



Abstract

Hypothesis / aims of study

The long-term changes of symptoms in Overactive bladder (OAB) patients are not fully understood. The purpose of this study is to analyze the severity of OAB symptoms and symptom-specific bother in long term and investigate the prognostic factors of symptomatic change.

Study design, materials and methods

We retrospectively analyzed hospital record of female patients who visited our clinic from January 2008 to December 2014 and were diagnosed as OAB. The severity of OAB symptoms and the bother specific to each OAB symptom were assessed using 2 questionnaires the OAB symptom score (OABSS) (Homma 2006) and the visual analogue scale (VAS) questionnaires for each OABSS (OABSS-VAS)(Fujihara 2013), respectively.

Results

This study was conducted with the approval of the institutional ethical committee.

We had 613 female OAB patients in those seven years. Among those patients, we analyzed patients in detail with whom we could observe more than 3 years and compare OABSS and OABSS-VAS before and after treatment. In those patients, the median (range) age was 71 (22-87) years, and the median follow-up period was 67(36-130) months. The number of wet OAB patients was 85 and that of dry OAB was 7. Median number of past usage of anti-muscarinic agents was 3 (0-6) and 62 patients had previous history of usage of mirabegron. In comparison of symptom and bother/QOL scores between before and after treatment, there were significant improvement in symptom scores, including OABSS-nocturia (Q2) (p=0.0057), OABSS-urgency (Q3) (p<0.0001), OABSS-urge incontinence (Q4) (p=0.0002), and total scores of OABSS (p<0.0001); similarly, there were significant improvement in QOL/bother scores including VAS- daytime frequency (Q1) (p=0.0009), VAS-nocturia (Q2) (p=0.0201), VAS-urgency (Q3) (p<0.0001), VAS-urge incontinence (Q4) (p=0.0003), respectively. We found also significant improvement of VAS-QOL score(p<0.0001). Among wet OAB patients, 71 patients (83.5%) suffered from UUI after OAB treatment. On the other hand, UUI was disappeared in 14 patients (16.5%) of wet OAB patients. Among dry OAB patients, UUI was newly occurred in 5 patients (71.4%). According to OABSS, in 25 patients (27.2%) total OABSS score were increased after treatment and in 10 patients (10.9%) disease severity were increased. When taking account of the past history in relation to the OAB symptom or QOL, there were no significant correlations of symptomatic aggravation with age, treatment period, and co-existing disease such as hypertension, DM, cerebral vascular disease. However, we found significant correlations between OAB symptomatic aggravation and co-existing cardiovascular disease (p<0.0001).

Interpretation of results

There were few reports about long-term (>12 months) outcome in OAB treatment. Our study showed symptomatic change of OAB during over a 5-year follow-up. In our study, as in Fig.3, the decrease in OABSS and OABSS-VAS score has been demonstrated at the beginning of the treatment with maintaining of the decreased score with only small fluctuations. However, in 25 patients (27.2%) total OABSS score were increased during the follow-up and in 10 patients (10.9%) disease severity were increased. Interestingly, there were significant correlations between OAB symptomatic aggravation and co-existing cardiovascular disease (p<0.0001), while no significant correlations with treatment period or age. As reported, the prevalence of cardiovascular comorbidities was significantly higher in patients with than without OAB (KE Andersson 2010), the patients who has cardiovascular disease may have the risk for treatment-resistance against OAB.

Concluding message

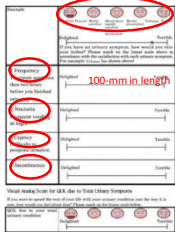
At a mean follow up of approximately 5.5 years, the OAB symptom severity were getting better in about 40% of OAB patients; while getting worse in about 10% of OAB patients despite undergoing various treatment. Patients who has cardiovascular disease may have the risk of treatment-resistant against OAB.

Methods

OABSS and OABSS-VAS questionnaires

Question	Frequency	score
Q1. How many times do you typically urinate from waking in the morning to going to sleep at night? Daytime frequency	7 or less 8-14 15 or more	0 1 2
Q2. How many times do you typically wake up to urinate at night? Nocturia	None 1 2 3 or more	0 1 2 3
Q3. How often do you have a sudden desire to urinate that is difficult to defer? Urgency	None Less than once a week Once a week or more About once a day 2-4 times a day 5 times a day or more	0 1 2 3 4 5
Q4. How often do you leak urine because you cannot defer the sudden desire to urinate? Urinary urge incontinence	None Less than once a week Once a week or more About once a day 2-4 times a day 5 times a day or more	0 1 2 3 4 5

(Homma et al., 2006 Uro)



VAS questionnaire to assess bother or satisfaction regarding patient QOL specific to each of 4 OABSS items, using VAS scale with 10 cm line.

