

Original Article

Therapeutic effect of solifenacin combined with tamsulosin on benign prostatic hyperplasia with overactive bladder

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Received June 13, 2018; Accepted August 25, 2018; Epub December 15, 2018; Published December 30, 2018

Abstract: Objective: To observe the clinical efficacy of solifenacin combined with tamsulosin in benign prostatic hyperplasia (BPH) with overactive bladder (OAB). Methods: One hundred and six patients with BPH and OAB were enrolled in Department of Urology Surgery, Ruian City People's Hospital. The patients were divided into control group and study group (53 cases for each group). In the control group, tamsulosin was used alone for 12 weeks. In the study group, solifenacin was added on the basis of the control group method for 12 weeks. International prostate symptom score (IPSS), overactive bladder symptom scores (OABSS), urine storage period symptom score (USPSS), voiding symptom score (VSS), maximum urinary flow rate (Qmax), residual urine volume (RUV), total effective rate, quality of life index (QOL), urinary nerve growth factor, and adverse reactions were analyzed and compared. Results: The general data of the two groups were statistically insignificant and comparable ($P > 0.05$). After treatment, the patients in the study group were superior to those in the control group in IPSS, OABSS, USPSS, VSS, and Qmax indicators. And the results of two groups were statistically different ($P < 0.05$). There was no significant difference in the residual urine volume between the two groups ($P > 0.05$). In terms of total efficiency, the study group was superior to the control group with statistical differences ($P < 0.05$). In terms of quality of life scores, the two groups were significantly improved after treatment ($P < 0.05$), and the quality of life scores in the study group after treatment were significantly better than those in the control group ($P < 0.05$). In terms of urine nerve growth factor, the two groups of patients significantly improved after treatment ($P < 0.05$), and the study group was statistically superior to the control group ($P < 0.05$). There was no statistical difference in the incidence of adverse reactions between the two groups ($P > 0.05$). Conclusion: The clinical efficacy of solifenacin combined with tamsulosin on benign prostatic hyperplasia combined with overactive bladder patients is better than that of tamsulosin alone and does not increase the incidence of side effects. It is worthy of clinical application.

Keywords: Solifenacin, tamsulosin, benign prostatic hyperplasia, overactive bladder, curative effect observation

Introduction

The clinical manifestations of overactive bladder (OAB) include urinary frequency, urinary urgency, urinary incontinence, and nocturnal urinary frequency. Symptoms during urinary storage are more pronounced and the incidence of this disease is higher in foreign countries than in China [1]. Benign prostatic hyperplasia (BPH) occurs frequently in middle-aged and elderly men, and often leads to bladder outlet obstruction and OAB, which seriously affects the patient's quality of life and increases patient's psychological and economic pressure [2, 3]. Previously $\alpha 1$ blocker tamsulosin

was used commonly in the treatment of BPH, but the efficacy of tamsulosin in OAB is not significant [4]. Solifenacin has been used clinically as a new type of M3 receptor antagonist, its mechanism is to act on the M3 receptors in the bladder and urethra, therefore the contraction of bladder smooth muscle can be suppressed, and the symptoms of OAB can be improved [5, 6]. In this study, the two drugs were used in combination to explore the combined effects on BPH and OAB, and whether the combined use of these drugs increased the incidence of adverse reactions. Based on this, we selected 106 male patients in this hospital with BPH and OAB, and studied the clinical efficacy and safety

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Table 1. Comparison of general data between the two groups of patients

Project	Study Group	Control Group	t/ χ^2	P value
Number of cases	53	53		
Age (years)	55.74 ± 7.89	56.32 ± 8.01	0.793	0.421
Prostate volume (mL)	41.68 ± 15.67	42.01 ± 15.26	0.745	0.498
BMI (kg/m ²)	24.39 ± 5.27	24.25 ± 5.39	0.159	0.784
Systolic pressure (mmHg)	126.67 ± 13.51	125.47 ± 12.97	1.147	0.685
Diastolic pressure (mmHg)	95.34 ± 10.25	95.18 ± 9.89	1.126	0.697
Heart rate (beats per minute)	77.28 ± 7.92	76.58 ± 7.72	0.107	0.845
Concomitant underlying disease (n, %)				
Hypertension	39 (73.58)	41 (77.36)	0.498	0.894
Type 2 diabetes	19 (35.85)	18 (33.96)	0.574	0.901
Hyperlipemia	37 (69.81)	39 (73.58)	0.426	0.812

Note: BMI, body mass index.

of solifenacin combined with tamsulosin treatment.

Materials and methods

General information

In the Department of Urology of Ruian People's Hospital, 106 patients with BPH with OAB were enrolled from January 2015 to December 2017. All patients were randomly divided into experimental and control groups (53 patients in each group). All patients aged 45-78 years old, with an average age of 55.96 ± 8.69 years.

