

Clinical Factors Associated With Dose Escalation of Solifenacin for the Treatment of Overactive Bladder in Real Life Practice

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Purpose: To determine the baseline clinical characteristics associated with dose escalation of solifenacin in patients with overactive bladder (OAB).

Methods: We analyzed the data of patients with OAB (micturition frequency ≥ 8 /day and urgency ≥ 1 /day) who were treated with solifenacin and followed up for 24 weeks. According to our department protocol, all the patients kept voiding diaries, and OAB symptom scores (OABSS) were monitored at baseline and after 4, 12, and 24 weeks of solifenacin treatment.

Results: In total, 68 patients (mean age, 60.8 ± 10.0 years) were recruited. The dose escalation rate by the end of the study was 41.2%, from 23.5% at 4 weeks and 17.6% at 12 weeks. At baseline, the dose escalator group had significantly more OAB wet patients (53.6% vs. 20.0%) and higher total OABSS (10.2 ± 2.4 vs. 7.9 ± 3.5 , $P = 0.032$) than the nonescalator group. OAB wet (odds ratio [OR], 4.615; 95% confidence interval [CI], 1.578–13.499; $P < 0.05$) and total OABSS (OR, 1.398; 95% CI, 1.046–1.869; $P < 0.05$) were found to be independently associated with dose escalation.

Conclusions: Patients who have urgency urinary incontinence and high total OABSS have a tendency for dose escalation of solifenacin.

Keywords: Overactive urinary bladder; Muscarinic antagonists; Solifenacin

INTRODUCTION

The International Continence Society defines overactive bladder (OAB) as urgency with or without urgency urinary incontinence (UUI), usually accompanied by daytime frequency and nocturia, in the absence of urinary tract infection (UTI) or other obvious pathology [1]. The overall prevalence of lower urinary tract symptoms was 61.4% (53.7% of men, 68.9% of women) in the Korean EPIC study [2] and 11.8% (10.8% of men, 12.8% of women) in the international EPIC study [3], and the prevalence of OAB increased with age. OAB has a marked influence on quality of life. Liberman et al. [4] reported that individuals with OAB experienced decreased quality of life relative to community controls, even if they did not have incontinence.

Current treatment options include lifestyle modifications, behavioral therapy, pharmacotherapy, intravesical injection of botulinum toxin, and surgical procedures such as bladder augmentation or sacral neuromodulation. However, antimuscarinic agents represent the mainstay of OAB treatment. Flexible dosing of anticholinergic drugs is useful in clinical practice for achieving the maximal effect with minimal side effects [5].

Data from numerous flexible-dose studies of solifenacin demonstrated significantly improved urgency, frequency, and nocturia symptoms and increased volume voided in OAB dry patients [6-9]. However, these clinical trials were conducted with OAB patients for 14 weeks and offered only one opportunity for dose escalation.

The aim of the present study was to determine the baseline

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clinical characteristics associated with solifenacin DE in practice. In addition, we assessed the efficacy of solifenacin DE in reducing OAB symptoms after DE. We provided two opportunities for DE (after 4 and 12 weeks), and the patients were followed up for 24 weeks.

MATERIALS AND METHODS

This was a retrospective investigation of the factors associated with solifenacin DE in a population with OAB symptoms according to the protocol of our hospital. We reviewed 2,332 patients with OAB who received 5-mg solifenacin between August 2010 and January 2012. Men and women aged ≥ 20 years with a mean micturition frequency ≥ 8 /day, urgency episodes ≥ 1 /day in a 3-day voiding diary at baseline, and follow-up of at least 24 weeks were selected. Patients were excluded if they were taking alpha blockers or 5-alpha reductase inhibitors or had done so in the previous 2 months, had undergone pelvic surgery within 1 year (hysterectomy, sling operation, etc.), had received previous OAB treatment with antimuscarinics within 3 months, or had specific comorbidities such as known neurogenic bladder, history of acute urinary retention requiring catheterization, predominant stress urinary incontinence, significant pelvic organ prolapse, or lower urinary tract surgery within 6 months.

