Treatment compliance of working persons to high-dose antimuscarinic therapies: a randomized trial

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Abstract

Aim: The aim of this work was to study the factors affecting the stability of working patients in antimuscarinic (AM) drug treatment.

Background: The prevalence of urge urinary incontinence (UUI) is an average of between 8.2% and 16.0% of the population. UUI is a condition that adversely affects the health-related quality of life. The first-line therapy in managing UUI is AM treatment.

Methods: In 1006 patients between 18 and 60 years old (627 women, 379 men, mean age 69.4) who received AM treatment for one year, the possible demographic, socioeconomic and health factors influencing compliance were studied. Also, the functional state of the lower urinary tract (LUT) was studied in this randomized, prospective survey. The study instruments were the documents of employers, tax offices, outpatient records, OABq-SF (overactive bladder - short form) questionnaires, MOS SF-36 (Medical Outcomes Study short form-36), voiding charts, and uroflowmetry data.

Results: The compliance to AM treatment within 6 months was retained in 49.5% patients; during the year, in 32.3% of patients. The average time for reaching the 30-day break in taking trospium was 194 days. In the course of the experiment it was revealed that compliance to AM treatment was significantly higher in patients taking solifenacin and trospium in high dosages ($p \leq 0.01$, $p \leq 0.05$), suffering from severe symptoms of urgency ($p \leq 0.01$), and having a low level of side effects ($p \leq 0.01$). A satisfactory level of compliance is characteristic of patients with a high level of monthly and annual income ($p \leq 0.01$, $p \leq 0.01$), a low percentage of expenses to AM ($p \leq 0.05$), and rarely changing employers ($p \leq 0.05$). In addition, the compliance to treatment is higher in older adults ($p \leq 0.05$), living in the urban district ($p \leq 0.01$), and working in educational ($p \leq 0.05$) and health ($p \leq 0.01$) institutions, having a high level of the indices of Social Functioning ($p \leq 0.05$), Role-Emotional ($p \leq 0.05$), and Mental Health ($p \leq 0.01$).

Conclusion: As a result of this study, under the control of the objective functional state of LUT, the influence of various factors on the patients' stability in the treatment with AM drugs was revealed.

Keywords: antimuscarinic, lower urinary tract, urinary incontinence, adherence, working persons

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Introduction

The prevalence of urgency urinary incontinence (UUI) is between 8.2% and 16.0% of the world population [Coyne *et al.* 2013]. UUI reduces health-related quality of life, adversely affects the capacity to work, and can be accompanied by emotional stress, reduced social status, and economic problems [Patrick *et al.* 2013; Coyne *et al.*

2014]. The first-line therapy in managing UUI is antimuscarinic (AM) drug treatments [Felicilda-Reynaldo, 2013]. The first generation of AM treatments were of limited efficacy, had significant side effects and had inconvenient dosing regimens, but recently the drugs used for UUI treatment are almost free of these drawbacks [Oefelein, 2011]. However, the compliance to

AM treatment remains low [Basma *et al.* 2009; Benner *et al.* 2009]. In earlier studies, we also noted this problem [Kosilov *et al.* 2014, 2015]. The main reasons of refusals or long breaks in treatment are often specified as the lack of efficacy, occurrence of side effects, high cost of medicines, and lack of income. Some researchers add to this list a low awareness of the patients about their disease, young age of the patients, and other factors [Veenboer and Bosch, 2014; Mauseth *et al.* 2013; Kleinman *et al.* 2014; Harpe *et al.* 2007]. Some researchers consider ‘medical reasons’ of refused treatments to be basic ones, influencing patients’ motivation in almost all cases [Yu *et al.* 2005; Chapple *et al.* 2008]. There are data on the significant differences between the compliance to different AM treatments [Basma *et al.* 2009; Benner *et al.* 2009], which are refuted by other studies’ results [Gopal *et al.* 2008; Gomelsky and Dmochowski, 2010; Chancellor *et al.* 2013].

