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OAB in Asia Today
A Matter of Urgency

Highlights of Second OAB Advisory Board Meeting
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This advisory board meeting was held on the sidelines of the 3rd Pan Pacific Continence Society Meeting held in Kaohsiung, Taiwan. Leading urologists from Korea, Taiwan, and Japan met to discuss the standards of evaluation of overactive bladder (OAB) in Asia, unsolved issues including treatment strategies for unsatisfied patients, and management of male lower urinary track syndrome (LUTS). The meeting was chaired by Professor Osamu Yamaguchi of Fukushima Medical University, Japan.

Inside This Issue

Reporter: Mary Nishikawa, Medical Tribune, Inc.

Effective Tools for Identifying OAB

Diagnostic tools for doctors and self-check tools for patients

Dr. Won Hee Park, Inha University Hospital, Incheon, Korea

As we consider tools for the diagnosis or self-check of overactive bladder (OAB), how do we define OAB and explain urgency to our patients? The International Continence Society (ICS) defines ***Urgency*** as, "a sudden compelling desire to pass urine, which is difficult to defer" and the ***Overactive Bladder Syndrome*** as "urgency, with or without urge incontinence, usually with frequency and nocturia."[1]

A patient presents with a urinary complaint, and during the consultation the doctor suspects OAB and describes the syndrome. The patient may have trouble understanding the difference between the healthy sensation of "urge" and symptomatic "urgency." The doctor might not be able to describe these two clearly enough, if there is only one word describing both in the language. Instead of using "urgency" to define OAB, Dr. Yamaguchi has proposed to describe OAB as a hypersensitivity disorder.[2]

On the other hand, patients often deny having urgency, even though they exhibit habitual frequency, defensive voiding and toilet mapping (confirming locations of toilets before venturing outside the home). Diagnostic questionnaires help convince patients that they have OAB and assist busy clinicians to identity patients who may benefit from medical intervention. Self-check questionnaires encourage patients to seek medical attention.

Diagnostic tools for doctors

Various questionnaires are now being employed in Korea to diagnose OAB. The Korean Continence Society has linguistically validated versions of OAB-q[3] and ICIQ-OAB[4] in their native language though these still require psychometric validation.

User friendly diagnostic tools are now available in Asia.

Dr. Oh and Dr. Choo have recently finished a Korean version of the Overactive Bladder Symptom Score (OABSS) (Table 1).[5]

A Korean version of OABSS is available now.

The OABSS is obtained as the sum (Table 2) of four symptom scores that address daytime voiding, nighttime voiding, urgency, and urgency incontinence. It is being using throughout Asia in clinical studies and daily practice.

Table 2. Overall Score*

Sum of Scores	Urgency Grade
5 or less	Mild
6-11	Moderate
12 or more	Severe

**The overall score is the sum of the four scores of the OABSS.*

Table 1. Overactive Bladder Symptom Score (OABSS)*

Question	Frequency	Score
How many times do you typically urinate from waking in the morning until sleeping at night?	7 or less 8-14 15 or more	0 1 2
How many times do you typically wake up to urinate from sleeping at night until waking in the morning?	0 1 2 3 or more	0 1 2 3
How often do you have a sudden desire to urinate, which is difficult to defer?	Not at all 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
How often do you leak urine because you cannot defer the sudden desire to urinate?	Not at all 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

**Patients were instructed to circle the score that applied best to their urinary condition during the past week.*

Reproduced from *Urology*.[5]

Self-check tools for patients

Physicians in Korea commonly use a self-check tool that queries the patient on nine items: frequency, urgency, toilet mapping, being inconvenienced by lack of facilities, urge incontinence, fluid restriction, interruption of work, pad usage and nocturia. A patient with one or more of these symptoms might have OAB. Questionnaires written and validated in our own language helps in the clarification of urgency and symptoms of OAB.