Inclusion criteria: Patients aged 45 years or older (including 45 years old), conformity with the diagnosis of BPH and OAB [7]. Diagnosis of OAB was made based on the clinical symptoms, overactive bladder symptom scores (OABSS) and urinalysis of the patient [8].

Exclusion criteria: Urinary tract infections; lower urinary tract obstruction; allergies of study drugs; patients with psychiatric symptoms who do not cooperate; abnormal urethra caused by neurogenic bladder; patients with peptic ulcer disease, glaucoma, or myasthenia gravis who cannot use research drugs.

This study was approved by the Ethics Committee of Ruian People's Hospital. All patients included in the study had completed the informed consent form.

Methods

All patients admitted to the hospital were examined by relevant checks, routine treatments

such as fluid infusion to correct the balance of water and electrolytes, antibiotics and anti-infective treatment for the infection, etc. Therapeutic scheme of the control group: routine treatment and tamsulosin hydrochloride capsules (Astellas Pharma Inc., Japan) 0.2 mg q.d. by oral administration after breakfast. Therapeutic scheme of the study group: treatment regimen of the control group combined with solifenacin succinate tablets (Astellas Pharma, Inc., Japan) 5 mg q.d. by oral administration after breakfast. Treatments of the two groups were taken by the patients for 12 weeks followed by the efficacy evaluation [9].

Observation indicators

Main outcome indicators: International prostate symptom score (IPSS): There are 7 questions in this table, and the total score is 35 points. According to the score, the Lower Urinary-Tract symptoms (LUTS) can be divided into three levels. Among them, ≤ 7 is divided into mild degrees, 8-19 is moderate, and ≥ 20 is divided into severe [10].

OABSS: Patients were scored according to the daytime urination number, night urination number, urgency urination and urge urinary incontinence, patients with more than 3 points can be diagnosed as OAB [8].

Urine Storage Period Symptom Score (USPSS): In the IPSS table, items 2, 4 and 7 are used as USPSS [10].

Voiding Symptom Score (VSS): In the IPSS table, items 1, 3, 5, 6 are used as VSS [10].

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Table 2. Comparison of various indicators before and after treatment in two groups of patients

	Before treatment				After treatment			
	Study Group	Control Group	t value	P value	Study Group	Control Group	t value	P value
IPSS	18.57 ± 2.29	17.86 ± 2.92	0.954	0.389	9.85 ± 3.02*	15.80 ± 3.29*	5.981	0.002
OABSS	10.27 ± 1.76	10.37 ± 2.28	0.576	0.673	5.28 ± 1.24*	9.59 ± 2.73#	4.198	0.019
USPSS	14.76 ± 2.17	12.95 ± 3.18	0.792	0.742	8.29 ± 1.74*	12.28 ± 3.08#	4.698	0.008
VSS	5.12 ± 2.47	5.23 ± 2.26	0.189	0.741	3.41 ± 1.68*	4.94 ± 1.72#	4.165	0.016
Qmax (mL/s)	8.69 ± 2.73	8.39 ± 2.24	0.802	0.562	16.68 ± 4.15*	9.26 ± 2.39#	3.125	0.041
RUV (mL)	18.67 ± 12.39	17.87 ± 9.37	0.658	0.502	16.72 ± 10.16#	15.76 ± 9.64#	0.795	0.421

Note: P value represents the comparison between the two groups before and after treatment, *represents the comparison between the project after and before treatment and $P < 0.05$, #represents the comparison between the project after and before treatment and $P > 0.05$. IPSS, international prostate symptom score; OABSS, overactive bladder symptom scores; USPSS, urine storage period symptom score; VSS, voiding symptom score; Qmax, maximum urinary flow rate; RUV, residual urine volume.

Qmax: The amount of urine discharged per unit time is called the urinary flow rate, and Qmax is the most significant of the urinary flow rate parameters [10]. Under normal circumstances, when the urine volume is more than 150 mL, the Qmax of an adult male should be greater than or equal to 15 mL/s, if the Qmax is less than 10 mL/s, it represents obstruction.

Residual urine volume (RUV) determination: The patient after urination should do a B-ultrasound check to determinate the residual urine volume of the bladder [11].

Secondary indicators: Quality of life index (QOL): The score for this table is 0-6 points, the higher the score, the severer the patient's symptoms would be. The highest score is 6 points, in this case the patient feels very painful about the current symptoms [11].

Determination of urinary nerve growth factor (NGF): Took 20 mL urine in the bladder filling period before and after treatment, and detected the urinary NGF levels [12].

Adverse reactions: Observed the adverse reactions during drug use in both groups to record and treat accordingly.