Many experimenters point out the importance of subjective psychological factors, such as aversion to taking medication, and fear of side effects [Benner *et al.* 2009]. Attention is drawn to the significant impact of cost and other economic and social factors when the patients decide against treatment [Kleinman *et al.* 2014; Clifford and Coyne, 2014].

Most manuscripts discussing the problems of AM drugs compliance are limited to retrograde analysis of any one group of factors, which are related to either the pharmacological properties of AM drugs or their cost and the financial problems of patients, or restricted social and working activity of persons with UUI. In such resources as Scopus, WoS, and PubMed, the data from prospective observations of patients’ compliance to AM treatment with objective control of the functional state of LUT, psycho-emotional stress, as well as socio-economic status are currently unavailable. Some observations are based on data about prescriptions that may not always provide the necessary level of confidence in the result.

Against this background, we have attempted to conduct a comprehensive assessment of the impact of diverse medical, economic, and sociodemographic factors on the working patient’s compliance to AM treatment.

Materials and methods

The study involved 1006 patients aged 18–60 years, including 627 women (mean age 53.6

years) and 379 men (mean age 49.9 years). The allocation of patients into groups depending on the AM drug administered was performed using a simple randomization method. The individuals, who got a particular AM drug prescribed having sought medical advice in odd-numbered days of the week, were admitted to participate in the study. A random number generator, working on the principle of congruent method, was used to randomize experiment participants for each group by age and sex. The individuals who got odd numbers and met all other inclusion criteria were enrolled in the group. The sample size calculation was carried out taking into account the need to identify sign differences between the groups at the end of the study. A probabilistic loss of the adherence was determined in 70% of the experiment participants [Basma *et al.* 2009; Veenboer and Bosch, 2014; Mauseth *et al.* 2013]. The desired power of the study constituted 90%, and the threshold confidence level was 5%. Patients’ data were depersonalized by assigning random numbers. The treatment was appointed by independent urologists who were not part of the research team.

The study was conducted from 6 January 2013 up to 15 January 2015 in the Urology Department of Vladivostok City Polyclinic No.3 and the Far Eastern Federal University. The criteria for inclusion in the group were: Diagnosis: Urinary Incontinence (UI N39.41) [Schafer *et al.* 2002], appointment of AM drugs in standard high doses for long periods of time (per day: solifenacin 10 mg, 20 mg, or tadalafil 30 mg, 60 mg, oxybutynin 20 mg, tolterodine 4 mg, darifenacin 15 mg) [Felicilda-Reynaldo, 2013]. Due to the data available on the high efficacy and safety of using higher-dose solifenacin and tadalafil, we also included in the study individuals who were recommended elevated doses of these drugs (20 mg and 60 mg per day respectively) [Horstmann *et al.* 2006; Amend *et al.* 2008; Kosilov *et al.* 2014].

The exclusion criteria were oncological diseases in the terminal stage, taking medications with a therapeutic effect similar to AM treatment, chronic infection of LUT, and change of QT interval.

The regression percentage of patients adherent to treatment under various influencing factors was classified as the primary outcome. A comparison of quantitative indicators of health, economic, social and psychological factors in patients with different

levels of adherence to treatment, as well as the evaluation of side effects of the drug administration, was classified as the secondary outcome. Interim evaluations of observations were performed on a monthly basis, the final (the control point) at the end of the study (12 months after the beginning).

The compliance level was assessed by a waiting model of a 30-day break in taking the AM drug [Kleinman *et al.* 2014; Clifford and Coyne, 2014]. To determine the relation between compliance and factors of significance, the general group was split into three cohorts: dedicated employees (i.e. those with compliance of $\geq 80\%$), poorly-dedicated employees (i.e. those with compliance of $< 80\%$ yet $\geq 50\%$) and nondedicated employees (i.e. those with compliance of $< 50\%$) [Kleinman *et al.* 2014]. The last group was considered as a control group.

