



## Management of Overactive Bladder (OAB) in Elderly Men and Women with Combined, High-Dosed Antimuscarinics without Increased Side Effects

Kirill Kosilov, Sergey Loparev, Marina Ivanovskaya, Lily Kosilova

Submitted April 16, 2013 - Accepted for Publication July 14, 2013

### ABSTRACT

**Objectives:** Numerous elderly patients with overactive bladder (OAB) demonstrate insufficient treatment results under antimuscarinic monotherapy with dose increase. To reduce the OAB symptoms and to estimate safety and tolerability of non-invasive treatment, we evaluated the use of combined antimuscarinics as the alternatives.

**Methods:** Eighty-one patients older than 65 years, both male and female, who earlier received (for 6 months or more before our study) double-dose antimuscarinic monotherapy (trospium), whose initial symptoms did not resolve (or the improvement was short lived), and who experienced mild or no side effects, were included in this study. The patients demonstrated urodynamic-proven overactive bladder with daily incontinence, increased intravesical pressure, and reduced bladder capacity. Taking into account the strength of the initial study treatment, they were distributed into 3 groups and treated with 2 antimuscarinics. The patients underwent urodynamic examination before enrollment in the sixth week and in the fourth month. During the whole treatment period, they kept special bladder diaries where they, among other issues, described side effects during treatment.

**Results:** Significant changes were noted at the 6-week follow-up in all 3 groups. The average number of daily incontinence events decreased from 6 to 2 events. The average maximum bladder capacity (177 to 356 mL) and reflex volume (149 to 284 mL) increased; detrusor compliance also improved (average, 16 to 37 mL/cm H<sub>2</sub>O). Twenty-four patients reported side effects; 3 of them discontinued the successful treatment due to this reason. Seven other patients did not receive any noticeable improvement of detrusor dysfunction, although they did not report any side effects.

**Conclusion:** The majority of elderly patients, who previously demonstrated unsatisfactory results under dose-escalated monotherapy, were treated successfully with combined high-dosage antimuscarinics (87.6 %). The quantity of side effects was comparable to that of normal-dosed antimuscarinics.

**Take-Home Message:** The majority of elderly patients, who continued to suffer from symptoms of overactive bladder after dose-escalated antimuscarinic monotherapy, showed subjective and objective treatment success. The therapy used the combination of high-dosed antimuscarinics (87.6%). Obtained side effects were comparable to (did not exceed) the single-drug treatment.

### INTRODUCTION

The current outlook of the European population reveals an increasing proportion of people aged > 65 years old, with a rise

in those aged > 75 years; thus, it is reasonable to expect that the overactive bladder (OAB) sickness rate will also increase.

The abundance of overactive bladder increases permanently in association with an increasing average, susceptible to its

**KEYWORDS:** Overactive bladder, aging population, pharmacologic treatments, muscarinic antagonists, side effects, tolterodine, trospium, oxybutynin, solifenacin, combination antimuscarinics, urodynamic monitoring

**CORRESPONDENCE:** Kirill Kosilov, Far Eastern Federal University, Department of Neurourology-Urodynamics, Primorsky Regional Diagnostic Center, Vladivostok, Russian Federation (oton2000@mail.ru)

**CITATION:** *UroToday Int J.* 2013 August;6(4):art 47. <http://dx.doi.org/10.3834/uij.1944-5784.2013.08.06>

influence on 41% of men and 31% of women aged > 75 years [1,2]. Many older women use pads to manage the problem. Men are more likely to seek earlier help because of the recognized association between lower urinary tract symptoms (LUTS) and prostatic pathology.

As it is known, OAB is a chronic disorder characterized by symptoms of urinary urgency with or without urgency incontinence, usually accompanied by frequency and nocturia in the absence of infection or obvious neurologic pathology. The OAB-symptom complex is the commonest cause of urinary incontinence in the elderly, usually due to underlying detrusor overactivity, and as such is a treatable condition [1,2]. The elderly, as a rule, have more severe disease than younger people. Studies using urodynamic data show that senior citizens with OAB have a depressed bladder capacity and usually have urgency at lower volumes of filling than younger adults with this status, despite the fact that older adults with no evidence of OAB have a depressed sensation of bladder filling [3]. The elderly patient's main problem is involuntary loss of urine induced by sudden and strong bladder retraction that causes stress in patients, resulting in a distinct reduction in quality of life [4].

