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ORIGINAL ARTICLE

Persistence with first line anticholinergic medication in treatment-naïve overactive bladder patients

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Abstract

Objective. The aim of this study was to evaluate the persistence of first line anticholinergic medication use by patients with overactive bladder (OAB). Data from a hospital outpatient database were matched with information obtained by a telephone survey of patients to determine which patients discontinued use of anticholinergic medication and to identify the reasons underlying discontinuation. *Material and methods.* The study group included 377 OAB patients (52 men, 325 women) with a mean age of 60.29 ± 13.84 years. In total, 189 patients (50.1%) were treated with trospium (median dose 27.86 ± 12.73 mg), 41 patients (10.9%) with propiverine (28.17 ± 4.97 mg), nine patients (2.4%) with extended-release tolterodine (4.0 ± 0 mg), 48 patients (12.7%) with solifenacin (5.94 ± 1.97 mg) and 90 patients (23.9%) with fesoterodine (6.09 ± 2.01 mg). *Results.* The median time for persistence with the first line anticholinergic treatment was 6.53 ± 3.84 months. Persistence was significantly higher in patients treated with anticholinergic medication with an extended-release formulation than in patients treated with immediate-release anticholinergics. The most common reasons for termination of treatment were healing/resolution of symptoms (35.9%), low effectiveness (30.9%) and side-effects (23.7%). *Conclusions.* More than half of the OAB patients were not satisfied with their first line treatment. Other treatment options should be sought, such as changing the medication or dosage, or possibly combining treatments.

Key Words: *Anticholinergics, overactive bladder, persistence*

Introduction

Overactive bladder (OAB) is defined as a serious urgency with or without urgency incontinence, usually accompanied by frequency and nocturia. Urgency is defined as the sudden urge to void, which is very difficult to resist [1]. OAB has a substantial impact on the quality of life of affected individuals [2]. The prevalence of OAB in the adult population is estimated to be 10–12% [3].

Anticholinergics are considered the first line pharmacological treatment for OAB. The effectiveness and safety of anticholinergics have been confirmed in numerous clinical trials and meta-analyses [4]. Owing to the chronic nature of OAB, long-term use of anticholinergics is required for successful treatment [5].

OAB is often associated with the term "persistence". Medication persistence is defined as "the duration of time from initiation to discontinuation of therapy" [6]". Data from clinical trials indicate relatively good persistence with anticholinergic therapy in patients with OAB; that is, the percentage of patients who prematurely discontinue treatment is low. Especially in short-term 12-week trials, the reported percentage of discontinuation ranges between 4% and 31%. However, one might assume that the patients enrolled in these clinical trials are probably very

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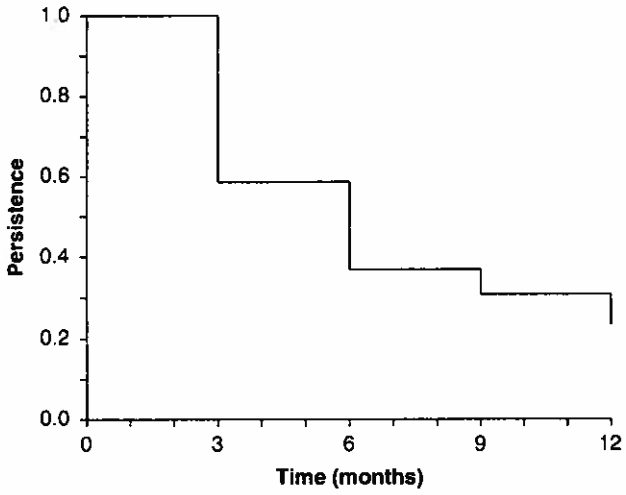

Figure 1. Persistence with treatment for overactive bladder with first line anticholinergics (study population; $n = 377$).

cooperative and particularly motivated. Notably, the percentage of patients with prematurely discontinued therapy in long-term clinical trials (i.e. in trials with follow-up periods of 1 year or longer) is 20–54% [7].

There is a limited number of studies describing anticholinergics persistence in real-life clinical setting. The aims of this study were to assess the persistence of first line anticholinergic medication in yet-untreated patients with OAB and to determine the reasons for therapy termination. Therefore, the data from a tertiary hospital outpatient database were matched with information obtained during a telephone survey carried out among these patients.

Material and methods

The study was undertaken in the outpatient clinics of the Department of Urology and Department of Gynaecology and Obstetrics of the University Hospital Ostrava, Czech Republic. The study protocol was approved by the ethics committee of the hospital.