The control of the functional state of the LUT and treatment efficacy was carried out with the help of a voiding diary supplemented by graphs of AM drug intake (daily) [Amundsen, 2006], uroflowmetry [Schafer *et al.* 2002] and OABq-SF [Coyne *et al.* 2015] (monthly). Incontinence of more than three episodes a day was considered a severe symptom [Kurita *et al.* 2013]. The medicinal factors included AM drug type, presence of side effects (extra graph in voiding chart), severity of urgency urinary symptoms, comorbidity and polypragmasy level [Chapple *et al.* 2008; Chancellor *et al.* 2013; Gopal *et al.* 2008]. The control of social and psychological status, and the influence of health conditions on quality of life was carried out using the questionnaire MOS-36 [Yang *et al.* 2013] (monthly). The patients' awareness of UUI treatment methods was carried out using a questionnaire at the start of the experiment [Jin *et al.* 2008].

The demographic data were verified by outpatient medical records (form 25U) and data from social protection services. The economic factors included income and expenses level related to the acquisition of AM drugs, other medicines, health care, number of disability days, and a number of factors that characterize the economic activity and the financial viability of the patients. The control of these factors was carried out according to the documents of tax offices and employers with written informed consent of the patients [Kleinman *et al.* 2014; Clifford and Coyne, 2014]. The level of income and expense is specified for inflation to the US dollar price as of 1 June 2013.

To study the stability of patients and trait survival time (compliance) the Weibull distribution with type I right censoring was used. The models with Weibull distribution, as well as gamma distribution and a log link function, controlled all major medical and socio-economic factors of compliance to treatment.

A Hollander-Proschan test and resampling method were used to adjust the likelihood in the case of incomplete data. In cases of abnormal distribution, two-component regression models were used. In some cases, Spearman's rank correlation coefficient was used to study the relationship of regression curves. The differences were considered significant at $p < 0.05$, all p -values are two-sided. All statistical analyses were performed using SAS version 8.0.2 (SAS Institute Inc., Cary, NC, USA). The study was performed in compliance with the principles of the Helsinki Declaration. Design and the protocol of the experimental was approved by the local ethics committee.

During the experiment, 79 people (7.8%) did not participate in it due to external reasons (moving, oncological disease in the terminal stage, taking other anticholinergic drugs, and death).

Results

The compliance to AM treatment within 6 months was retained in 49.5% of patients and, during the year, in 32.3% of patients. The average time of reaching the 30-day break in taking tiroprism was 194 days.

The primary outcomes are presented in Figure 1. In the simulation, the regression of the percentage of adherent patients under the influence of various factors, it was found that medical (0.5% $\rightarrow$ 34.9%) and economic (0.4% $\rightarrow$ 23.0%) factors were the most frequent reasons for treatment refusal or long breaks in treatment. The curves of compliant patients' percent changing under the influence of these two factors had a high level of correlation ($r = 0.89$, $p \leq 0.01$). Not more than 10% of refused treatments in all cohorts were associated with social or psychological factors.

The secondary outcomes are presented in Tables 1–4. Tables 1 and 2 present the data obtained at the beginning of the study, but allocation of patients into groups with different adherence levels was performed at the control point, after the experiment had ended. Assessing the quantitative parameters of the LUT status, side effects, and

Figure 1. Model of the impact that various factors have on patient compliance with the treatment by antimuscarinic drugs.

the symptom severity (Tables 3 and 4), the data of the current survey in a month preceding the discontinuation of the AM treatment administration were used (if it was discontinued). Significant differences were found between the cohort of stable patients and cohorts of moderately and weakly-compliant patients by age ($p \leq 0.05$), and place of residence ($p \leq 0.05$, $p \leq 0.01$). In the cohort of stable patients, the majority were working in the education and health fields ($P_{2/3}$, $p \leq 0.05$, $p \leq 0.01$; $P_{1/3}$, $p \leq 0.05$, $p \leq 0.01$), followed by trade and agriculture ($P_{2/3}$, $p \leq 0.05$, $p \leq 0.01$; $P_{1/3}$, $p \leq 0.05$, $p \leq 0.01$; Table 1).