For many cases of OAB, the underlying etiology is not entirely understood. The forming of idiopathic OAB is often one of the symptoms associated with weakening nervous system effectiveness as a whole in the elderly population. In the older bladder, there is an increase in the collagen-to-muscle ratio and a decrease in the amount and level of innervation, resulting in less cholinergic transmission [5]. This is reflected in a negative correlation of receptor numbers in the detrusor muscle as people age and selective age-related decreases in mRNA for muscarinic M3 (but not M2) receptors in both male and female bladders. These findings correspond with reports of decreased detrusor contractility with aging, and many of them occur in response to obstruction and ischemia. The role of suburothelial M2 receptors in DO is now better understood. They are well preserved in older bladders and might be involved in the appreciation of urgency [2,6].

As reported by several researchers, OAB-associated diseases include neurological impairment (multiple sclerosis, spinal cord injury), neurological degeneration (Parkinson's disease, multi-system atrophy), and bladder outflow tract obstruction. The underlying cerebrovascular disease and lumbar spondyloarthropathy have also been associated with the development of DO in older men with prostatic disease [7]. Other associated conditions include UTIs, skin infections, sleep disorders, urogenital atrophy, and depression [8]. Reduced physical and cognitive function with aging and the influence of coexisting medication are already known to be important. Older people might be unable to compensate for the impact of

other coexistent diseases that limit their ability to remain dry.

The occurrence of OAB also has important quality-of-life and economic consequences, and the presence of incontinence is associated with a greater likelihood of nursing-home placement and other adverse factors [9-13].

Although treatment for idiopathic OAB has been extensively studied, therapy for the elderly population has not been thoroughly evaluated. Long years of research and multiple clinical studies with antimuscarinic drugs have proved their effectiveness in treating neurogenic bladder dysfunction.

Most elderly patients have already received oral antimuscarinic treatment. Nevertheless, for some older patients, these antimuscarinic drugs often fall short because of insignificant effect taken on the continuing incontinence [1,3,5,14]. Several articles on this issue noted that side effects with increasing dosages and the number of drugs did not occur more often or more severely than with the recommended dosage of a single drug [15]. Based on initial research with the population of elderly patients, we have assumed that another antimuscarinic drug could be combined with the existing medication to advance the continence, bladder capacity, and pressure in the bladder.

## PATIENTS AND METHODS

The study was a double-blind, phase II clinical trial with 2 parallel treatments, performed in the Regional Diagnostic Center in Vladivostok, Russia. From 2008 to 2010, 81 patients older than 65 years, both male and female, who earlier received double-doses of antimuscarinic monotherapy (trospium), whose initial symptoms did not resolve and who experienced mild or no side effects, were enrolled.

In accordance with the experience protocol, patients with OAB had to be 65 to 79 years of age, with normal body weight, vital signs, and age-appropriate ECG. Therefore, the study group consisted of 51 male and 30 female patients with the average age of 67.9 years (range: 65–79 years).

The main signs of exclusion included closed-angle glaucoma, tachydysrhythmias, urinary outlet obstruction, myasthenia gravis, allergies, and other severe diseases. Contemporaneous treatment with other anticholinergics, antidepressants,  $\alpha$ -blockers, and  $\beta$ -sympathomimetics was not allowed. The experience was performed in accordance with Good Clinical Practice (GCP) and the Declaration of Helsinki [16]. Prior written and informed consent on the study was obtained from each patient. The study was agreed and approved by the local ethics committee.

Patients in the group showed (both in the antecedent study

and present study) urodynamically proven idiopathic OAB dysfunction with incontinence, reduced bladder capacity, and increased intravesical pressure. Based on previous surveys, using double monotherapy, the patients in the present study were allocated into 3 pre-determined treatment groups; we took the double-dose drug from the initial study and added the second antimuscarinic drug at the usual recommended dosage to reduce any risk of adverse events [4,15]. We decided to proceed with the drug from the primary study (trospium), because this drug was well tolerated by the patients, and added 3 new drugs, 1 for each group. Patients were accurately monitored for 6 weeks under a consistent drug setting for possible side effects. The dosage of each of these drugs was changed as needed according to patient feedback and a review of their diaries while ensuring that the combination was uneventfully generally tolerated and urodynamic results were also sufficiently positive.