According to our department protocol, all the patients kept 3-day voiding diaries, and OAB symptom scores (OABSS) [10] were monitored at baseline and after 4, 12, and 24 weeks of solifenacin treatment. The subjects recorded the time of every micturition and rated the sensation associated with each using the 5-point urinary sensation scale (USS) [11].

Urgency grade was defined as the mean of urgency episodes of USS ratings for all micturitions reported during the 3-day voiding diary period. All the patients received 5-mg solifenacin once daily before sleep for 4 weeks. After 4 weeks, the subjects either maintained the solifenacin dosage at 5 mg once daily (nonescalators) or increased their dose to 10 mg once daily for the remainder of the study (escalators), based on discussions between the subjects and the investigator regarding their subjective assessment of treatment efficacy and tolerability. Similarly, after 12 weeks, the patients either remained at the baseline dose or increased it for the remaining 12 weeks of the study (escalators) after consultation with the investigator regarding efficacy and tolerability. This study did not need an institutional review board approval because all the patients were followed up according to the protocol of our hospital, the data were collect-

ed by retrospective chart reviews of existing medical records, and the data were recorded by the investigator anonymously to protect the patients' identities.

The patients were divided according to "no escalation" (NE) or "dose escalation" (DE). The DE group consisted of the patients who elevated their solifenacin dose from 5 to 10 mg at either week 4 or 12.

Patients were considered to have OAB-Wet if they had OAB symptoms of urgency and frequency with urge urinary incontinence. OAB-Dry was defined as patients with symptoms of urgency and frequency but lacked urge urinary incontinence.

Changes in OAB symptoms were evaluated from baseline to 4, 12, and 24 weeks for both groups. The baseline clinical factors associated with DE were assessed using a logistic regression model. The baseline demographic characteristics of the NE and DE groups were evaluated for statistical differences using the analysis of variance or t-tests for continuous variables and chi-square tests for categorical variables. The baseline clinical risk factors for DE over the entire study period and at 4 and 12 weeks were examined by univariate and multivariate analyses using a logistic regression model. Both absolute (numeric mean) and relative (%) changes in efficacy variables were assessed because of the potential for baseline differences in OAB symptom severity between the NE and DE groups.

Least-squares (LS) mean differences in changes from baseline in the DE and NE groups were assessed using a linear mixed model. Relative percent changes in efficacy variables from baseline to 4 and 12 weeks within each DE group were assessed using a Wilcoxon signed-rank test at the 5% significance level. Relative differences in mean percent changes between the NE and DE groups were assessed by two-sided paired t-tests. All the reported P-values were two-sided, and $P < 0.05$ was deemed statistically significant. Data manipulation and statistical analyses were conducted using SAS ver. 9.2 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Subjects

In total, 68 patients (54 women and 14 men; mean age, 60.8 ± 10.0 years) were selected. The NE and DE groups were comparable with respect to baseline demographics (Table 1). Thirty six percent of male patients (4/11) were taking alpha-blockers over 2 months at the beginning of the medication with solifenacin. The one of the exclusion criteria was taking alpha-blocker

Table 1. Baseline demographic characteristics of the nonescalators and escalators group

Parameter	Nonescalators	Escalators	P-value
Sex			0.082
Male	11 (16.2)	3 (4.4)	
Female	29 (42.6)	25 (36.8)	
Age (yr)	61.9±9.4	59.9±10.5	0.430
Body mass index (kg/m ²)	24.8±3.5	23.8±2.5	0.316
OAB type			0.004 ^{a)}
OAB dry	32 (47.0)	13 (19.1)	
OAB wet	8 (11.8)	15 (22.1)	
Diary variables per 24 hr			
Micturitions	10.7±4.0	11.5±3.2	0.204
Urgency episodes	6.2±5.0	8.4±4.4	0.055
UUI episodes	0.4±1.2	1.1±2.1	0.079
Urgency grade	3.2±0.3	3.4±0.9	0.055
Questionnaire scores			
OABSS	7.9±3.5	10.2±2.4	0.032 ^{a)}
OABSS-3Q	3.0±1.2	3.8±1.1	0.048
Uroflowmetry			
Voiding volume (mL)	256.5±115.8	219.8±110.8	0.196
Peak flow rate (mL/sec)	22.6±9.2	23.2±11.4	0.806
Postvoided residual urine (mL)	27.4±38.7	23.3±45.5	0.693

Values are presented as number (%) or mean ± standard deviation. OAB, overactive bladder; UUI, urgency urinary incontinence; OABSS, OAB symptom scores.