Assessment of the factors affecting patient stability, by calculating the regression models of the influence of economic factors, allowed us to determine that the stable patients have a higher annual and monthly income ($p \leq 0.05$, $p \leq 0.01$), and a lower percentage of wages spent on AM treatment ($p \leq 0.05$). The stable patients were much more likely to be working for the same employer for a long time ($p \leq 0.05$; Table 2).

The percentage of stable patients treated with solifenacin at 20 mg/day (72.5%), and trospium at

60 mg/day (55.1%) was significantly higher than the percentage of patients in the other cohorts ($p \leq 0.01$; $p \leq 0.05$; Table 3). The percentage of patients with severe urinary incontinence symptoms (42.9%) exceeded the percentage of patients moderately (22.6; $p \leq 0.01$) and weakly (8.5; $p \leq 0.01$) compliant to treatment. Among the stable patients, there proved to be significantly more patients who had a good knowledge of urinary incontinence treatment methods ($p \leq 0.01$). The mean value of side effects in stable patients differed significantly from patients in the other groups. Statistical heterogeneity between the groups with different compliance (Table 4) was found in uroflowmetry parameters, as well as in urgency ($P_{1/2}$, $p \leq 0.05$, $P_{2/3}$, $p \leq 0.05$, $P_{1/3}$, $p \leq 0.01$) and urge incontinence ($P_{1/3}$, $p \leq 0.01$).

When studying the influence of health conditions on quality of life, it was found that in evaluating the indices: Role Physical, Social Functioning, Role Emotional, and Mental Health, the mean score at the experiment conclusion was significantly higher in the stable patients than in the cohort of weakly-compliant patients ($p \leq 0.05$, $p \leq 0.05$, $p \leq 0.05$, $p \leq 0.01$).

Table 1. Socio-demographic characteristics of persons aged 18–60 years who were taking various antimuscarinic drugs at the start of the study ($N = 1006$).

Level of adherence	Adherence <50% ($n = 372$)		Adherence ≥50% <80% ($n = 265$)		Adherence ≥80% ($n = 369$)		<i>p</i> -value		
Parameters	Mean or <i>N</i>	SD or %	Mean or <i>N</i>	SD or %	Mean or <i>N</i>	SD or %	<i>P</i> _{1/2}	<i>P</i> _{2/3}	<i>P</i> _{1/3}
Age	41.2	6.8	51.0	3.7	57.3	7.8	≥0.05	≥0.05	≤ 0.05
Female	214	57.5	182	68.6	231	62.6	≥0.05	≥0.05	≥0.05
Married	258	69.3	177	66.8	249	67.5	≥0.05	≥0.05	≥0.05
Not married	114	30.6	88	43.6	120	32.5	≥0.05	≥0.05	≥0.05
Family members living together	1.9	0.5	2.2	1.0	2.2	0.8	≥0.05	≥0.05	≥0.05
Number of children	1.3	0.7	1.5	0.6	1.1	1.0	≥0.05	≥0.05	≥0.05
Lives in the city district	113	30.4	142	53.5	279	75.6	≤ 0.05	≤ 0.05	≤ 0.01
Lives in rural areas	259	69.5	123	46.4	90	24.3	≤ 0.05	≤ 0.05	≤ 0.01
Field of activity: Industry	41	11.0	54	20.3	61	16.5	≥0.05	≥0.05	≥0.05
Transportation	25	6.7	42	15.8	32	8.7	≥0.05	≥0.05	≥0.05
Retail	89	23.9	25	9.4	45	12.2	≥0.05	≤ 0.05	≤ 0.05
Agriculture	114	30.6	77	29.0	11	3.0	≥0.05	≤ 0.01	≤ 0.01
Education	57	15.3	32	12.1	99	26.8	≥0.05	≤ 0.05	≤ 0.05
Medicine	21	5.6	24	9.0	102	27.6	≥0.05	≤ 0.01	≤ 0.01
Other	25	6.7	11	4.1	19	5.1	≥0.05	≥0.05	≥0.05

