2.69±1.46	2.44±1.37		
	On the day of stent removal	2.90±1.65	3.67±1.94	2.87±1.87	2.69±1.31		

IPSS/QoL: International Prostate Symptom Score and Quality of Life, VAPS: Visual analogue pain scale, ^a: one-way repeated measures ANOVA, ^b: one-way ANOVA, ^c: p-value of interaction, ^d: the same letters indicate non-significant difference between groups based on Tukey's multiple comparison test

of urinary tract diseases. For example, for the prevention of ureteral obstruction and recovery of damaged ureter tissue, narrowing the expansion of the ureter and the stone will help with emissions [2]. Ureterscopy, especially after ureteroscopic lithotripsy, routinely make use of ureteral stents [6]. The use of ureteral stents aids in the improvement of urinary tract disease, whereas patients with indwelling stents have been known to complain of a variety of stent-related symptoms. In fact, flank pain, lower abdominal pain or loin pain, frequency, urgency, infection, and hematuria are known stent-related symptoms [7]. Joshi et al reported that, because of these stent-related symptoms, 80% of patients have a reduced HRQoL and need continued understanding and interest about their symptoms [8]. To solve these problems, studies have been run in several ways. First, stent material changes have been tried to reduce the symptoms. For example, double-J stents with a tapered distal end made with a hydrophilic material were introduced [9]. In addition, studies about the relationship between stent length and morbidity have been reported. If a ureteral stent is needed after endoscopic surgery, ureteral length should be measured so that an appropriate stent can be used in patients, which can reduce distal migration and stent-related symptoms [10]. Periureteral injection of botulinum toxin type A after stent insertion has been shown to decrease pain and narcotic requirement [11].

We believe that new stent development is difficult. In addition, the cost and technical difficulties of botulinum toxin treatment are considered to be problems. We therefore sought safe and convenient ways to improve stent-related

symptoms and we researched pharmacologic management as one of those ways. Stent-related symptoms are similar to the benign prostatic hyperplasia symptoms caused by urethral and bladder resistance and bladder instability [12]. For this reason, some studies have reported that selective alpha-1-blockers improve stent-related symptoms. Beddingfield et al reported that patients taking alfuzosin 10 mg daily had improved frequency and flank pain [13]. Furthermore, improvement of sleep disorders and daily life were also reported. Deliveliotis et al reported that alfuzosin improved stent-related symptoms and pain as well as sexual function and general health [14]. Wang et al suggested that the selective alpha-1-blocker tamsulosin improved urinary symptoms, flank pain, and pain during voiding [15]. In addition, Damiano et al reported that the administration of tamsulosin improved urinary symptoms, VAPS, and QoL [12]. In our study, the IPSS total score, irritative subscore, QoL, and VAPS did not show statistically significant differences. However, the difference in the obstructive subscore was statistically significant.

Stent-related symptoms are similar to overactive bladder symptoms (urinary frequency, urgency, and urge incontinence) caused by involuntary bladder contraction mediated by muscarinic receptors [16]. Antimuscarinic agents have been used to improve overactive bladder symptoms. Norris et al reported that there were no significant differences between an oxybutynin-treated group and a placebo group [17]. But those authors argued that further ongoing research is needed. Agarwal et al reported that bladder discomfort was improved in an oxybutynin or

tolterodine administration group compared with a placebo group before surgery [18]. In our study, the solifenacin 5 mg daily group had statistically significant differences in the total score and irritative subscore. The other scores were not significantly different.

Lee et al compared combination treatment with tamsulosin and tolterodine with a placebo group [19]. Each group showed no significant differences in the IPSS or VAPS. They reported that correct stent location was more effective for the improvement of stent-related symptoms. In the present study, however, IPSS and QoL showed statistically significant differences in the tamsulosin and solifenacin combination treatment group. However, there was no significant difference in the VAPS.

The limitations of this study are as follows. Some patients did not complete the ureteral stent symptom questionnaire on the preoperative day. Therefore, we could not use this questionnaire. The small groups of each scale made it difficult to verify the statistical significance. Because this was a nonrandomized and retrospective study, we did not get useful and entirely credible information. Therefore, further large-scale, randomized, prospective study is needed to get more accurate information.

CONCLUSIONS

Combination therapy with tamsulosin and solifenacin improved obstructive and irritative symptoms and QoL more than in the control group. Therefore, combination therapy with tamsulosin and solifenacin should be strongly considered for patients who complain of stent-related symptoms. In the future, large-scale, prospective, and randomized study will be needed.

Conflicts of Interest

The authors have nothing to disclose.

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