All OAB patients in the outpatient hospital database who received prescribed anticholinergic treatment for OAB between 1 January 2009 and 31 December 2010 were retrospectively identified.

OAB was defined according the International Continence Society [1]. The diagnosis was based mainly on non-invasive urodynamic tools (history, bladder diary, urine examination, physical assessment). Subjects with the following conditions were excluded from participation in the study: urinary infections, significant prolapse of the pelvic organs, history of previous malignant disease in the pelvic area, previous irradiation therapy of the pelvis or neurogenic bladder.

A total of 926 OAB patients was identified. Patients with any previous anticholinergic treatment (started before 1 January 2009) were excluded. Altogether, 377 patients were considered to be treatment-naïve patients (target population).

After identification of patient records, patient data were monitored for the following 12 months. During this time, type of anticholinergic treatment prescribed, persistence according to the patient records and possible reasons for discontinuation of the therapy were evaluated.

A telephone survey of the patients was performed between February and June 2012.

All patients gave oral informed consent at the beginning of the interview. They were subsequently asked whether they were still using the prescribed anticholinergic medication. If they had discontinued the medication, they could select one most significant among seven precoded reasons for discontinuing anticholinergic medication.

In total, 377 OAB treatment-naïve patients (52 men, 325 women) with a mean age 60.29 ± 13.84 years were included in the study group. Pharmacotherapy was initiated in 189 patients (50.1%) with trospium (median daily dose 27.86 ± 12.73 mg), in 41 patients (10.9%) with propiverine (28.17 ± 4.97 mg), in nine patients (2.4%) with extended-release tolterodine (4.0 ± 0 mg), in 48 patients (12.7%) with solifenacin (5.94 ± 1.97 mg) and in 90 patients (23.9%) with fesoterodine (6.09 ± 2.01 mg).

Statistical analysis was performed using NCSS statistical software. The period of medication use was evaluated with the Kaplan–Meier estimate; the concordance of the period of use according to individual types of medication was evaluated with the log-rank test. A two-sample t test was used to evaluate the concordance of persistence among immediate- and extended-release anticholinergics. The reasons for discontinuation of the treatment were assessed with the chi-squared test.

Results

The median time to discontinuation of the first line anticholinergics in the monitored sample was 6.53 ± 3.84 months. After initiation of therapy, persistence in this group was 3 months for 59.7% of the patients, 6 months for 39.3%, 9 months for 33.6% and 12 months for 27.2% (Figure 1).

No statistically significant difference in persistence was observed in women versus men ($p = 0.180$; log-rank test). However, when persistence was assessed according to the type of medication, a significantly longer use of solifenacin was observed compared with other medications.

Table I. Reasons for discontinuation of anticholinergics, in total.

Reason for discontinuation	No. of patients (%)
Treatment not effective	81 (30.9)
Side-effects	62 (23.7)
Other health issues	4 (1.53)
Recommendation of family members or friends	1 (0.38)
Healing/resolution of symptoms	94 (35.9)
Symptoms persisted and patient learned to cope with them	10 (3.82)
Other	10 (3.82)

The patients were divided into two groups to assess the persistence for immediate-release versus extended-release preparations. Group A included 230 patients who were prescribed an immediate-release anticholinergic treatment (trospium or propiverine), and group B included 147 patients who were prescribed an extended-release anticholinergic (tolterodine with extended-release solifenacin or fesoterodine). The observed persistence in group A was 6.18 ± 3.75 months, while persistence in group B was 7.10 ± 3.90 months. The difference in persistence between groups A and B was statistically significant ($p = 0.023$; two-sample t test).

The reasons cited most frequently for discontinuation of treatment were healing/resolution of symptoms (35.9%), low effectiveness (30.9%) and medication side-effects (23.7%). The results are summarized in Table I. The most frequent reasons for discontinuation of anticholinergic medication in group A patients (who used immediate-release anticholinergics) were compared with those in group B patients (who used extended-release anticholinergic medication). The overall frequency of the reasons cited most often for discontinuation of medication, which were reasons 1, 2 and 5, were not significantly different in groups A and B ($p = 0.079$; χ^2 test). The results are presented in Table II. However, the frequencies of citing reason 5 for groups A and B were so high that this seemed to indicate a reason that might have statistical significance. Therefore, this reason was analysed separately.

Odds ratios were used to calculate the probability of symptom resolution (reason 5). The odds ratio for patients who stated healing/resolution of symptoms as the reason for discontinuation of medication was 1.98 (95% confidence interval 1.13–3.49). This shows that the probability of healing/resolution of symptoms in group B was significantly higher than in group A.