Discussion

The OABSS[5] is becoming available as a diagnostic tool across Asia, and the Screening Questionnaire for OAB (SQOAB)[6] is used for self-check (Table 3) in Japan. The OABq (V8)[3] is used in Korean during routine examinations and it was stressed that short questionnaires are the most acceptable to the general population. Questionnaires are being used more often after their inclusion in local OAB guidelines.

Table 3. Screening Questionnaire for Overactive Bladder (SQOAB)*

Do you have the following symptoms?
☐ I urinate frequently.
☐ It is difficult to hold on when I have the sudden compelling desire to urinate.
☐ I leak urine because I cannot hold on.

**People with at least one of the above symptoms may have overactive bladder.*

Reproduced from *Clinical Guidelines for Overactive Bladder*[6] with permission from Blackwell Publishing.

Evaluation and Issues of Present OAB Treatments

Standards for selection and efficacy evaluation of antimuscarinic drugs

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Antimuscarinic drugs are the first-line therapy for OAB. The ideal drug should suppress involuntary bladder contractions without inhibiting volitional bladder emptying, and be close to 100% bladder selective thereby exhibiting fewer side effects (dry mouth, constipation, blurred vision and drowsiness). It should be easy to administer and lacking in drug-drug interactions.

Drugs are ranked according to the number of large-scale random control trials showing favorable results for OAB variables, tested with proven methods.

Methods used to confirm efficacy of drugs for treating OAB

- Sensation-Related Bladder Diary (SR-BD)
- Warning Time (WT)
- Urgency Perception Score (UPS)
- Indevus Urgency Severity Scale (IUSS)
- Patient Perception of Bladder Condition (PBC/PPBC)

An antimuscarinic drug will receive a grade of A if it is supported by at least two level I clinical studies (large scale and randomized controlled).[6] The International Consultation

on Incontinence (ICI) has assessed solifenacin, tolterodine, trospium, and darifenacin to be level I, grade A as reported in the 3rd ICI 2004 Conference, co-sponsored with the World Health Organization (WHO).[7] These antimuscarinics decrease frequency, nocturia, micturitions, and post-void urine, and increase bladder capacity.

The efficacy of solifenacin has been confirmed in the following random controlled clinical trials

- VENUS[8] (VESIcare® Efficacy and Safety in Patients with Urgency Study) significantly increased WT at therapeutic dosage
- SUNRISE[9] significantly reduced urgency episodes per 24 hours
- VERSUS[10] improved severe symptom bother with residual urgency
- VOLT[11] (Open-Label Trial with Solifenacin) improved patient-reported outcomes

Discussion

Diagnostic methods, like IUSS, are used during clinical trials to grade urgency though they might not be practical to use in the clinical setting. Urgency is very subjective and hard to evaluate. Other tests are too involved for the patients, requiring them to record their activities in a diary. It was recommended to use OABSS[5] in the clinical setting because the questions are straightforward and easy to answer.

Patients have trouble describing their urgency or using a bladder diary, so simpler questionnaires such as OABSS are best to use in the clinical setting.

Cause and prevention of treatment failure and how to treat unsatisfied patients

Dr. Myung-Soo Choo, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

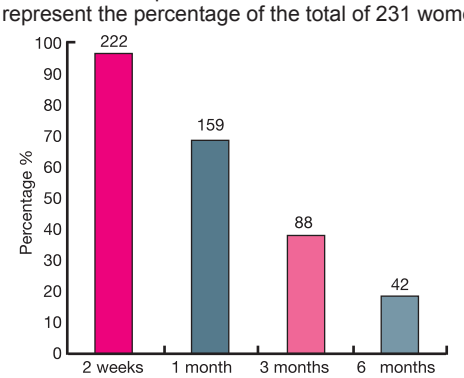
Antimuscarinic agents are the mainstay of treatment for OAB though low patient adherence is a major concern. Failure to recognize poor adherence to drug therapies can lead to inappropriate dose escalation, changes in medication, invasive investigations, and increased cost of disease management.