^{a)}P < 0.05.

within 2 months, so this 4 patients were included to present study finally. No other patients add with alpha-blockers or 5-alpha reductase inhibitor during the study except this 4 patients.

The rate of DE from the starting dose of 5-mg solifenacin to 10-mg solifenacin over the entire treatment period was 41.2% (28/68), from 23.5% (16/68) at 4 weeks and 17.6% (12/68) at 12 weeks. After 12 weeks, however, one patient reduced the dose until the end of treatment because of an adverse effect (dry mouth).

The DE group shows higher mean values for baseline micturitions (11.5 ± 3.2/24 hours vs. 10.7 ± 4.0/24 hours, P = 0.204), urgency episodes (8.4 ± 4.4/24 hours vs. 6.2 ± 5.0/24 hours, P = 0.055), UUI episodes (1.1 ± 2.1/24 hours vs. 0.4 ± 1.2/24 hours, P = 0.079), and urgency grade (3.4 ± 0.9/24 hours vs. 3.2 ± 0.3/24 hours, P = 0.055) than the NE group, even though it was not statistically significant. This results showed that the DE

group had more severe objective OAB symptoms than NE group. Compared with the NE group, the DE group also showed significantly higher baseline OABSS (7.9 ± 3.5 vs. 10.2 ± 2.4, P = 0.032) and OABSS-3Q (3.0 ± 1.2 vs. 3.8 ± 1.1, P = 0.048). Baseline voiding parameters such as voiding volume, maximal urinary flow rate, and postvoided residual urine were generally similar in both groups (all P > 0.05).

Factors Associated With DE

The univariate analysis indicated that age, sex, body mass index, and voiding parameters did not influence the DE outcome in the DE group (Table 2). Patients with OAB wet (odds ratio [OR], 4.615; 95% confidence interval [CI], 1.578–13.499; P = 0.002) and higher total OABSS (OR, 1.398; 95% CI, 1.046–1.869; P < 0.05) were more likely to escalate the dose than patients with OAB dry in the total DE group. The number of urgency and UUI episodes per 24 hours were marginally associated with DE in the total DE group (OR, 1.109; 95% CI, 0.998–1.224; P = 0.058 and OR, 1.704; 95% CI, 0.977–2.975; P = 0.073). The multivariate analysis indicated that no factor was independently associated with solifenacin DE. UUI episodes and OABSS-Q3 were excluded from the multivariate analysis because these factors were related to multicollinearity of risk factors.

In the 4-week escalators (4WE), OAB wet and voiding volume were associated with DE in the subgroup univariate analysis (OR, 9.351; 95% CI, 1.092–19.422; P = 0.039 and OR, 0.994; 95% CI, 0.988–1.000; P = 0.045) (Table 3). The number of urgency episodes and total OABSS per 24 hours were marginally associated in the 4WE (OR, 1.188; 95% CI, 0.996–1.254; P = 0.058 and OR, 1.289; 95% CI, 0.954–1.741; P = 0.098). In the 12-week escalators, only urgency grade was associated with DE (OR, 4.060; 95% CI, 1.126–14.630; P = 0.032) in the subgroup univariate analysis.