Efficacy evaluation: The clinical efficacy included cure (clinical symptoms completely disappeared after treatment), effective (all clinical symptoms had improved after treatment), valid (clinical symptoms were partially improved after treatment), invalid (no clinical change or even worse after treatment). The total effective rate is the ratio of the sum of cure, effective, and valid cases to the total number of cases.

Statistical analysis

Statistical analysis was performed using SPSS 17.0 software. Measured data were expressed as mean ± sd. The measurement data that matched the normal distribution were analyzed using t-test, denoted by t. Enumeration data is expressed in percentage, using chi-square test and Fisher's exact probability method, represented by chi-square. The difference is statistically significant at $P < 0.05$.

Results

Comparison of general information

A total of 106 male patients were included in the study, including 53 in the study group, aged 46 to 78 years with an average age of 55.74 ± 7.89 years. The mean prostate volume was 41.68 ± 15.67 mL, mean body mass index (BMI) was 24.39 ± 5.27, mean systolic and diastolic pressure were 126.67 ± 13.51 mmHg and 95.34 ± 10.25 mmHg, mean heart rate was 77.28 ± 7.92 beats per minute. Patients combined underlying disease included 39 cases of hypertension, 19 cases of type 2 diabetes and 37 cases of hyperlipemia. There were 53 patients in the control group, aged 45 to 76 years with an average age of 56.32 ± 8.01 years. The mean prostate volume was 42.01 ± 15.26 mL, mean body mass index (BMI) was 24.25 ± 5.39, mean systolic and diastolic pressure were 125.47 ± 12.97 mmHg and 95.18 ± 9.89 mmHg, mean heart rate was 76.58 ± 7.72 beats per minute. Patients combined underlying disease included 41 patients with hypertension, 39 patients with hyperlipid-

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Table 3. Comparison of effective rate after treatment between two groups of patients

Curative Effect	Before treatment (n, %)	After treatment (n, %)	χ^2	P value
Cured	12 (22.64)	9 (16.98)		
Effective	17 (32.08)	15 (28.30)		
Valid	20 (37.74)	19 (35.85)		
Invalid	4 (7.54)	10 (18.87)		
Effective rate	49 (92.46)	43 (81.13)	2.694	0.034

emia and 18 patients with type 2 diabetes mellitus. In terms of general data and clinical scores, there was no statistically significant difference between the two groups ($P > 0.05$). See **Table 1**.

Comparison of various indicators before and after treatment in two groups of patients

There was no statistical difference in IPSS, OABSS, USPSS, VSS, Qmax and RUV between the two groups before treatment ($P > 0.05$). In the study group, there were statistically differences in IPSS, OABSS, USPSS, VSS and Qmax before and after treatment ($P < 0.05$), while there was no significant difference in RUV before and after treatment ($P > 0.05$). In the control group, there was statistically difference in IPSS before and after treatment ($P < 0.05$), while there were no significant difference in OABSS, USPSS, VSS, Qmax and RUV before and after treatment ($P > 0.05$). There was no significant difference in the RUV between the two groups after treatment ($P > 0.05$). In the IPSS, OABSS, USPSS, VSS and Qmax, the study group was better than the control group after treatment, there were statistical differences ($P < 0.05$). See **Table 2**.

Comparison of clinical efficacy between two groups of patients

After treatment, there were 12 cured cases, 17 effective cases, 20 valid cases and 4 invalid cases in the study group. The total effective rate was 92.46%. In the control group, there were 9 cured cases, 15 effective cases, 19 valid cases and 10 invalid cases. The total effective rate was 81.13%. There was significant difference between the two groups in total effective rate, the statistics showed that the total effective rate of the study group was better than that of the control group ($P < 0.05$). See **Table 3**.

Comparison of quality of life scores between two groups of patients

Before treatment, there was no difference in quality of life scores between the two groups ($P > 0.05$), both groups had significant improvement after treatment ($P < 0.05$). There was a statistical difference in quality of life scores between the study group and the control group

after treatment, the study group was better than the control group ($P < 0.05$). See **Table 4**.

Comparison of urine nerve growth factor between two groups of patients

Before treatment, there was no difference in urinary NGF between the two groups ($P > 0.05$), both groups of patients had significant improvement after treatment ($P < 0.05$). There was a statistical difference in urinary NGF between the study group and control group after treatment, the study group was better than the control group ($P < 0.05$). See **Table 5**.