### *Statistical Methods*

The indicators were processed with Excel (Microsoft-Rus, Moscow, Russia) and analyzed with SAS JMP Statistical Discovery 8.0.2 (SAS Institute, Cary, NC, USA). Wilcoxon and Kruskal-Wallis tests were used to compare results in each treatment group before and after supplement of another drug. The one-way analysis of variance (ANOVAs) with the Tukey-Kramer method were used to compare effects in the 3 groups; a post-hoc analysis was performed for individual changes in each of the criteria. P values of < 0.05 were considered statistically significant.

### *Urodynamic Studies*

It is known that urodynamic studies reproduce the patient's symptoms during the test to assure the validity of urodynamic findings. This is not always easy for several reasons, particularly in the elderly. Such a survey is performed in unfamiliar surroundings, which includes the presence of the examiner and staff as well as the equipment.

In addition, the insertion of 1 or 2 catheters transurethraly into the bladder and 1 more catheter into the rectum can be quite uncomfortable. A number of potential pitfalls may have been encountered in a urodynamic study relating to fluid fill rate and the level of the liquid temperature, the patient's position, and the presence of significant genital prolapse. However, despite all these features, most researchers recognize urodynamics as a secure and completely reliable method of studying the state of lower urinary tract health in the elderly [17-20].

Before the start of the study, the urine status was verified to exclude incorrect measurements due to urinary infection. If any urinary infection had been found, the patient received an appropriate treatment and was examined again in 2 to 3 weeks. If the infection had been found repeatedly (2 episodes), the patients were excluded from the study. In addition, each

patient carried out a urodynamic examination to confirm the diagnosis of OAB. The urodynamic state of the lower urinary tract was evaluated in accordance with the International Continence Society (ICS) guidelines [16, 21].

A UDS "Relief-01" (DALPRIBOR, Vladivostok, Russia) with double catheter (8 Ch; 1,7 I.D., 2,7 O.D., Apexmed International B.V., Netherlands) was used for the standard urodynamic procedure. The following data was recorded and analyzed: 1) maximal bladder capacity, 2) reflex volume of the bladder, 3) maximum detrusor pressure, and 4) detrusor compliance.

The bladder was filled with 98.6 °F of isotonic solution (0.9% NaCl) via the transurethral micro-tip catheter at the filling rate of 20 mL/min. For calculating the pressure in the bladder, a rectal balloon catheter was inserted into the rectum to register the intra-abdominal pressure. The urodynamic unit also recorded the pelvic floor muscle activity by electromyogram with adhesive electrodes attached to the perineum.

Pending the survey and the 6-week and 4-month follow-up under the effective or tolerated antimuscarinic dosage, the patients underwent urodynamic examination. Urodynamic parameters for effective treatment were defined as follows: 1) intravesical pressure less than 40 cm H<sub>2</sub>O, 2) less than 2 incontinence events per day, 3) a bladder capacity of at least 300 mL, and 4) a bladder compliance greater than 25 mL/cm H<sub>2</sub>O. The study terminology and the urodynamic parameters followed the International Continence Society guidelines [16].

### *Bladder Diaries*

All participants of this survey had a bladder diary at their disposal to fix the amount of urine while urinating, mark the time of taking medications, the time and amount of fluid intake, incontinence events and their description, as well as occurrence of side effects. The fluid intake recording was necessary to ensure a patient's constant hydration during the study [22-24].

### *Treatment Algorithm*

Group A (N = 27; mean age 69.1 yr; SD ± 8.9) received 60 mg of trospium and oxybutynin dosages between 10 and 25 mg (Table 1). Group B (N = 31; mean age, 68.2 yr; SD ± 8.4) received 60 mg of trospium and tolterodine dosages between 4 and 8 mg. Group C (N = 23; mean age, 66.8 yr; SD ± 5.9) received 60 mg of trospium and solifenacin dosages between 20 and 40 mg.

## **RESULTS**

### *Reports on Side Effects*

All patients had to pay attention to and describe the following disorders in their diaries: dry mouth, blurred vision, dizziness,

Table 1. Dosing of antimuscarinic drugs to patients in the target groups (n = 81).