A total of 3 people with adherence <50%, 11 employees with adherence ≥50%, but <80%, and 2 employees with adherence ≥80% had missing information about professional activity.
SD, standard deviation.

Discussion

During the experiment, it was found that the stable patients were older, lived mainly in the city, and often worked in the field of education and health. Regression calculation of compliant patients under the influence of economic factors led to the conclusion that the stable patients had a higher annual and monthly income, lower percentage of income spent on AM treatment, and they worked for the same employer for a long time. Among the stable patients was a high number of patients with severe symptoms of incontinence, high treatment efficacy, and taking solifenacin and trospium in high dosage. Also, there were significantly more stable patients who had a good knowledge of UUI treatment methods. The percentage of side effects in stable patients was less than in other cohorts. It was found that the level of social and role functioning, and the mental health of stable and unstable patients was statistically nonhomogeneous. The highest percentage of refused treatments in cohorts observed was associated with medicinal and economic factors (34.9% and 23.0% of the sample, respectively). The impact of social and psychological factors was lower (9.7% in total).

The results obtained are in some contradiction with the assessment of the significance of the factors of influence on compliance, claimed by some authors. Thus, according to Benner and colleagues, in 89% of cases, refused treatments are caused by unsatisfactory results and side effects [Benner *et al.* 2009]. According to our data these reasons caused the refusals of not more than 34.9% of the patients who participated in the experiment, or 52.8% of all cases of refusal to continue treatment, which is close to the data of other researchers [Mauseth *et al.* 2013; Chancellor *et al.* 2013; Brubaker *et al.* 2010].

Unlike most quoted sources, in our experiment the subjective evaluations of efficacy were confirmed by instrumental study of the functional state of the LUT. In a number of cases, we noted the discrepancy between the declared refusal reasons (e.g. lack of efficacy) with a significant change in the functional state of the LUT. The optimization of the urine evacuation phase found during the research process can probably be explained by the relatedness of innervation mechanisms of different parts of the LUT, as well as an

Table 2. Quantitative comparison of the economic characteristics of persons aged 18–60 years who were taking various antimuscarinic drugs at the start of the study (N = 1006).