Efficacy

After 4 weeks, significant percentage improvements in mean micturitions, urgency episodes, and UUI episodes were observed from the baseline in both groups (Table 4). In the NE group, micturitions (50.9%), urgency episodes (85.4%), and UUI episodes (77.0%) decreased from the baseline (all P < 0.05). In the DE group, micturitions (25.5%), urgency episodes (57.4%), and UUI episodes (18.8%) decreased from the baseline (all P < 0.05). The mean percentage change in the NE group was significantly higher than that in the DE group (all P < 0.05). When mean changes were assessed, all the diary variables per

Table 2. Factors related to solifenacin dose escalation in the total dose escalators

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Sex (female)	0.334	0.170–1.825	0.334			
Age	0.980	0.933–1.030	0.424			
Body mass index	0.899	0.761–1.105	0.899			
OAB type						
OAB wet	4.615	1.578–13.499	0.002 ^{a)}	1.234	0.916–1.662	0.167
Diary variables per 24 hr						
Micturitions	1.101	0.946–1.281	0.213			
Urgency episodes	1.109	0.988–1.244	0.058			
UII episodes	1.704	0.977–2.975	0.073			
Urgency grade	0.569	0.218–1.488	0.251			
Questionnaire scores						
OABSS	1.398	1.046–1.869	0.024 ^{a)}	0.784	0.572–1.074	0.125
OABSS-3Q	1.853	0.989–3.475	0.172			
Uroflowmetry						
Voiding volume	0.997	0.993–1.002	0.196			
Peak flow rate	1.003	0.960–1.055	0.802			
Postvoided residual urine	0.996	0.986–1.009	0.688			

OR, odds ratio; CI, confidence interval; OAB, overactive bladder; UII, urgency urinary incontinence; OABSS, OAB symptom scores.

^{a)}P < 0.05.

24-hour period in the NE group were significantly greater than those in the DE group (Fig. 1). The mean numbers of micturitions (–2.94 vs. –0.87; LS mean difference, 2.07; P > 0.05), urgency episodes (–4.53 vs. –3.64; LS mean difference, 0.89; P > 0.05), UII episodes (–0.41 vs. 0.09; LS mean difference, 0.50; P > 0.05), and urgency grade (–1.57 vs. –0.43; LS mean difference, 1.14; P > 0.05) per 24 hours in the NE group were higher than those in the DE group (Fig. 1).

After 12 weeks, significant mean percentage improvements were observed in all the voiding diary variables compared with the baseline in both groups (Table 4). In the NE group, micturitions (18.9%), urgency episodes (85.4%), and UII episodes (84.6%) decreased from the baseline (all P < 0.05), as well as in the DE group at 22.4%, 75.0%, and 59.8%, respectively (all P < 0.05). When the mean percentage change was assessed, the improvement in UII episodes per 24 hours in the NE group was significantly greater than that in the DE group after 12 weeks (P = 0.034).

The DE group showed an improvement in micturitions and urgency episodes per 24 hours, as did the NE group (P = 0.831 and P = 0.466). In contrast to the week 4 results, the mean numbers of micturitions (–3.13 vs. –3.15; LS mean difference, 0.02;

P > 0.05), urgency episodes (–4.67 vs. –5.45; LS mean difference, 0.78; P > 0.05), and UII episodes (–0.44 vs. –0.53; LS mean difference, 0.09; P > 0.05) per 24 hours, showed similar or greater reductions in value in the DE group compared with the NE group except urgency grade (Fig. 1).

After 24 weeks, significant mean percentage improvements were observed from the baseline in all the voiding diary variables in both groups (Table 4). In the NE group, micturitions (64.7%), urgency episodes (96.3%), and UII episodes (92.3%) decreased from the baseline (all P < 0.05), as well as in the DE group at 62.6%, 79.6%, and 75.6%, respectively (all P < 0.05). No significant differences in mean percentage changes in the diary variables were observed between the two groups (all P > 0.05). Following DE, the drug efficacy was continuous and improved in both groups. The mean numbers of micturitions (–3.49 vs. –3.44; LS mean difference, 0.05; P > 0.05), urgency episodes (–4.92 vs. –5.97; LS mean difference, 1.05; P > 0.05), and UII episodes (–0.38 vs. –1.32; LS mean difference, 0.94; P > 0.05) per 24 hours were greater in the DE group compared with the NE group. Only the urgency grade (–2.43 vs. –1.53; LS mean difference, 0.90; P > 0.05) per 24 hours was lower in the DE group compared with the NE group (Fig. 1).