Ordinal day of treatment Group of patients		Recom. dosage	Doubled dosage	Second study																	41 Last day of the study
				1	2	3	4	5	6	7	8	9	10	11	12	13	14	23	37		
Group A qty. of patients: 27	First trospium (mg)	30	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
	Second oxybutynin (mg)			10	10	15	15	20	20	25	25	15	15	20	20	20	20	20	20	20	20
Group B qty. of patients: 31	First trospium (mg)	30	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
	Second tolterodine (mg)			4	4	4	4	8	4	4	6	6	6	6	6	6	6	6	6	6	6
Group C qty. of patients: 23	First trospium (mg)	30	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
	Second solifenacin (mg)			20	20	20	20	40	40	40	20	20	20	20	20	20	30	30	30	30	30

Total time of the study: 6 weeks

Remark: Gray shading = dropouts due to side effects; hazel shading = dropouts due to unsatisfactory outcome

nausea, vomiting, rash, dry skin, nervousness, sleep disorders, cognitive impairment, memory impairment, hallucination, confusion, stomach pain, bloating, or gas, as well as any other breach of health [25,26]. Twenty-eight patients reported side effects under the combined therapy with 2 antimuscarinic drugs (Table 2).

Twenty patients had poorly expressed side effects; therefore, the combined therapy was continued. In 3 remaining patients, the combined therapy was stopped soon after the beginning of the study because of the side effects (in 2 cases, it was intolerable dry mouth (groups A, C), in 1 case, insomnia (group A)) despite their attaining objective and subjective treatment success.

*Eliminated Because of Poor Results*

Seven patients (3 patients in groups A and B, and 1 in group C) did not experience any satisfactory benefit or improvement under the combined antimuscarinic therapy (Table 1 and Table 2), although they also received double doses of the second antimuscarinic drug.

*Results Urodynamic and Bladder Diaries*

In all groups, positive results were observed. In group A (trospium + oxybutynin), the incontinence events reduced from the range of 3 to 11 (median 6.3), to 0 to 5 (median 2.3). The urodynamic study found an increase in reflex volume (from a median of 165 mL to 291) as well as an increase in maximal bladder capacity (183 to 320 mL) and increased bladder compliance (22 to 35 mL/cm H<sub>2</sub>O). In group B (trospium + tolterodine) incontinence events reduced from the range of 3 to 13 (median 5.5) to 0 to 4 (median, 2.4). Reflex volume increased from the median of 135 mL to 265 mL and increased as the maximum capacity of the bladder from 171 mL to 380 mL was recorded, and the bladder compliance advanced from 10 to 35 mL/cm H<sub>2</sub>O. In group C (trospium + solifenacin), the incontinence events reduced from the range of 4 to 15 (median 7.5) to 0.5 to 5 (median 2.2). Reflex volume in patients in this group increased (median 130 to 295 mL), and the maximal capacity increased from 175 to 340 mL, with detrusor compliance increasing from 13 to 39 mL/cm H<sub>2</sub>O (Table 3). Table 3 shows the same average values for all 3 groups.

As mentioned above, improvement was noted in all groups.

Table 2. Side effects and patients dismissed.

	Group A	Group B	Group C
Dry mouth	4 (1)	2 (0)	1(1)
Blurred vision	1	1	2
Dizziness	1	1	0
Nausea, vomiting	0	1	0
Rash	2	0	0
Dry skin and intense itching	2	0	1
Nervousness	0	0	1
Sleep disorders	2 (1)	0	0
Cognitive impairment	0	0	0
Memory impairment	0	0	0
Hallucination	0	0	0
Confusion	0	0	0
Stomach pain, bloating, gas	1	0	0
Other breach of health	1	0	0
Discontinuation due to side-effects	2	0	1
Discontinuation due to unsatisfactory outcome	3	3	1

Remark: Parentheses indicate the number of cases to refusal of further therapy because of side effects.

With regard to episodes of incontinence, group C showed somewhat greater improvement after treatment compared with other groups, but differences were not statistically significant ( $P = 0.78$ ). Enhancement of reflex volume was equally and highly statistically significant in groups A and C ( $P < 0.001$ , ANOVA) and slightly lower in group B ( $P < 0.005$ , ANOVA). The most significant improvement in terms of bladder capacity was observed in patients of group B ( $P < 0.0005$ , ANOVA), and difference indicators in 2 other groups were also at acceptable levels. Finally, the assessment of bladder function by the criterion of detrusor compliance found that the most significant differences in comparison to the original data were available in groups B and C ( $P < 0.001$ , ANOVA).

The results shown are derived from the 6-week evaluation. The final evaluation (diary and urodynamic) was performed at the fourth month, the results of which were almost identical to the 6-week follow-up. As a result of this similarity, the 4-month

results were not reported separately.

Parameters such as “frequency of urination during daytime” and “frequency of urination at night” were down in synchronization with events of incontinence, but the significance of differences in most cases was not sufficient. Index Sudden Urge (urgency) correlated with incontinence events, and it was noted as a significant decrease in all groups with  $P < 0.01$ .