A medium-term analysis of subjective efficacy of treatment for women with detrusor instability and low bladder compliance reported[12] that about half of patients stopped treatment before therapeutic levels were reached at 3 months, with most abandoning treatment between 4 to 6 months (Figure 1). Improved patient adherence has been reported in long-term studies (Table 4).[13-18] In a 1-year study for solifenacin,[17] discontinuations due to adverse events were only 4.7%, of which 0.4% were due to dry mouth.

Social and cultural factors, socioeconomic status, education, smoking and alcohol consumption have an impact on adherence to drug treatment. Patients may refuse to reduce fluid or caffeine intake, or imagine that their condition is untreatable. Patients may stop their treatment when side effects are encountered. Antimuscarinic treatment may fail because of the presence of other diseases or misdiagnosis by the physician. The dosage may be incorrect or side effects may prohibit adequate dosing. Physicians can evaluate the failure of initial therapies by performing urodynamic studies (UDS) or requesting patients to record their symptoms in voiding diaries.

Figure 1. The number and percentage of women continuing anticholinergic medication between 2 weeks and 6 months

Values above the bars represent the number of women, and the bars represent the percentage of the total of 231 women.



Reproduced from *Br J Obstet Gynaecol*[12] with permission from the publisher.

To prevent treatment failure, we can

- Provide a thorough initial consultation, that is, ask about painful voiding with a full bladder during the first visit to rule out interstitial cystitis (IC)
- Provide adequate counseling from the start, including behavior modification. With drug therapy, patients need to be made aware that the course of treatment requires 2 to 3 months with adequate dosing, and that side effects are common but not serious
- Allow dose flexibility, adjusted according to the appearance of side effects
- Reduce the frequency of the dose to improve compliance
- Provide better follow up to rule out an incorrect diagnosis
- Be aware of social and cultural factors

Treatment failure is preventable.

Table 4. Long-Term Studies of Antimuscarinic Agents

Study	Study design	Adherence	Adverse events/discontinuation
ER oxybutynin[14]	1-year extension study: 1067 participants started on 5 mg, followed by weekly 5 mg increments, until the patient was continent or until there was optimum balance between symptom control and tolerability.	63% of patients who continued therapy >3 months remained on medication at 1 year	Dry mouth reported by 8.4% Discontinuation due to adverse events 24%
Darifenacin[15]	24-month extension study: 719 participants received 7.5 mg for the first 2 weeks of the study, and then offered dose escalation to 15 mg.	475 (63%) completed the study >85% of the study participants achieved >80% compliance at 2-year follow-up	Discontinuation due to: insufficient clinical response 9.5%; adverse events 8.9%
IR tolterodine[16]	1-year extension study of 3 mg, twice daily; 712 participants.	62% (441) completed the study 23% required dose reduction	Discontinuations due to adverse events 15%, of which 10% were due to dry mouth
Solifenacin[17]	1-year extension study: 1633 participants commenced on 5 mg, then offered dose escalation to 10 mg.	1329 (81%) patients completed study	Discontinuations due to adverse events 4.7%, of which 0.4% were due to dry mouth
Trospium[18]	9-month extension study: 407 participants commenced on trospium 20 mg twice daily.	265 (65%) patients completed study	Discontinuations due to adverse events 9%

Table adapted from original Table 2 in *BJU Int*[13] with permission from the publisher.

Discussion

We agreed that first-line therapy for OAB treatment is an antimuscarinic drug; however, for those who are refractory to treatment various options were discussed. Botulinum toxin (Botox) and neuromodulation were recommended. The Botox is applied locally, so its effects on the bladder are favorable. Though neuromodulation is efficacious, an instrument is required to be inserted into the body and is often refused by Asian patients. Sometimes imipramine can be used in low dose, but its side effects must be strictly monitored. ExMI and biofeedback were also recommended, though ExMI requires many visits to the hospital (twice a week for 2 or 3 months), which is difficult for some patients. Pelvic floor exercises are recommended.