Table 3. Univariate analysis of the factors related to solifenacin dose escalation in the 4-, and 12-week dose escalators

Variable	4 Weeks			12 Weeks		
	OR	95% CI	P-value	OR	95% CI	P-value
Sex (female)						
Age	2.100	0.417–10.569	0.368	4.550	0.544–38.023	0.162
Body mass index	0.990	0.936–1.048	0.728	0.964	0.909–1.023	0.229
OAB type	1.137	0.849–1.524	0.389	0.842	0.654–1.084	0.183
OAB wet	9.351	1.092–19.422	0.039 ^{a)}	4.245	0.646–8.143	0.199
Diary variables per 24 hr						
Micturitions	1.131	0.977–1.310	0.100	0.906	0.739–1.109	0.339
Urgency episodes	1.188	0.996–1.254	0.058	1.004	0.892–1.130	0.947
UUI episodes	1.112	0.806–1.534	0.519	1.593	0.916–1.754	0.153
Urgency grade	0.654	0.256–1.674	0.376	4.060	1.126–14.630	0.032 ^{a)}
Questionnaire scores						
OABSS	1.289	0.954–1.741	0.098	1.237	0.932–1.724	0.131
OABSS-3Q	1.502	0.759–2.974	0.243	1.413	0.675–2.957	0.359
Uroflowmetry						
Voiding volume	0.994	0.988–1.000	0.045	1.000	0.994–1.005	0.866
Peak flow rate	0.983	0.929–1.041	0.555	1.019	0.965–1.077	0.498
Post-voided residual urine	1.003	0.990–1.013	0.650	0.987	0.966–1.007	0.197

OR, odds ratio; CI, confidence interval; OAB, overactive bladder; UUI, urgency urinary incontinence; OABSS, OAB symptom scores.

^{a)}P < 0.05.

Table 4. Mean percentage changes in efficacy parameters from baseline for the nonescalators and escalators (Mann-Whitney test)

Diary variables per 24 hr	4 Weeks			12 Weeks			24 Weeks		
	Nonescalators	Dose escalators	P-value	Nonescalators	Dose escalators	P-value	Nonescalators	Dose escalators	P-value
Micturitions	–50.9 ^{a)}	–25.5 ^{a)}	0.007	–18.9 ^{a)}	–22.4 ^{a)}	0.831	–64.7 ^{a)}	–62.6 ^{a)}	0.826
Urgency episodes	–85.4 ^{a)}	–57.4 ^{a)}	0.002	–85.4 ^{a)}	–75.0 ^{a)}	0.466	–96.3 ^{a)}	–79.6 ^{a)}	0.357
UUI episodes	–77.0 ^{a)}	–18.8 ^{a)}	0.039	–84.6 ^{a)}	–59.8 ^{a)}	0.034	–92.3 ^{a)}	–75.6 ^{a)}	0.239

For the UUI episodes, only the patients with UUI episode at baseline characteristics were analyzed.

UUI, urgency urinary incontinence.

^{a)}P < 0.05 versus the baseline (Wilcoxon signed rank test).

DISCUSSION

Of the patients' baseline characteristics, the values for OAB wet, all voiding diary variables, and total OABSS in the 10-mg solifenacin group were greater than those in the 5-mg solifenacin group. The key factors associated with DE were OAB wet and total OABSS across all DE groups. All diary variables decreased from baseline to 12 and 24 weeks throughout the study period in both groups.

Antimuscarinic drugs, which have proven efficacy in patients

who have OAB symptoms with or without urodynamically confirmed detrusor overactivity, were used as the first-line treatment [12]. Some agents are available in two or more dose strengths; a flexible dosing strategy can help to achieve the desired efficacy with minimal side effects [13].