## DISCUSSION

The practice of antimuscarinic therapy as the priority medication for the control of overactive bladder in the elderly is well established, and the effectiveness of antimuscarinics for the treatment of OAB is well documented. In general, antimuscarinic therapy is most effective in older patients with relatively mild to moderate bladder dysfunction [27-30]. Patients seeking help are usually concerned about urinary incontinence, frequent urination, and an urgent need to urinate, which decreases their quality of life. Receiving antimuscarinic drugs contributes to full or a partial relief of symptoms, but side effects such as dry mouth, blurred vision, dizziness, nausea, vomiting, rash, dry skin and intense itching, sleep disorders, and some others are extensively described by many authors and must be reconciled [31,32].

The action of antimuscarinic agents on detrusor muscles is well researched today. Oxybutynin hydrochloride is a moderately potent antimuscarinic agent with pronounced detrusor muscle relaxant activity. Oral administration effectivity has been shown in many publications. Its effectiveness has been established and described by many researchers [33]. Trospium effectiveness and safety was confirmed many times by meta analysis as well. It does not break the blood-brain barrier, and central nervous system side effects are therefore not expected [34]. Tolterodine is a competitive muscarinic receptor antagonist with better tolerability and comparable efficacy than in oxybutynin. Many authors have noted the therapeutic effect of increasing doses of the drug. Tolterodine was also one of the first new-generation antimuscarinics that was better tolerated due to reduced side effects [35]. According to some researchers, significant improvements in urgency and other diary-documented symptoms of OAB were noted in patients with urgency and other symptoms of overactive detrusor after treatment with solifenacin. Patients receiving solifenacin also had significant improvements in HRQL. Moreover, solifenacin, with its flexible dosing regimen, was found to be superior to tolterodine with respect to the majority of the efficacy indicators [36,37].

Nevertheless, after the use of antimuscarinics at the manufacturer's recommended dosage, approximately 1/3 of patients still do not experience sufficient efficacy [4,38]. In order to improve the effectiveness of treatment in these patients, we attempted to optimize the treatment. As it was established

Table 3. Comparative analysis of urodynamic and diary data in groups A, B, and C (n = 81 ).

	Bladder diary importance ( $\pm$ SD)								Urodynamics importance ( $\pm$ SD)					
	Incontinence events / day		Sudden Urge /day		Frequency of urination during daytime		Frequency of urination at night		Reflex volume (ml)		Bladder capacity (ml)		Detrusor compliance (ml/cm H <sub>2</sub> O)	
	Before treat	After treat	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Group A (trospium+oxybutynin)	6,3 (2,0)	2,3 (1,1)*	10,9 (3,6)	3,5 (1,0)**	5,6 (0,8)	5,1 (0,9)	2,1 (0,3)	0,7 (0,4)*	165,7 (23,2)	291,2 (61,2)**	183,5 (27,8)	320,3 (42,2)**	22,4 (7,6)	35,6 (9,0)*
Group B (trospium+tolterodine)	5,5 (2,6)	2,4 (1,2)*	9,8 (2,1)	4,1 (1,7)**	6,1 (0,5)	4,8 (0,4)*	1,5 (0,8)	0,9 (0,4)	135,4 (30,0)	265,9 (31,9)*	170,8 (11,9)	380,1 (34,8)***	10,8 (1,2)	34,9 (6,9)**
Group C (trospium+solfenacin)	7,5 (2,0)	2,2 (0,9)**	10,1 (2,6)	3,1 (2,0)**	6,6 (1,3)	5,8 (1,5)	1,5 (0,4)	0,7 (0,5)	130,7 (17,9)	295,5 (41,3)**	175,5 (33,5)	340,0 (49,8)**	13,6 (4,4)	39,1 (4,1)**
All groups	6,2 (2,2)	2,1 (1,0)*	10,4 (2,2)	3,6 (0,7)**	6,0 (1,7)	5,3 (1,9)	1,7 (0,3)	0,8 (0,2)*	148,9 (24,7)	283,8 (34,8)	176,9 (39,9)	356,6 (41,8)**	15,7 (3,4)	37,1 (5,7)**

Remark: SD = standard deviation. \* < 0.05; \*\* < 0.01; \*\*\* < 0.005. "Before" amounts taken at onset of study and considered baseline; "after" amounts taken at 6-week follow-up.

earlier [4,15], increased administration of antimuscarinic drugs was tolerated well. Therefore, we assumed that, since our patients did not experience a benefit from the doubled dosage in the first study, a different combination of antimuscarinics (with modified receptor selectivity) might be beneficial and result in an inconsiderable increase in side effects only. Thus, we decided to increase the initial dose of the antimuscarinic drug 1.5 to 2 times and introduce the second antimuscarinic drug in the second phase.

