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OVERACTIVE BLADDER: DIAGNOSIS AND MANAGEMENT



Overactive bladder (OAB)

- OAB is a symptom syndrome.
- ICS (International Continence Society, 2002) definition:
 - Urgency, with or without urge incontinence, usually with frequency and nocturia.
 - In the absence of obvious pathologic or metabolic disorders (such as UTI, BPE or bladder cancer, which might cause such symptoms).



Prevalence of OAB

- European: 16.6% female: 17.4% male: 15.6%
- USA: 16.4% female: 16.9% male: 16.0%
- Taiwan: 16.9% female: 18.3% male: 16.0%

 $(age \ge 40 \text{ y/o})$

(age > 18y/o)

(age > 30y/o)

Milsom et al. *BJU Int* 2001 Stewart et al. *World J Urol.* 2003 Yu et al. Urol Int 2006



OAB Symptoms

Frequency

- Daytime frequency: complaint by the patient who considers that they void too often by day
- Nocturia (urination at night): complaint that the patient has to wake up at night I or more times to void







OABSS

TABLE I. Overactive bladder symptom score *				
Question	Frequency	Score		
How many times do you typically urinate from waking in the morning until sleeping	≤7	0		
at night?	8–14	1		
	≥15	2		
How many times do you typically wake up to urinate from sleeping at night until	0	0		
waking in the morning?	1	1		
	2	2		
	≥3	3		
How often do you have a sudden desire to urinate, which is difficult to defer?	Not at all	0		
	Less than once a week	1		
	Once a week or more	2		
	About once a day	3		
	2–4 times a day	4		
	5 times a day or more	5		
How often do you leak urine because you cannot defer the sudden desire to	Not at all	0		
urinate?	Less than once a week	1		
	Once a week or more	2		
	About once a day	3		
	2–4 times a day	4		
	5 times a day or more	5		

* Patients were instructed to circle the score that best applied to their urinary condition during the past week; the overall score was the sum of the four scores.

Homma et al. Urology 68(2), 2006



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OAB-q

	Yes	No
Do you urinate more than 8 times in a 24-hour period?		
Do you frequently get up 2 or more times during the night to go to the bathroom?		
Do you have the uncontrollable urges to urinate that sometime resulted in wetting accidents?		
Do you frequently limit your fluid intake when you are away from home so that you won't have to worry about finding a bathroom?		
When you are in a new place, do you make sure you know where the bathroom is?		
Do you avoid places if you think there won't a bathroom nearby?		
Do you frequently have strong, sudden urges to urinate?		
Do you go to he bathroom so often that it interferes with the things you want to do?		
Do you use pads to protect your clothes from wetting?		



Goal for treatment of OAB

- To improve symptoms that cause a problem for the individual patient.
- Urgency is the key symptom to OAB treatment.



Management of OAB

- Standard first-line therapy
 - Behavior therapy
 - Pharmacological therapy
- Specialized therapy
 - Neuromodulation
 - Reconstructive and invasive surgery
 - Botulinum neurotoxin-A injections



Behavior therapy

Initial treatment (first line) (level 1 evidence)

- Lifestyle intervention (behavior modification)

- Weight reduction, caffeine reduction, smoking cessation, modified fluid intake (fluid reduction, avoid watercontaining foods, avoid fluid intake from 4 hours before sleep, empty bladder before sleep or going out)
- Pelvic floor muscle training
- Bladder retraining



Pharmacotherapy for OAB

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Pharmacological therapy *Anticholinergic agents*

• Antimuscarinics are efficacious, safe, and welltolerated treatments for OAB.

• These agents currently remain the first-line pharmacologic treatment for OAB.

Chapple CR, Eur Urol 2008



Antimuscarinic mechamism of action

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- Detrusor muscle
 - →inhibit Ach binding to M receptor
 - → stablize det muscle
 - $\rightarrow \uparrow$ bladder capacity
- Sensory receptors in uro/suburothelium
 - $\boldsymbol{\rightarrow}$ $\boldsymbol{\downarrow}$ afferent nerve activity (A\delta-fiber and C-fiber)
- Significant reductions in urinary frequency, urgency and UUI episodes



EUROPEAN UROLOGY 54 (2008) 543-562

The Effects of Antimuscarinic Treatments in Overactive Bladder: An Update of a Systematic Review and Meta-Analysis

Christopher R. Chapple^{a,*}, Vik Khullar^b, Zahava Gabriel^c, Dominic Muston^c, Caty Ebel Bitoun^d, David Weinstein^d

- All antimuscarinics reviewed were more effective than placebo
- Mean changes in
 - Number of incontinence episodes
 - Number of micturitions per day
 - Volume voided per micturitions
 - Number of urgency episodes per day (fesoterodine, propiverine, solifenacin, tolterodine)*

The data for the remaining drugs in the study was not available for these parameters



Antimuscarinic agents

FIGC		Level	Grade	
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	Tolterodine	1	Α	(highly recommended)
	Trospium	1	Α	(highly recommended)
	Darifenacin	1	Α	(highly recommended)
	Solifenacin	1	Α	(highly recommended)
	Propantheline	2	В	(Recommended)
	Atropine, hyoscyamine	3	С	(optional)
	Mixed Action Drugs			
	Oxybutynin (muscle relaxant effect)	1	А	(highly recommended)
	Propiverine (CC blocker)	1	Α	(highly recommended)
	Dicyclomine	3	С	(Optional)
	Flavoxate	2	D	(possible)



Adverse events of antimuscarinics

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- Due to inhibition of muscarinic receptors in organs other than bladder
- Dry mouth: most common
- Constipation: 2nd most common
- **Blurred** vision
- CNS effect: Dizziness, insomnia, cognitive impairment



Pharmacotherapy for OAB

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Novel 63 agonist

- Japan approval in 2011: 25 mg/day dose level
- FDA approval in 2012 June: 25 or 50 mg/day dose in the USA
- Europe and Canada
- For symptomatic treatment of urgency, increased micturition frequency and/or UUI~ OAB syndrome.



Anticholinergic drugs vs. β3 agonist

Anticholinergic drugs:

~first-line pharmacologic treatment for OAB

• β3 agonist :

- ~As second-line treatment for OAB p'ts who are poor responders or intolerant to anticholinergics.
- ~ May be considered as first-line treatment in the future



Toxins

	Level of evidence	Grade of recommendation
Botulinum toxin (neurogenic)	2	A
Botulinum toxin (idiopathic)	3	В
Capsaicin (neurogenic)	2	С
Resiniferatoxin (idiopathic)	2	С