Overactive Bladder
Drugs, Botox or Neurostimulation?
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The Annual Women’s Health Update

Definition
- International Continence Society (ICS) definition of overactive bladder
- Urgency with or without urge incontinence, usually with increased frequency and nocturia
  - Frequency > 8 times in 24 hours
  - Nocturia > 1 time per night
  - Urge incontinence
  - Distinguish from stress or overflow

Prevalence
- Prevalence 12-17%
- Increases with age
  - 22% men and women 70-74yo
  - 42% men and 31% women >75yo

Impact
- Lower work productivity
- Travel and activity restriction
- Sexual dysfunction
- Depression
- Interrupted sleep
- Falls
- Fractures

Table 1. Definitions of overactive bladder syndrome

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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</thead>
<tbody>
<tr>
<td>Detrusor overactivity</td>
<td>A dynamic overactivity characterized by involuntary spontaneous or provoked detrusor contractions during the filling phase</td>
</tr>
<tr>
<td>Nocturnal polyuria</td>
<td>An excess (&gt;25-50%) proportion of urine excruted at night</td>
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<tr>
<td>Polyuria</td>
<td>&gt;40 mL/night body weight during 24 hours</td>
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<tr>
<td>Posterior residual volume</td>
<td>The volume of fluid remain in the bladder at the completion of miction</td>
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<tr>
<td>Urgency</td>
<td>A sudden, compelling desire to void that is difficult to delay</td>
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<tr>
<td>Urinary frequency</td>
<td>&lt;8 mictions/24 hours</td>
</tr>
<tr>
<td>Urgency urinary incontinence</td>
<td>Involuntary loss of urine associated with urgency</td>
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Overactive Bladder Syndrome: Management and Treatment options.

http://classes.midlandstech.edu/carterp/Courses/bio211/chap25/chap25.htm
Pathophysiology

- Detrusor muscle overactivity
  - Upregulation of muscarinic receptors M2, M3
  - Increased release of stretch-related acetylcholine
  - Supersensitivity to acetylcholine
  - Ischaemia, nerve injury, smooth muscle damage → DHIC


Pathophysiology

- Bladder outlet obstruction or inflammation
  - Increased nerve growth factor and neuronal enlargement
  - Altered smooth muscle structure and function
  - Enhanced spinal micturition reflex


Pathophysiology

- Neurogenic bladder
  - Damage cerebral inhibitory centre
  - Alter dopamine-glutamatergic mechanisms
  - Loss of inhibitory substantia nigra cells in basal ganglia
  - Increased mechanosensitivity of capsaicin-sensitive C fibers


Differentials

- UTI
- Medications / caffeine
- Polydipsia / Nocturnal polyuria
- Constipation
- Prolapse / Vaginitis
- BPH / Stricture
- Surgery / radiotherapy
- Pelvic mass
- Diverticulitis
- Endometriosis
- Diabetes
- Neurogenic bladder
- Malignancy
- Bladder stones
- Painful bladder syndrome

Assessment

<table>
<thead>
<tr>
<th>Table 3. Investigations for overactive bladder syndrome</th>
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<tbody>
<tr>
<td>Initial investigations:</td>
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<tr>
<td>- Ultrasound to exclude infection, haematuria and glycosuria</td>
</tr>
<tr>
<td>- Urinary tract ultrasound and measurement of postvoid residual volume</td>
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<tr>
<td>- Pregancy/Volume of Shift for at least 3 days</td>
</tr>
<tr>
<td>- Bladder diary for a minimum of 3 days</td>
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<tr>
<td>Secondary investigations:</td>
</tr>
<tr>
<td>- Urine cytology</td>
</tr>
<tr>
<td>- Urine bacterial culture</td>
</tr>
<tr>
<td>- Proteinuria</td>
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<tr>
<td>- Imaging of upper urinary tract or spine</td>
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</tbody>
</table>


Behavoural therapy

- Response rate
  - Initial 85%
  - 3 year 48%
- Reduction in number of incontinence episodes
  - Behavioral therapy 80.7%
  - Drug 68.5%
  - Placebo 39.4%

Behavioural therapy

- Dietary strategies
  - Caffeine, alcohol, irritants, avoid constipation
- Bladder retraining
  - Timed voids, deferral strategies, voids 3-4 hourly
- Fluid management
  - Adequate hydration 1.5L per day
- Pelvic floor muscle exercises

Pharmacotherapy

- Alpha blockers
- Anticholinergics – M3 antagonists
  - Non-selective – Oxybutynin
  - Selective M3 – Solifenacin
- Tricyclic antidepressants
  - Amitriptyline – not first-line
- Sympathomimetics – B3 agonists
  - Mirabegron

Novel Therapy

- Botulinum toxin A (Botox)
- Posterior tibial nerve stimulation (PTNS)
- Sacral nerve modulation (SNM)

Botulinum Toxin A

- PBS listing 2012, 2014
- Anticholinergics ineffective
- >/= 14 UUI episodes/week
- Achieve >50% reduction in UUI episodes
- Willing to self-catheterise
- 100 IU DO, 200 IU NDO

Botulinum Toxin A

- Onset 1-2/52, lasts 9-12/12
- Urinary retention risk
  - 36 of 552 patients (6.5%)
  - CISC required for <6 weeks in >50%
  - Higher risk with DM
- 60-65% improved

PTNS

- FDA approved 2000
- Needle placement
- Weekly stimulation x12
- Monthly maintenance
- RCT PTNS vs sham
  - 54.5% vs 20.9%
- RCT PTNS vs tolterodine
  - 79.5% vs 54.8%


**SNM**

- FDA approved 1997
- S3 nerve foramen
- Implant permanent lead with temporary extension wire for trial phase 1-2 weeks
- Implant pulse generator and battery if trial effective

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**SNM**

- MRI contraindicated
- Response rate 33-88%
- High correlation between 1 and 5 year success rates – 84%

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**SNM**

- 3 year study (Siegel)
  - 59% UUI patients significantly improved
  - 46% UUI patients completely dry
  - 56% urgency-frequency patients had >50% reduction in frequency
  - 70% retention patients had >50% reduction in catheter volume per catheterisation
- 5 year study (van Kerrebroeck)
  - 68% UUI patients, 56% urgency-frequency, 71% retention patients had >50% improvement from baseline

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**SNM**

- Complication risks
  - Pain at implant site
  - Lead migration
  - Wound complication
  - Bowel dysfunction
  - Generator problem
  - Infection
  - Battery life 5-7 years

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**Take Home Messages**

- Recognise and exclude differentials
- History and examination important
- Initiate behavioural therapy
- Drugs – anticholinergics, B3 agonists
- Adjuncts – urodynamic studies, cystoscopy
- Botox vs sacral neuromodulation