Various options can be considered for patients refractory to antimuscarinic drug therapy

- Surgical option: denervation or augmented cystoplasty
- Modulatory therapies: electromagnetic stimulation, neuromodulation, extracorporeal magnetic innervation (ExMI)
- Different classes of drug having other modes of activity: botulinum toxin (Botox), producing muscle relaxation by blocking the release of acetylcholine within the alpha motor neuron; capsaicin and resiniferatoxin, acting on c-fibers that stimulate bladder activity and release tachykinins, desensitizing bladder afferents
- Referral to other specialists because of concurrent diseases that may be affecting treatment

How do we treat unsatisfied patients?

Treatment strategies and challenges for male OAB and LUTS

Dr. Alex Tong-Long Lin, National Yang-Ming University, Taipei Veterans General Hospital, Taipei, Taiwan

There are multiple factors that may contribute to LUTS (Lower Urinary Tract Syndrome) and OAB in the male patient. The following case studies show the complexity of symptoms and concomitant disease that are required to be diagnosed before beginning treatment for OAB and LUTS.

How do we treat male patients with OAB?

CASE STUDY 1

- Male, 75 years old
- OAB-related symptoms: urgency, nocturia (4 to 5 episodes/night), urge urinary incontinence (UUI), occasional
- Other symptoms: slow urinary stream
- Clinical tests: uroflowmetry (UFR) - volume, 172 mL; Qmax, 13 mL/sec; shape, bell curve; tmax, lower than normal; ultrasound - prostate size 57 by 46 by 52 mm (70.9 mL)

The major concern of CASE STUDY 1 was urinary urge incontinence. At first, an antimuscarinic drug was prescribed, but it did not seen to have an effect; so urodynamic studies were done, which revealed a small bladder capacity (bladder outlet obstruction, BOO) with detrusor overactivity (DO) (residual urine of 172 mL with a Qmax of 13 mL/sec). Ultrasound revealed an enlarged prostate, so the patient was started with an alpha antagonist. Because the patient did have urge incontinence, an antimuscarinic was added to the treatment. We can conclude that BOO-induced detrusor overactivity was better managed with an alpha antagonist. The alpha blocker may have improved the storage symptoms because it reduced the BOO and blocked the increased alpha

adrenergic activity in the detrusor. Prostate size and shape should be important in managing male LUTS although published reports tell us that prostate size does not correlate with patient symptoms. Experience tells us that if the prostate is really large we should consider it in the management of symptoms.

The initial diagnosis for CASE STUDY 2 was BOO with DO.The patient was treated with both an alpha blocker and antimuscarinic, but neither drug improved the symptoms. For the re-evaluation, the patient was requested to record his symptoms in a voiding diary for 3 days. Urine chemistries were also taken. Desmopressin was prescribed to reduce urine volume.

The final diagnosis was complex. The patient had BOO due to benign prostatic hyperplasia (BPH) and the DO might have been secondary to the BOO. He also had nocturnal polyuria and sleep apnea. Multiple factors might contribute to male LUTS and OAB. We need to pay attention to prostate size and urine volume, and when there is poor response to medication it is advisable to inquire about snoring and possibly suspect sleep apnea.

CASE STUDY 2

- Male, 83 years old
- OAB-related symptoms: frequency, urgency, nocturia 10 episodes/night, urgency, UUI (occasional)
- Other symptoms: Slow urinary stream, loud snoring for over 10 years (tested and diagnosed: sleep apnea)
- Clinical tests: UFR, 173 mL; ultrasound - prostate size, 47 by 44 by 39 mm (42 mL)
- Physical exam: no leg edema, no varicose veins, moderate enlargement of prostate, normal perianal sensations and anal tone
- Pressure flow study: bladder capacity, 59 mL

Discussion

Nocturia is bothersome and often difficult to manage with anticholinergics because it is a multi-etiological condition. Desmopressin is used in nocturnal polyuria cases but it should be used with caution in the elderly (>65 yrs) due to its CV side effects. For patients with sleep apnea and improved nocturia, it was suggested that an antimuscarinic plus a mild sedative could be prescribed. With these complex cases, it is recommended to seek the advice of a specialist, especially to rule out diabetes or cardiovascular disease.