	Adherence <50% (n = 372)			Adherence ≥50%, <80% (n = 265)			Adherence ≥80% (n = 369)			Mean difference	p-value
	Adjusted mean, \$ or rate (%)	Adjusted standard error	Median	Adjusted mean, \$ or rate (%)	Adjusted standard error	Median	Adjusted mean, \$ or rate (%)	Adjusted standard error	Median		
Annual salary	\$6,745	1,127	\$6,573	\$9,518	2,156	\$8,945	\$17,891	3,822	\$16,189	-2,773 -8,373 -11,146	≥0.05 ≤ 0.05 ≤ 0.01
Average monthly income	\$562.10	93.9	\$512.40	\$793.20	179.6	\$760.50	\$1,490	238.4	\$1,337	-231.1 -696.8 -927.9	≥0.05 ≤ 0.05 ≤ 0.01
Annual expenses on AM drugs	\$367.20	37.6	\$347.30	\$371.20	32.6	\$338.50	\$372.4	46.4	\$366.30	-4.0 -1.2 -5.2	≥0.05 ≥0.05 ≥0.05
AM drug costs as % of wages	5.4	1.1	5.3	3.9	0.9	3.7	2.1	0.9	2.0	1.5 1.8 3.3	≥0.05 ≥0.05 ≤ 0.05
Annual expenses on other drugs	\$217.50	\$31.60	\$199.60	\$258.50	\$48.20	\$250.10	\$251.50	\$39.5	\$241.90	-41.0 7.0 -34.0	≥0.05 ≥0.05 ≥0.05
Annual medical costs	\$344.50	\$31.20	\$331.40	\$422.30	\$52.30	\$385.70	\$387.0	\$63.20	\$354.50	-77.8 35.3 -42.5	≥0.05 ≥0.05 ≥0.05
Short-term disability days	3.5	1.1	3.3	3.6	0.9	3.4	2.1	0.5	1.9	0.9 -1.3 -0.6	≥0.05 ≥0.05 ≥0.05
Long-term disability days	11.2	3.9	10.2	6.9	1.5	7.2	10.6	1.7	9.9	-1.0 -1.1 -2.1	≥0.05 ≥0.05 ≥0.05
Full working days	223.7	27.5	119.3	237.2	46.4	230.3	243.6	37.5	235.6	-13.5 -6.4 -19.9	≥0.05 ≥0.05 ≥0.05
Constant work, years	7.4	5.6	7.5	10.4	5.6	10.1	17.6	5.3	17.3	-3.0 -7.2 -10.2	≥0.05 ≥0.05 ≤ 0.05
Combining work	0.33	0.30	0.29	0.51	0.28	0.42	0.61	0.52	0.59	-0.18 -0.1 -0.28	≥0.05 ≥0.05 ≥0.05
Remark. A total of 9 patients with adherence <50%, 5 employees with adherence ≥50%, but <80%, and 5 employees with adherence ≥80% had missing information about salary and expenses. AM, antimuscarinic.											

Table 3. Medical characteristics and parameters related to the health and side effects of patients with UUI aged 18–60 years who were taking various antimuscarinic drugs at the control point ($N = 1006$).

Level of adherence		Adherence <50% ($n = 372$)		Adherence ≥50%, <80% ($n = 265$)		Adherence ≥80% ($n = 369$)		Total		p-value		
Parameters		N or scores	% or SD	N or scores	% or SD	N or scores	% or SD	N		$P_{1/2}$	$P_{2/3}$	$P_{1/3}$
solifenacin 10 mg/day ($n = 158$)		19	12.0	69	43.7	70	44.3	158		≤0.05	≥0.05	≤0.05
solifenacin 20 mg/day ($n = 131$)		10	7.6	26	19.8	95	72.5	131		≥0.05	≤0.01	≤0.01
trospium 30 mg/day ($n = 170$)		79	46.5	41	24.1	50	29.4	170		≤0.05	≥0.05	≤0.05
trospium 60 mg/day ($n = 136$)		34	25.0	27	19.8	75	55.1	136		≥0.05	≤0.05	≤0.05
oxybutynin 20 mg/day ($n = 119$)		82	68.9	22	18.5	15	12.6	119		≤0.01	≥0.05	≤0.01
tolterodine 4 mg/day ($n = 138$)		84	60.9	41	29.7	13	9.4	138		≤0.05	≤0.05	≤0.01
darifenacin 15 mg/day ($n = 154$)		64	41.5	39	25.3	51	33.1	154		≤0.05	≥0.05	≤0.05
Severe symptoms (EUI ≥ 3/day)		25	8.5	72	22.6	138	42.9	235		≤0.05	≤0.01	≤0.01
Awareness of treatment options of UUI		89	30.5	211	66.3	293	91.3	593		≤0.01	≤0.01	≤0.01
Taking medications to treat comorbidities		283	96.9	286	89.9	293	91.3	862		≥0.05	≥0.05	≥0.05
Charlson Comorbidity Index		7.1	2.1	9.1	4.2	9.5	3.1	–		≥0.05	≥0.05	≥0.05
Side effects 1		39 (27)	10.5 (7.2)	28 (24)	10.6 (9.0)	9 (2)	2.4 (0.5)	76 (53)		≥0.05	≤0.05	≤0.05
Dry mouth												
Dizziness		16 (10)	4.3 (2.7)	7 (3)	2.6 (1.1)	5 (2)	1.3 (0.5)	28 (15)		≥0.05	≥0.05	≤0.05
Nausea		6 (6)	1.6 (1.6)	10 (3)	3.8 (1.1)	5 (3)	1.3 (0.8)	21 (12)		≥0.05	≥0.05	≥0.05
Dry skin		19 (15)	5.1 (4.0)	7 (5)	2.6 (1.9)	5 (2)	1.3 (0.5)	31 (22)		≥0.05	≥0.05	≤0.05
Cognitive		4 (1)	1.1 (0.3)	1 (0)	0.4 (0.0)	2 (1)	0.5 (0.3)	7 (2)		≥0.05	≥0.05	≥0.05
Other		8 (2)	2.1 (0.6)	5 (2)	1.9 (0.7)	2 (2)	0.5 (0.5)	15 (6)		≥0.05	≥0.05	≥0.05
Total		92 (61)	24.7 (16.4)	58 (37)	21.9 (13.9)	28 (12)	7.6 (3.2)	178 (110)		≥0.05	≤0.05	≤0.01
Remark.												
EUI, episodes of urge incontinence; SD, standard deviation; UUI, urge urination incontinence.												
¹ In parentheses indicate the number of cases of refusal of further therapy because of side effects.												