To eliminate the influence of discontinuation of medication due to healing/resolution of symptoms (reason 5) on overall persistence, the length of use of anticholinergic therapy was assessed in subgroups of patients who did not cite reason 5 as the cause for therapy discontinuation. Group A_1 included 177 patients, i.e. 230 patients who initiated therapy with group A anticholinergic medication minus the 53 patients who discontinued treatment owing to healing/resolution of symptoms. Group B_1 consisted of 106 patients, i.e. 147 patients who initiated therapy with a group B anticholinergic medication minus the 41 patients who discontinued treatment owing to healing/resolution of symptoms. The persistence in group A_1 was 6.24 ± 3.93 months, while persistence in group B_1 was 7.19 ± 4.09 months. The difference in persistence between groups A_1 and B_1 was statistically significant ($p = 0.048$; two-sample t test).

Discussion

Low patient persistence with OAB therapy in everyday practice decreases the quality of treatment and also increases medical costs [8]. Data from OAB patients who are not enrolled in clinical trials indicate short persistence with anticholinergics. For example, Keleher et al. reported that only 18% of female patients who initiated treatment with anticholinergics were still using the medication after 6 months [9]. Similarly, Echols et al. found that adherence after 12 months of therapy was only about 18% [10]. Data obtained from healthcare professionals also indicates a rather high rate of medication discontinuation, with only 10–20% of patients still taking anticholinergic medication 1 year after initiation of therapy [11]. The reasons for the low

Table II. Reasons for discontinuation of anticholinergics in group A (patients treated with immediate-release anticholinergics) and group B (patients treated with extended-release anticholinergics).

Reason for discontinuation	Patients who discontinued anticholinergics		
	Total (n = 262)	Group A (n = 174)	Group B (n = 88)
1. Low effectiveness	81 (30.9)	57 (32.8)	24 (27.3)
2. Side-effects	62 (23.7)	44 (25.3)	18 (20.5)
5. Healing/resolution of symptoms	94 (35.9)	53 (30.5)	41 (46.6)

Data are shown as n (%).

persistence with OAB treatment remain unclear. The persistence with anticholinergics seems to be worse than the persistence for other types of chronic medication, such as statins, per oral antidiabetic drugs, antihypertensive drugs and others [12].

The present analysis looked at the persistence of treatment with first line medication in treatment-naïve patients. It is well known that the persistence in clinical trials often substantially differs from that of "real-life" patients. The only way to evaluate actual persistence is in a retrospective study. That is why this retrospective analysis was performed using data from the hospital information database in combination with data from a telephone survey of patients. The overall persistence in this study was comparable with that found by others. For example, Gopal et al. reported 6-month persistence with anticholinergic medication of 41.2% and 12-month persistence of 23% [13]. However, comparison of the different studies is difficult because of the heterogeneous nature of the patient populations and dosage schemes. In addition, persistence is significantly influenced by differences in particular healthcare systems (e.g. the cost of medication for the patient, prescription of anticholinergics by a general practitioner versus prescription by a specialist). Nevertheless, a trend was observed during the assessment of individual types of anticholinergic medication, in that there seemed to be higher persistence with extended-release formulations. This finding corresponds with findings in other real-life retrospective studies [14]. Extended-release medication may have a better safety profile and a convenient once-daily dosing. These factors may be important reasons for higher persistence rates, which are seen not only for anticholinergic medication [15].

The assessment of reasons for medication discontinuation revealed a relatively high percentage of patients who reported healing/resolution of symptoms. This may be explained by the composition of the patient group, since in treatment-naïve patients, it is likely that a higher proportion of patients have mild symptoms. It may also be explained by the character of the natural course of OAB, in that OAB is chronic, shows slow progression of complex symptoms, and has periods of progression interspersed with periods of remission of variable length [16].

The most frequently reported reasons for discontinuation of medication in this study were similar to those found in other studies, i.e. low effectiveness of the treatment and treatment side-effects [17]. A total of 54.6% of the patients who discontinued first line medication cited one of these two reasons. In other words, more than half of the patients were not satisfied with the prescribed first line treatment. However, this should not prompt patients to terminate OAB treatment. On the contrary, physicians should work with patients, possibly offering another type of treatment, a change in the dosage of the anticholinergic drug, a transition to a different anticholinergic medication, suggesting the use of other methods, or some combination of these.

In conclusion, the search continues for an OAB treatment that is effective and satisfactory to patients, since more than half of OAB patients are not satisfied with their first line treatment. Physicians should explore other treatment possibilities, such as changes in medication or dosage, or the addition of other treatment methods.

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