How do we treat nocturia in patients with LUTS?

Japanese OAB Guidelines Update

Clinical guidelines for overactive bladder

Dr. Osamu Yamaguchi, Fukushima Medical University, Fukushima, Japan

A digest edition of Clinical Guidelines for Overactive Bladder was published in Japanese by Blackwell in 2008, with an English version now in press.[6] This digest will be particularly helpful, educating general practitioners (GPs) on symptom-based diagnosis, diagnosis by exclusion and treatments for OAB. Though OAB is prevalent in Asia, patients usually visit their doctors with other complaints, and with appropriate questioning, the physician makes a diagnosis of OAB.

8.1 million Japanese are estimated to have OAB.

The patient is then given a formalized questionnaire, like the OABSS (Table 1) which helps the GP make a diagnosis. Severity of the OAB symptoms can be classified according to the OABSS.[5]

OABSS is a simple questionnaire - it is appropriate for clinical practice.

Patients may have other diseases that are causing their symptoms and it is important to rule them out before beginning any course of treatment for OAB.

Major diseases to exclude

- **Bladder abnormalities**: bladder cancer, bladder stones, interstitial cystitis (painful bladder syndrome)
- **Pericystic abnormalities**: endometriosis
- **Prostate or urethral abnormalities**: prostate cancer, urethral calculus
- **Urinary tract infection**: bacterial cystitis, prostatitis, urethritis
- **Others**: urinary retention, polyuria, psychogenic urinary frequency

In the guidelines, there is a new section on drug therapies for treating OAB. Solifenacin has a grade A recommendation with fourteen level I clinical trial research reports (Table 5).[6]

Table 5. Solifenacin: Recommendation Grade and Ranking of Research Papers

Recommendation Grade	Number of research papers						
	General Remarks	Level I	Level II	Level III	Level IV	Level V	Total
A	-	14	-	1	-	4	19

There is a section in the guidelines[6] on the rules for treatment with anticholinergic drugs, classified by sex and age.

OAB in women

- Low-dose anticholinergic drugs can be administered immediately
- Women over 80 years old with voiding symptoms or copious residual urine should be referred to a urologist

OAB in men under 50 years of age

- Test for any underlying comorbidities such as neurological or urological diseases

OAB in men over 50 years of age (especially OAB complicated with BPH)

- Start with α1 blockers if voiding symptoms are confirmed
- If OAB symptoms do not improve, refer patients to a urologist who will coadminister an anticholinergic drug

A treatment algorithm, included in the guidelines,[6] provides the most suitable treatments and suggests referrals for patients with complex conditions. GPs can easily follow the flow chart to determine the best treatment regimen for their patients, which will depend on urinalysis results, presence or absence of pyuria or hematuria, and results of residual urine volume test.

With the inclusion of the OABSS,[5] drug treatments, special patient-type descriptions, and an evidence-based algorithm, it is hoped that the guidelines in digest form will be an indispensable aid to GPs.

Discussion

OABSS[5] measures OAB symptoms, but does not directly query the patient about Quality of Life (QoL) issues; therefore, the questions are more straightforward and easier for the patient to answer. It is recommended to measure QoL with other tools such as the International Prostate Symptom Score (IPSS) with The Disease Specific Quality of Life Question.[19]

It was agreed that the OAB voiding diary is not essential for diagnosis though useful for some patients. Residual urine measurements are recommended though the GP often does not have the ultrasound equipment to take the measurement. In cases where it might not be practical to request the patient to keep a voiding diary or the physician does not have the means for measuring residual volume, it was recommended to start with low dose solifenacin.

Residual urine should be measured in both elderly men and women to avoid safety risks.

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