Table 4. Change in OABq-SF, diaries of urination and uroflowmetry at the start and after treatment ($N = 1006$).

Level of adherence parameters	Adherence <50% (<i>n</i> = 372)		Adherence ≥50%, <80% (<i>n</i> = 265)		Adherence ≥80% (<i>n</i> = 369)		<i>p</i> -value (after treatment)
	Start	Finish	Start	Finish	Start	Finish	<i>P</i> _{1/2} <i>P</i> _{2/3} <i>P</i> _{1/3}
OAB-SF questionnaire (in scores, [SD])							
Daytime urination	4.6 [1.1]	4.4 (1.5)	4.6 [1.4]	3.4 (1.0)	4.2 [1.2]	1.2 (0.7)*	≥0.05, ≥0.05, ≤ 0.05
Night urination	5.2 [0.8]	5.1 (1.6)	4.1 (1.3)	2.3 [0.8]	3.9 [1.5]	2.5 (1.3)*	≥0.05, ≥0.05, ≥0.05
Urgency	4.9 [1.1]	4.5 (1.5)	4.5 [1.3]	3.7 (0.6)	4.2 [1.3]	0.9 (0.6)*	≥0.05, ≤ 0.01 , ≤ 0.01
Urge incontinence	5.1 [0.9]	4.7 (1.0)	4.1 [1.0]	3.0 (0.8)	4.3 [1.4]	1.5 (0.9)*	≥0.05, ≥0.05, ≤ 0.05
Diaries of urination (the number of episodes per day, [SD])							
Daytime frequency	10.7 [2.2]	8.4 [1.5]	10.3 [1.5]	7.2 [1.5]	11.0 [1.4]	6.1 [1.5]*	≥0.05, ≥0.05, ≥0.05
Night frequency	1.9 [0.5]	1.0 [1.1]	2.2 [0.7]	1.3 [0.8]	2.1 [0.7]	0.5 [0.5]*	≥0.05, ≥0.05, ≥0.05
Urgency	7.9 [1.6]	6.5 (1.4)	7.5 [1.2]	3.9 (0.4) *	7.7 [1.2]	1.2 (1.3)*	≤ 0.05 , ≤ 0.05 , ≤ 0.01
Urge Incontinence	3.5 [2.1]	2.5 (0.8)	3.7 [0.9]	1.2 (1.1)	3.5 [0.95]	0.7 (0.6)	≥0.05, ≥0.05, ≤ 0.05
Urodynamic parameters (uroflowmetry, [SD])							
<i>Q</i> _{aver} , ml/sec	17.5 [5.5]	18.1 (2.4)	15.9 [2.0]	17.9 (2.5)	17.0 [1.5]	24.9 (2.9)*	≥0.05, ≤ 0.05 , ≤ 0.05
<i>Q</i> _{max} , ml/sec	19.1 [3.1]	22.2 (2.6)	18.8 [3.1]	22.9 (2.3)	18.5 [2.7]	29.3 (4.1)*	≥0.05, ≥0.05, ≤ 0.05
Bladder volume, ml	203.4 [31.5]	253.2 (34.0)	183.2 [25.6]	267.2 (25.1)*	191.0 [26.4]	323.6 (43.8)*	≥0.05 ≤ 0.05 ≤ 0.05
Remark. Bladder volume, bladder volume at first desire to void (ml); SD, standard deviation is indicated in parentheses; significance of differences in the same group before and after treatment is denoted as *(<i>p</i> ≤ 0.05). OABq-SF, Overactive Bladder questionnaire - short form; <i>Q</i> _{aver} , average flow rate; <i>Q</i> _{max} , maximum flow rate; SD, standard deviation							