We did not know of that decision before, but we knew that a group of authors [4] used combined treatment with high doses of antimuscarinic drugs. However, these researchers used a different combination of drugs and the study was not conducted specifically in elderly patients. In addition, we investigated the greatly expanded list of side effects studied.

As in most similar studies, in the beginning, the majority of patients experienced feelings of anxiety because of increased side effects due to the use of a second antimuscarinic, which soon disappeared. In the data (Table 3) for our all study groups, which were obtained in a population of elderly patients, our statistical analysis demonstrated confident results with an increase in reflex volume, maximal bladder capacity, and detrusor compliance under the combined treatment. The main positive clinical result, the improvement of patient quality of life, with an acceptable level of confidence, was connected with reduction of incontinence events [39,40]. The most patients were positive that the declined frequency of incontinence events positively affected their quality of life.

In all 3 groups satisfactory options for urodynamic parameters and patient satisfaction were achieved. Reflex volume increase

was the greatest in group C, and the largest increase in absolute values in the bladder capacity was found in group B. The most significant increase in the values of detrusor compliance was also noted in group C. The number of episodes of incontinence decreased most significantly in group C, as well. Differences in the dynamics of these indices between groups were statistically insignificant.

Nearly 2 decades ago, it was found that the action of antimuscarinic agents was to suppress overactive contractions of the bladder acting via M3- receptors, although data to support this were inconsistent [41]. It is now well known that the M2-muscarinic receptor is the predominant receptor in the urinary bladder. M3-muscarinic receptors are represented in a lower amount but they are more efficient. It is also known that pre-junctional-inhibiting M2- or M4-muscarinic receptors, as well as M1-muscarinic receptors, were detected in the urinary bladder. The interaction of the subdivision of these muscarinic receptors is currently not well understood. Currently, there are strong indications of the presence of muscarinic receptors in various tissues, including M1-receptors in the brain, sympathetic ganglia, and salivary glands; M2-receptors in cardiac tissue (heart frequency), brain, and smooth muscle (bladder and stomach); M3-receptors in salivary glands, eyes, and especially smooth muscle (bladder contraction, intestinal movement, accommodation); M4-receptors in the brain and salivary glands; and M5 receptors in the brain, eyes, and also the urinary bladder [35,42,43].

It is also believed that trospium with its continuous affinity to all receptors (M1 to 5) showed milder side effects; this is why we chose it as the basic antimuscarinic drug for all 3 groups of elderly patients.

We assume that the interaction of receptors on different parts of the bladder wall or a synergistic activation of different muscarinic receptors might be 1 of the explanations for the present study's positive results. The reason for the poor efficiency of conventional doses of drugs might be the insufficient study of the rate of metabolism of antimuscarinics. This requires an increase in their dosage to improve the therapeutic results. Further research may show us that down-regulation of antimuscarinic receptor subdivisions under monotherapy may lead to better susceptibility of other subdivisions when treated with the second drug in older patients.

We failed to find any published explanation of receptor interaction under the combined administration of antimuscarinics, with a moderate increase in tolerable side effects, in Medline. Further studies are also necessary for the verification of long-term efficacy, including the analysis of receptor selectivity and its interactions. We expect that including new drugs into combined regimens for elderly patients who do not receive enough benefit from the usual dosage, as well as escalating the dosages, could further enrich treatment efficacy without side-effect increases.

In conclusion, it should be noted that the force of antimuscarinic drugs on all levels of the central nervous system are currently the focus of several investigations [44-51]. A promising direction of this treatment option would be to explore the reduction of combined oral medication doses.

## CONCLUSION

Our study in a group of elderly patients showed that the combination of antimuscarinic drugs in a dosage that is higher than the usual recommended one is an effective treatment option for patients with OAB in those cases where treatment with 1 antimuscarinic drug was poorly effective. Side effects occurred almost equally in patients treated with only 1 antimuscarinic drug compared to the combined dosage. We are planning further studies to obtain data on long-term results and side effects, as well as the results of combined therapy with antimuscarinic agents for a new generation of both male and female elderly patients. This regimen could be offered to elderly patients with OAB until the appointment of invasive treatment.

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