Several studies have evaluated baseline characteristics associated with DE in OAB patients. Most studies of solifenacin flexible-dose strategies were performed using a 12- to 16-week study period [6,8,9]. After 4 or 8 weeks of treatment, the patients had a single opportunity either to continue with their original dose

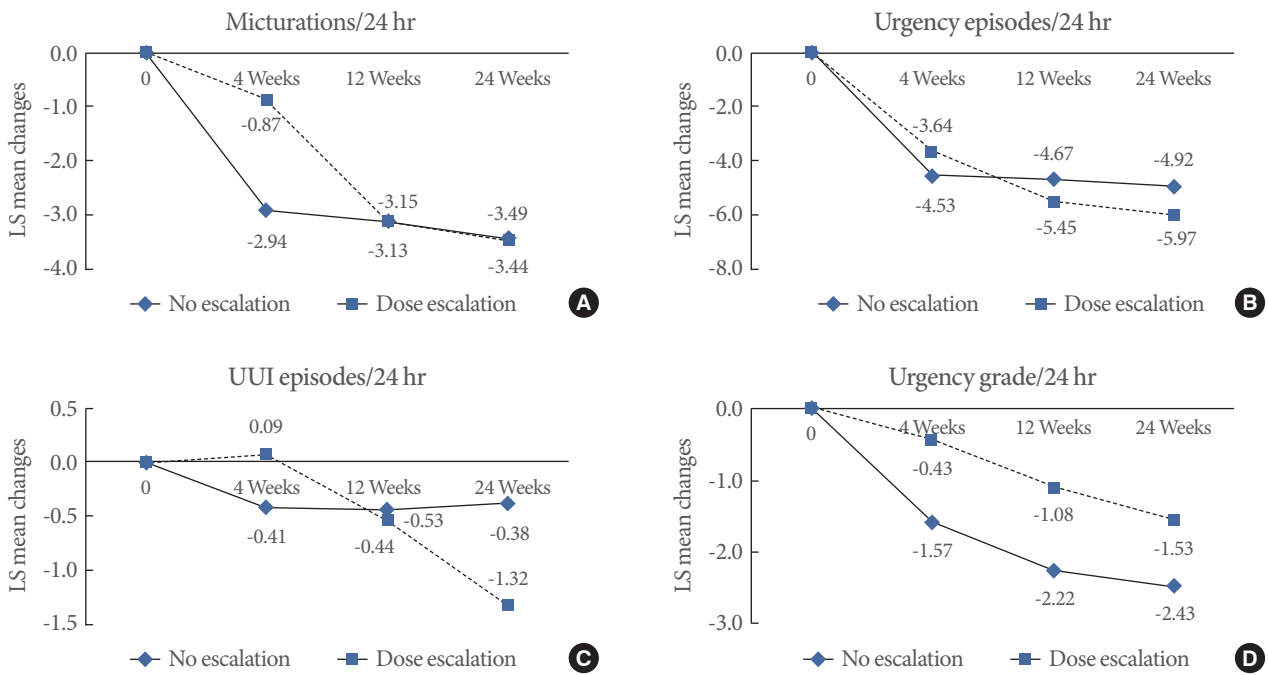


Fig. 1. Least-squares (LS) mean changes from baseline in number of (A) micturations, (B) urgency episodes, (C) UUI episodes, and (D) urgency grade per 24 h in the groups of patients who did or did not request a dose escalation from 5- to 10-mg solifenacin at 4, 12, and 24 weeks (Mann-Whitney test). UUI, urgency urinary incontinence.

or to request a dose increase based on their satisfaction with treatment efficacy and tolerability and discussion with the investigator. These previous studies did not compare between nonescalators and escalator but rather between a placebo group and a drug administration group (including 5- or 10-mg solifenacin). Recently, the SUNRISE study investigated the relationship between the severity of baseline OAB symptoms and requests for a solifenacin dose increase and the efficacy of 5- and 10-mg solifenacin doses in relieving OAB symptoms in patients who requested a dose increase [14]. In the 16-week, prospective, double-blind, double-randomized, parallel-group, multicenter study, 591 patients received 5- or 10-mg solifenacin once daily in a flexible-dose regimen. The present study examined the differences between escalators and non-escalators (DE group vs. NE group) using a flexible-dose solifenacin regimen with a 3-day voiding diary, OAB questionnaires, and uroflowmetry for 24 weeks in a real clinical setting [3].

