THE ROLE OF OVERACTIVE BLADDER TREATMENT

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Ngompol dengan desakan berkemih
Sering berkemih
(kurang dari 2 jam)
Desakan yang kuat untuk berkemih
Toilet dependence
Overactive Bladder (OAB)
What is Overactive Bladder (OAB)

Overactive Bladder (OAB) is a “symptom syndrome suggestive of lower urinary tract dysfunction”

It is specifically defined as:

- Urgency, with or without urge incontinence,
- Usually with frequency and nocturia

Standardisation Subcommittee of the International Continence Society (ICS)

- OAB is used in the absence of proven infection or other obvious pathology
- Usually suggestive of detrusor overactivity, but can be due to other urethro-vesical dysfunction.

International Continence Society definitions

Urgency  A sudden compelling desire to pass urine, which is difficult to defer

Incontinence  Any involuntary leakage of urine

Frequency  Voiding too often – usually defined as 8 or more times in 24 hours

Nocturia  Waking more than once at night to void

# Impact of OAB

<table>
<thead>
<tr>
<th>Emotional effects</th>
<th>Disruption to activities of daily life</th>
<th>Economic</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ embarrassment</td>
<td>♫ proximity to toilets is important</td>
<td>♦ spend on incontinence pads</td>
</tr>
<tr>
<td>✓ shame</td>
<td>♫ reduced fluid intake</td>
<td>♦ loss of employment</td>
</tr>
<tr>
<td>✓ social withdrawal</td>
<td>♫ avoidance of sexual intimacy</td>
<td>♦ direct costs of laundry</td>
</tr>
<tr>
<td></td>
<td>♫ loss of independence</td>
<td></td>
</tr>
</tbody>
</table>
Normal detrusor function allows bladder filling with little or no change in pressure. No involuntary phasic contractions occur despite provocation.
Filling Cystometry (CMG) (Normal)
Involuntary Detrusor Contractions (Abnormal)

Namiki M, 1998
Detrusor overactivity is a urodynamic observation characterised by involuntary detrusor contractions during the filling phase which may be spontaneous or provoked.

1. Neurogenic detrusor overactivity
   - When there is a relevant neurological condition
   - This term replaces the term “detrusor hyperreflexia”

2. Idiopathic detrusor overactivity
   - When there is no defined cause → Non-neurogenic
   - This term replaces the term “detrusor instability”

Unstable detrusor (what is called Unstable bladder, =Detrusor instability) in the previous version (1989) → Deleted

Possible neurogenic causes of incontinence

- Stroke
- Dementia
- Tumour
- Trauma
- Multiple sclerosis
- Parkinson’s disease
- Stroke
- Multiple sclerosis
- Childbirth
- Straining at stool
- Diabetes
- Pelvic surgery
- Spinal injury
- Tumour
- Spina bifida
- S2
- S3
- S4

Diagram showing the brain, spinal cord, and bladder with pathways indicating neurogenic causes of incontinence.
The unstable bladder

Failure of inhibition of detrusor contraction

Sensation of urgency

Sensation relayed to brain

Failure of inhibition

Reflex arc completed

Bladder contracts involuntarily
OAB is Nearly as Common as Arthritis and Sinusitis

Overall, 16.5% of the population aged > 18 years (~ 33 million people) had symptoms of OAB.

Prevalence of OAB increases with age.

Stewart W et al World J Urol. 2002 Available at http://link.springer.de/link/service/journale/00345

*N=5,204

*>micturitions per day*
Overall, 16.5% of the population aged > 40 years in 6 European countries have symptoms of OAB.

Prevalence of OAB increases with age.

* >8 micturitions per day or nocturia 2x

Milson I et al BJU Int. 2001;87:760-766
53% of Asian Women Have Symptoms of OAB

- Urgency: 65%
- Frequency: 55%
- Incontinence: 21%
- Percent Seeking Treatment: 21%

OAB is undertreated

Questionnaire survey of 5,502 women from 11 countries in Asia

Urgency and frequency are the most common LUTS

Storage Symptoms and Incontinence

In a recent US survey (n = 5204), 16.5% of individuals in the general population met the criteria for OAB.

SUI: stress urinary incontinence
UUI: urge urinary incontinence
Mixed SUI/UUI (2.7%)
"OAB dry" urgency frequency nocturia (10.3%)
"OAB wet" (6.1%)

Overactive bladder

Frequency

Urgency

Urge incontinence

SYMPTOM OVERACTIVE BLADDER
DIAGNOSTIC OVERACTIVE BLADDER (OAB)

HISTORY

PHYSICAL EXAMINATION

LABORATORY TEST

URINARY DIARY

URODYNAMICS
1. LABORATORY TESTS

- Urinalysis
  - to rule out hematuria, pyuria, bacteriuria, glucosuria, proteinuria

- Blood work as appropriate
  - glucose
  - prostate specific antigen
  - others
# DIAGNOSTIC INCONTINENCE URINE

## 1. URINARY DIARY

Your Daily Bladder Diary

This diary will help you and your healthcare team. Bladder diaries help show the causes of bladder control trouble. The “sample” line (below) will show you how to use the diary.

