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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% (age ≥ 40 y/o)
  female: 17.4%
  male: 15.6%
- USA: 16.4% (age > 18y/o)
  female: 16.9%
  male: 16.0%
- Taiwan: 16.9% (age > 30y/o)
  female: 18.3%
  male: 16.0%

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 1 or more times to void

**Urgency (core symptom)**
- Sudden, compelling desire to pass urine that is difficult to defer

**Urge Incontinence**
- Involuntary leakage preceded by urgency

OAB
Impact on Quality of Life

Physical
- Limitations or cessation of physical activities

Sexual
- Avoidance of sexual contact and intimacy

Occupational
- Absence from work
- Decreased productivity

Domestic
- Requirements for specialized underwear, bedding
- Special precautions with clothing

Psychological
- Guilt/depression
- Loss of self-esteem
- Fear of
  - being a burden
  - lack of bladder control
  - urine odor

Social
- Reduction in social interaction
- Limiting and planning travel around toilet accessibility

Quality of Life
# TABLE I. *Overactive bladder symptom score* *

<table>
<thead>
<tr>
<th>Question</th>
<th>Frequency</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>How many times do you typically urinate from waking in the morning until sleeping at night?</td>
<td>(\leq 7)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>8–14</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>(\geq 15)</td>
<td>2</td>
</tr>
<tr>
<td>How many times do you typically wake up to urinate from sleeping at night until waking in the morning?</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>(\geq 3)</td>
<td>3</td>
</tr>
<tr>
<td>How often do you have a sudden desire to urinate, which is difficult to defer?</td>
<td>Not at all</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Less than once a week</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Once a week or more</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>About once a day</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>2–4 times a day</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>5 times a day or more</td>
<td>5</td>
</tr>
<tr>
<td>How often do you leak urine because you cannot defer the sudden desire to urinate?</td>
<td>Not at all</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Less than once a week</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Once a week or more</td>
<td>2</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td></td>
<td>2–4 times a day</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>5 times a day or more</td>
<td>5</td>
</tr>
</tbody>
</table>

* 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.
### OAB-q

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you urinate more than 8 times in a 24-hour period?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you frequently get up 2 or more times during the night to go to the bathroom?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you have the uncontrollable urges to urinate that sometime resulted in wetting accidents?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>When you are in a new place, do you make sure you know where the bathroom is?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you avoid places if you think there won’t a bathroom nearby?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you frequently have strong, sudden urges to urinate?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you go to the bathroom so often that it interferes with the things you want to do?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you use pads to protect your clothes from wetting?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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 water-containing 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
Pharmacological therapy

Anticholinergic agents

• Antimuscarinics are efficacious, safe, and well-tolerated treatments for OAB.

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

Chapple CR, Eur Urol 2008
Antimuscarinic mechanism of action

– Detrusor muscle
  → inhibit Ach binding to M receptor
  → stabilize det muscle
  → ↑ bladder capacity

– Sensory receptors in uro/suburothelium
  → ↓ afferent nerve activity (Aδ-fiber and C-fiber)

– Significant reductions in urinary frequency, urgency and UUI episodes
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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Level</th>
<th>Grade</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimuscarinics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tolterodine</td>
<td>1</td>
<td>A</td>
<td>(highly recommended)</td>
</tr>
<tr>
<td>Trospium</td>
<td>1</td>
<td>A</td>
<td>(highly recommended)</td>
</tr>
<tr>
<td>Darifenacin</td>
<td>1</td>
<td>A</td>
<td>(highly recommended)</td>
</tr>
<tr>
<td>Solifenacin</td>
<td>1</td>
<td>A</td>
<td>(highly recommended)</td>
</tr>
<tr>
<td>Propantheline</td>
<td>2</td>
<td>B</td>
<td>(Recommended)</td>
</tr>
<tr>
<td>Atropine, hyoscyamine</td>
<td>3</td>
<td>C</td>
<td>(optional)</td>
</tr>
<tr>
<td>Mixed Action Drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxybutynin (muscle relaxant effect)</td>
<td>1</td>
<td>A</td>
<td>(highly recommended)</td>
</tr>
<tr>
<td>Propiverine (CC blocker)</td>
<td>1</td>
<td>A</td>
<td>(highly recommended)</td>
</tr>
<tr>
<td>Dicyclomine</td>
<td>3</td>
<td>C</td>
<td>(Optional)</td>
</tr>
<tr>
<td>Flavoxate</td>
<td>2</td>
<td>D</td>
<td>(possible)</td>
</tr>
</tbody>
</table>
Adverse events of antimuscarinics

- Due to inhibition of muscarinic receptors in organs other than bladder
- Dry mouth: most common
- Constipation: 2nd most common
- Blurred vision
- Cardiac effect: ↑HR, QT prolongation
- CNS effect: Dizziness, insomnia, cognitive impairment
Pharmacotherapy for OAB
**Novel β3 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

<table>
<thead>
<tr>
<th>toxin</th>
<th>Level of evidence</th>
<th>Grade of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botulinum toxin (neurogenic)</td>
<td>2</td>
<td>A</td>
</tr>
<tr>
<td>Botulinum toxin (idiopathic)</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>Capsaicin (neurogenic)</td>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>Resiniferatoxin (idiopathic)</td>
<td>2</td>
<td>C</td>
</tr>
</tbody>
</table>