The patients who chose DE tended to have more severe OAB symptoms at baseline; this was consistent across all the variables in NE versus DE. In the present study, OAB wet, all diary variables, and total OABSS were higher in baseline characteristics between the 5- and 10-mg solifenacin groups. Serati et al. [15] evaluate to identify the factors associated with the risk of solife-

nacin treatment failure. Specifically, the daily number of episodes of urgency, and the different symptoms severity scores (overactive bladder questionnaire-short form and USS) could be considered predictors of solifenacin failure. For these patients, an increase of the solifenacin dosage might be useful. Chapple et al. [13] reviewed data from several studies with solifenacin, darifenacin and oxybutynin extended-release that evaluated the impact of dose flexibility on clinical management. This study reported that patients with OAB refractory to initial treatment who requested dose increase, had often more severe symptoms at inclusion, especially in terms of number of episodes of urgency (with or without urge incontinence)

Large meta-analysis trials, including the STAR, SUNRISE, and VENUS studies, performed with this drug clearly demonstrated significant improvements in OAB symptoms compared with the placebo [16]. The drug effects were similar regardless of solifenacin dose (5 and 10 mg) at the end of the study period [16]. The 5-mg solifenacin group showed a reduction in mean micturations per day from -0.99 to -1.23 to -0.75 ($P < 0.01$) compared with the 10-mg solifenacin group (-1.3 to -1.56 to -1.04, $P < 0.01$). The mean values of urgency episodes and UUI episodes per day showed similar patterns in both groups. In contrast, our results indicate that improvements in mean epi-

sodes were maintained or further increased in the DE group compared with the NE group after 12 weeks (patients had a second opportunity for DE). A difference was observed in the results of the two groups caused by escalating the dose twice in the DE group.

Regardless of the dose escalator groups having lower drug efficacy before DE, a gradual reduction in the differences in OAB symptoms between the two groups was evident. By week 4, the mean percentage improvements in diary variables were significantly smaller in the DE group than in the NE group (all $P < 0.05$). Drug efficacy in the DE group became similar to that in the NE group. At week 12, the number of UUI episodes per 24 hours was the only variable that was statistically different between the two groups. At the end of the study, no statistical differences were observed between the groups for any diary variables.

It is difficult to compare our results directly with flexible-dose studies of other anticholinergics. In a fesoterodine study, at week 4 (before the decision to escalate), all the outcomes were significantly improved from the baseline in both groups (all $P < 0.05$), and no significant differences were observed between the non-escalators and escalators at week 12, except UUI episodes per 24 hours ($P < 0.05$) [17]. The fesoterodine study also showed similarities with our results in that the number of UUI episodes was the slowest variable to respond to the anticholinergic drug. A dose increase was requested by 41.2% of patients receiving 5-mg solifenacin after 4 or 12 weeks of active treatment. The incidence of DE in our study is similar to that in previous reports; a dose increase was requested by 48% of patients on solifenacin in the STAR study [8], 47% in the SUNRISE study [6], and 44.1% in the VENUS study [9].

This study had several limitations. It had a retrospective design, and only patients who continued the drug for 24 weeks were included, which is inherently a selection bias (all the patients who discontinued or did not comply for 24 weeks are not included in this population). There was great opportunity for bias in this small population, although the patients were followed up according to the protocol of our department. Objective parameters, including micturition, urgency episode, and urgency incontinence episode data, were used to make an objective comparison between dose escalators and nonescalators. However, a subjective measurement index of changes in urgency incontinence, treatment satisfaction, and quality of life was lacking.

In conclusion, the flexible-dose treatment with solifenacin improved OAB symptoms in the patients who chose to main-

tain the initial dose, as well as in 41% of those who chose to escalate the dose after 4 or 12 weeks. Although the reduction in OAB symptoms was insufficient in the DE group before DE, the gap narrowed steadily to be similar by the end of the study period (24 weeks). Patients with unfavorable initial symptoms had a tendency to escalate to 10-mg solifenacin and showed significant improvements in OAB symptoms. The use of flexible-dose solifenacin (5 or 10 mg) is associated with UUI and higher total OABSS.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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