<table>
<thead>
<tr>
<th>Time</th>
<th>Drinks</th>
<th>Urination</th>
<th>Accidental Leaks</th>
<th>Did you feel a strong urge to go?</th>
<th>What were you doing at the time?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sneezing, exercising, having sex, lifting, etc.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample</td>
<td>coffee</td>
<td>2 cups</td>
<td>12</td>
<td>large</td>
<td>large</td>
</tr>
<tr>
<td>6–7 AM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7–8 AM</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>8–9 AM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–10 AM</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>10–11 AM</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>11–12 PM</td>
<td></td>
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</tr>
</tbody>
</table>

Your name: J. Doe

Date: March 31, 2003
### CONTOH DAFTAR HARIAN BERKEMIH

<table>
<thead>
<tr>
<th>Interval waktu</th>
<th>Buang air kecil Biasa</th>
<th>Mengompol</th>
<th>Keinginan buang air kecil</th>
<th>Keadaan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tengah malam –1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1.00-2.00</td>
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<td>2.00-3.00</td>
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<td>3.00-4.00</td>
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<td>4.00-5.00</td>
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<tr>
<td>5.00-6.00</td>
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<td>6.00-7.00</td>
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<td>7.00-8.00</td>
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<td>8.00-9.00</td>
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<tr>
<td>9.00-10.00</td>
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</tr>
</tbody>
</table>

**KARTU CATATAN BUANG AIR KECIL**

<table>
<thead>
<tr>
<th>Tgl</th>
<th>y</th>
<th>y</th>
<th>y</th>
<th>y</th>
<th>m</th>
<th>m</th>
<th>d</th>
<th>d</th>
</tr>
</thead>
</table>

**Hari ke-1**
OVERACTIVE BLADDER TREATMENT

Conservative

- Bladder training
- Pharmacotherapy
Current approaches to OAB treatment

The challenge is to eliminate bladder overactivity without interfering with the function of other organ systems and without disturbing normal micturition

<table>
<thead>
<tr>
<th>Drugs licensed for OAB symptoms</th>
<th>Antimuscarinics are currently first-line therapy for OAB (eg tolterodine, oxybutynin [also has antispasmodic action], trospium, propiverine)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Antispasmodics (eg flavoxate, oxybutynin [also has antimuscarinic action])</td>
</tr>
</tbody>
</table>
| Other drugs used off-licence for OAB symptoms | Alpha blockers (eg doxazosin)  
Beta agonists (eg tarbutaline)  
Antidepressants (eg imipramine)  
Prostaglandin synthesis inhibitors (eg indomethacin)  
Vasopressin analogues (eg desmopressin)  
Miscellaneous (eg baclofen) |
| Non-pharmacological methods | Bladder retraining  
Pelvic floor exercises |

Garely AD and Burrows LJ Expert Opin Pharmacother 2002; 3(7):827-33
Antimuscarinic agents are the mainstay for treating OAB.

OAB symptoms are relieved by:

- inhibition of involuntary bladder contractions
- increased bladder capacity

Treatment can be limited by side effects such as dry mouth, GI effects (eg, constipation),...
Antimuscarinic drugs

- Mainstay of treatment for OAB
- Include:
  - Oxybutynin
  - Tolterodine
  - Flavoxate
  - Propiverine
  - Trospium
- Exerts bladder relaxation through antimuscarinic activity
- Also known as anticholinergics
Muscarinic Receptors

Five pharmacologically defined receptors, $M_1 - M_5$
Sigala et al 2002

Predominance of $M_2$ and $M_3$ receptors Yamaguchi et al 1996, Sigala et al 2002

$M_2$ receptors predominance 3:1 over $M_3$ receptors

Muscarinic receptors found

- Urotelial cells
- Suburotelial nerves
- Interstitial cells
- Chess-Williams 2002, Gillespie et al 2003
Lack of bladder selectivity results in anticholinergic adverse events in other organs:

- Salivary glands: dry mouth
- GI tract: constipation, nausea and vomiting, diarrhoea
- Eyes: blurred vision
- CNS: drowsiness, headache
- Heart: palpitations
- Skin: dryness
MUSCARINIC RECEPTOR DISTRIBUTION

- Iris/ciliary body —— Blurred vision
- Lacrimal gland —— Dry eyes
- Salivary glands —— Dry mouth
- Heart —— Tachycardia
- Stomach and esophagus —— Dyspepsia
- Colon —— Constipation
- Bladder (detrusor muscle)

Oxybutynin

- Tertiary amine that undergoes considerable first-pass metabolism
- Potent muscarinic receptor antagonist with some degree of selectivity for $M_3$, $M_4$, and $M_1$ receptors
- Local anesthetic as well as smooth muscle relaxant effects at doses higher than those used in clinical practice
- Lower doses used to improve tolerability profile

Tolterodine

Developed specifically for overactive bladder

Muscarinic receptor antagonist nonselective for the \( M_1 \) to \( M_5 \) receptors

Organ selective for bladder over salivary glands

Clinically proven to have fewer side effects than oxybutynin

Summary

1. Overactive Bladder (OAB) is a “symptom syndrome suggestive of lower urinary tract dysfunction”. It is specifically defined as Urgency, with or without urge incontinence, Usually with frequency and nocturia

1. Overactive Bladder syndrome (OAB) is highly prevalent condition that adversely affects the quality of life (QOL) of many individualy

1. Current approaches to OAB treatment, is Antimuscarinics (eg tolterodine, oxybutynin, trospium, propiverine) and Non-pharmacological methods (Bladder retraining Pelvic floor exercises)

THAK YOOU