Results

Table 1 Patients' demographic data

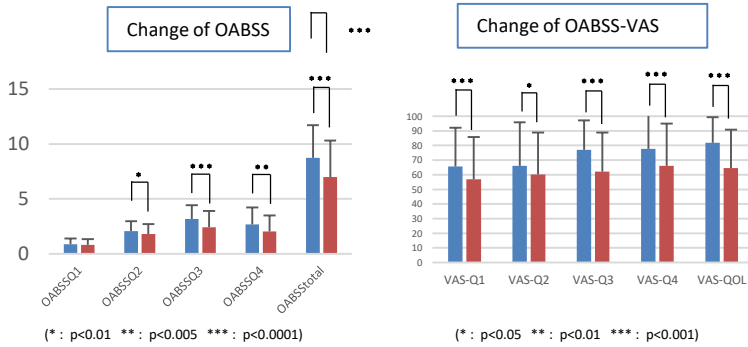
Age 71y.o. (22-87)
Following period (median) 67M (36-130M)
Wet OAB n=85 Dry OAB n=7
Treatment
previous anticholinergic agent (median) 3 (0-6)
previous usage of β3 agonist yes: 62 no: 30

Comorbidity

	yes	no
Hypertension	37	55
Cardiovascular disease	10	82
Cerebral vascular disease	11	81
Spinal disease	30	62
Diabetes	17	75

We had 613 female OAB patients in seven years, 2008-2014. Among those patients, we analyzed patients in detail with whom we could observe more than 3 years. Total number of the patients was 92. The number of wet OAB patients was 85 and that of dry OAB was 7. Median number of past usage of anti-muscarinic agents was 3 (0-6) and 62 patients had previous history of usage of mirabegron. UUI was resolved in 9 patients (10.6%) of wet OAB with the first drug which they had.

Fig.1 Comparison of symptom and QOL scores between before and after treatment



COMPARISON of symptom and QOL scores between before and after treatment:

*In OABSS questionnaires, there were significant improvement in symptom scores of OABSS-nocturia (Q2) (p=0.0057), OABSS-urgency (Q3) (p<0.0001), OABSS-urge incontinence (Q4) (p=0.0002), and total scores of OABSS (p<0.0001).
*In OABSS-VAS questionnaires, there were also significant improvement in QOL in each score of OABSS-VAS scores : VAS- daytime frequency (Q1) (p=0.0009), VAS-nocturia (Q2) (p=0.0201), VAS-urgency (Q3) (p<0.0001), VAS-urge incontinence(Q4) (p=0.0003), respectively.
*We found also showed significant improvement of VAS-QOL score : pre- 81.9±17.5 v.s. post-treatment 64.6±26.3, (p<0.0001).

Table 2 The change of OAB status after treatment

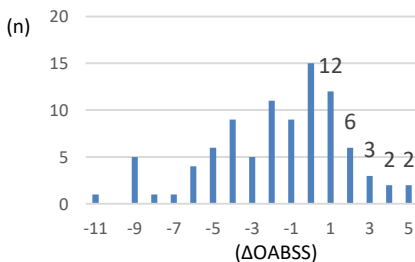
Dry OAB (n=7) → dry OAB (n=2)
wet OAB (n=5)

Wet OAB(n=85) → dry OAB (n=14)
wet OAB (n=71)

Among wet OAB patients, 71 patients (83.5%) suffered from UUI after OAB treatment. On the other hand, UUI was disappeared in 14 patients (16.5%) of wet OAB patients. Among dry OAB patients, UUI was newly occurred in 5 patients (71.4%).

Fig.2 The change of OAB severity after treatment according to OABSS

Change of OABSS total score between before and after treatment



This shows ΔOABSS total score (OABSS total score after treatment minus that of before treatment). Median of the score was -1 (-11- 5). In 25 patients (27.2%) total OABSS score were increased.

Change of OAB severity after treatment

Before	After
Mild (total of OABSS ≤ 5) n=13	mild (n=6) moderate (n=7)
Moderate (5<total of OABSS <12) n=59	mild (n=23) moderate (n=33) severe (n=3)
Severe (total of OABSS ≥ 12) n=20	mild (n=3) moderate (n=13) severe (n=4)

Fig.3 Correlations with symptomatic aggravation

Correlations with aggravation of OAB severity (univariate analysis)

	Aggravation (+; n=10); (-; n=82)	p value
Age	71±11 : 67±12	0.35
Treatment period	78±29 : 70±24	0.32
Number of past usage of anti-muscarinic agents	2.8±0.92 : 2.8±1.7	0.96
prior treatment with mirabegron	Usage (+)/(-) 7/3 : 55/27	0.85
comorbidity		
Hypertension	31:6	0.19
Cardiovascular disease	5:5	<0.0001
Cerebral vascular disease	8:3	0.066
Spinal disease	27:3	0.83
Diabetes	16:1	0.46

Correlations with ΔOABSS total score (univariate analysis)

	p value
Age	0.57
Treatment period	0.0085 (r=0.27)
Number of past usage of anti-muscarinic agents	0.093
prior treatment with mirabegron	0.47
Hypertension	0.48
Cardiovascular disease	0.029
Cerebral vascular disease	0.97
Spinal disease	0.57
Diabetes	0.45
Pretreatment total score of OABSS	<0.0001(r=-0.48)
Pretreatment score of OABSS-Q4	<0.0001(r=-0.45)
Pretreatment score of OABSS-Q3	<0.0001(r=-0.39)

There were significant correlation between ΔOABSS total score (OABSS total score after treatment minus that of before treatment) and treatment period, coexisting cardiovascular disease, pretreatment total score of OABSS, pretreatment score of OABSS-Q3 and pretreatment score of OABSS-Q4, respectively.

According to OABSS, 39 patients (42%) moved to better category (moderate→mild:23 patients, severe→mild: 3 patients, severe→moderate: 13 patients) and 10 patients (11%) moved to worse category (mild→moderate: 7 patients, moderate→severe: 3 patients).

Conclusions

- At a mean follow up of approximately 5.5 years, the OAB symptom severity were getting better in about 40% and were getting worse in about 10% of wet OAB patients despite the treatment.
- Coexisting cardiovascular disease had significant correlation with OAB symptomatic aggravation.

We analyzed the correlation with OAB symptomatic aggravation according to OABSS severity category. There was significant correlation with coexisting cardiovascular disease.