Comparison of adverse reactions between two groups of patients

Only one case of dry mouth, tachycardia, and nausea and vomiting occurred respectively in the experimental group during the course of medication. The incidence rate was 5.66% (3/53). In the control group there were 2 cases of nausea and vomiting, 2 cases of tachycardia, and 1 case of rash. The incidence rate was 9.43% (5/53). There was no statistical difference in the incidence of adverse reactions between the two groups ($P > 0.05$). Patients with adverse reactions were treated with rest and symptomatic treatment. If no remission, drug withdrawal treatment should be given to the patient. In this study, adverse reactions of patients were mild, no patient quitted after treatment.

Discussion

The incidence of OAB in China is 11.4%. The incidence of BPH for patients over 40 years is 10 times as much as the patients below 40 years could have. Benign prostatic hyperplasia is a common cause of overactive bladder symptoms by obstruction of the urethra in middle-

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Table 4. Comparison of quality of life between two groups of patients

Group	n	Before treatment	After treatment	t value	P value
Study group	53	4.92 ± 1.36	3.16 ± 0.73	8.098	0.001
Control group	53	4.96 ± 1.42	3.89 ± 1.02	4.287	0.015
t value		0.697	3.365		
P value		0.526	0.021		

Table 5. Comparison of urine nerve growth factor between two groups of patients

Group	n	Before treatment	After treatment	t value	P value
Study group	53	58.36 ± 6.12	18.63 ± 2.01	20.462	0.000
Control group	53	57.69 ± 6.02	30.63 ± 3.14	10.298	0.000
t value		0.602	3.698		
P value		0.612	0.015		

aged and elderly patients. Clinical efficacies are usually poor because of the age and combined chronic basal disease of patients [13, 14]. Clinical symptoms such as urinary frequency and urgency are seriously affecting the quality of life of patients [15]. The patients included in this study were all over the age of 45 years, and were combined with one or more underlying diseases, consistent with the results above. The α_1 receptor blocker is a common clinical treatment for patients with BPH combined with OAB, although it can improve the symptoms of patients with BPH but the improvement of OAB symptoms is not significant [16]. Solifenacin is a novel M3 receptor antagonist, when combined with M3 receptors it can inhibit detrusor contraction and improves OAB symptoms [5, 6]. Previous studies have shown that the combination of solifenacin and tamsulosin had a significant effect on patients with BPH combined with OAB [17]. In this study, after the combination of the two drugs, it was found that there was no difference between the two groups in the RUV, while the study group was better than the control group in the IPSS, OABSS, USPSS, VSS and Qmax, and the study group was more effective, consistent with the above study. Studies have found that patients with BPH combined with OAB have significant reduction in their quality of life due to the urinary frequency and urgency symptoms [15]. This study found that the quality of life of patients were low before treatment, the quality of life improvement of the study

group was better than that of the control group, consistent with the above studies.

So far, the pathogenesis of OAB is not clear, there are several conjectures [18]. The neurogenesis theory and efferent nerve theory are considered to be the most reasonable by our research team. The neurogenic theory suggests that due to the increase in the efferent nerve signals during the disease state, the micturition reaction is inhibited, which makes the micturition nerves unable to control properly, making the bladder overactive [19]. The efferent nerve theory suggests that due to peripheral and central sensory signals have changed during the conduction process, efferent nerves are believed to be extremely sensitive, filling feeling appears easily due to the small bladder capacity of BHP patients [20]. With the development of the disease, the afferent and efferent pathways are damaged, making the ability of the bladder to deal with afferent information to be weakened and the afferent activity of the reflected signal significantly increased [21]. Nerve growth factor is a neurotrophic factor that exists in many tissues and organs of the body. Its role is to promote nerve growth and nutrition nerves [12]. This study found that the levels of urinary NGF in the two groups were higher before treatment. After treatment, the level of NGF in the urine of the two groups significantly decreased, and the decline was more significant in the study group, which resulted in the regulation of bladder function and improvement of clinical symptoms.

group was better than that of the control group, consistent with the above studies.

In terms of adverse reactions, the use of M-adrenoceptor antagonists for acute urinary retention is widely concerned by clinics. In the previous studies, it was found that solifenacin combined with tamsulosin did not increase the incidence of acute urinary retention. The most common clinical side effect was dry mouth [22]. In this study, acute urinary retention did not occur. This may be related to the exclusion of patients with urinary tract obstruction and the small sample size in this study. The dry mouth in this study occurred only once in the study group, which may be related to the small

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sample size in this study, we could not consider that there is a difference in the incidence of dry mouth adverse reaction.

However, this study did not use multi-center samples, study cases came from a single source with a small sample size. We should expand the sample size and adopt a multi-center clinical study.

In summary, the clinical application of clinical trials of combined use of solifenacin and tamsulosin in patients with benign prostatic hyperplasia combined with overactive bladder is superior to that of tamsulosin alone and does not increase the incidence of side effects, which is worthy of clinical application.

Disclosure of conflict of interest

None.

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