increase in intravesical pressure caused by the AM treatment.

In addition, in the current study it became possible to confirm the connection of AM treatment type with compliance to treatment [Yu *et al.* 2005; Brubaker *et al.* 2010], to find that the severity of incontinence symptoms had a direct correlation to the 'survivability of trait' (i.e. to the stability of patients). The explanation of this effect may lie in the field of behavioral patterns: severe symptoms of urinary incontinence lead to rising psychological and social discomfort, and patients are forced to intervene more actively in control of the situation, including, to follow a doctor's prescription more exactly.

Attention given to the study of economic conditions for weak compliance to AM treatment was

noted above [Harpe *et al.* 2007; Wu *et al.* 2005; Sears *et al.* 2010]. According to our data, no less than 34% of the cases of refused treatment proved to be due to economic factors, and the regression model demonstrated the direct correlation between the level of income and an inverse correlation between the percentage of the costs of AM treatment on the one hand, and 'survivability of trait' on the other. However, in some cases, patient refusal for economic reasons coincided with objectively unsatisfactory results of treatment, confirmed instrumentally.

The results obtained in this experiment supplement and clarify the already known estimates; however, for the first time the result of the comprehensive study of various factors is obtained in the course of a randomized, prospective clinical trial, with the objective control of the functional

state of the LUT. The results may be significant for practicing urologists and allied physicians at the prognosis of AM treatment efficiency, and compliance to treatment in patients with different socioeconomic and medicinal status.

This study has a number of limitations. We have undoubtedly not studied all factors that could affect compliance with AM treatment. We have not studied factors that promote compliance before and during some period after the start of therapy. When controlling the severity of the patients' condition, we did not use cystometry and only used uroflowmetry, special questionnaires and bladder diaries, which might have caused certain inaccuracies in the estimation of urodynamic values. We have not considered additional expenditures of patients, nor income and expenditure, including unforeseen ones, of their families. In our calculations we have not referred to the time of side effect appearance, nor correlation between prices of solifenacin and other drugs taken by patients, as well as their specific share in overall expenditures of a patient and their family. All these issues are the theme of future studies.

Conclusion

In the course of the experiment, it was found that the compliance of patients to AM treatment was significantly higher when using solifenacin and trospium in high dosages, with considerable severity of urgency symptoms, and absence of side effects. The ability to follow doctor's prescriptions was significantly higher in patients with a high level of monthly and annual income, rarely changing employers, and was lower in those with a high percentage of expenditure on AM treatment. The compliance to AM treatment was high in patients in an older age group, living in an urban district, working in educational and health institutions, and having a high level of the indices of Social Functioning, Role Emotional, and Mental Health.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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