Diagnosis and treatment of BPH with idiopathic OAB

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- BPH
- Idiopathic OAB, not neurogenic
- Mechanism between them and recent treatment
Male and female LUTS

- Male and female
  - with urinary urgency, frequency and nocturia
    - antimuscarinic for female OAB
    - alpha blocker for male BPH

- Initial empiric diagnosis of BPH may be correct, in male
- But, not all cases of male LUTS equate to BPH
Shift in our understanding of LUTS in males

- 43% of older men with LUTS
  - suffer from DO, Not BOO


- Only 50% of men with preoperative DO
  - resolution of DO after outlet reduction surgery

paradigm shift for patient care

- men under 50 with LUTS, do not have BPH
  - symptoms are to another cause


- Regardless of the underlying cause,
  - if symptoms are not resolved as a result of prescribed therapy,
  - suffer needlessly or even undergo unnecessary prostate surgery
Definition of BPH

- **BPH**
  - Microscopic, prostatic hyperplasia,
  - benign proliferation of the prostatic stroma and epithelium

- **BPE**
  - enlargement of the prostate gland
  - diagnosed with clinical or ultrasound examinations

- **BOO**
  - Enlargement of the prostate with LUTS

Pathophysiology of LUTS and OAB

- LUTS, multifactorial
- OAB, a symptom complex, unknown aetiology
  - voiding symptoms of BPH
    - by prostatic enlargement
  - storage symptoms of BPH
    - by remains controversial
Identifying LUTS

- Screening tools
  - AUA symptom score, IPSS sheet

- History, physical and laboratory exam
  - identify other causes of the LUTS, reversible issues or comorbidities
  - medications, family history or prior surgeries

- Key to the proper evaluation of LUTS
  - voiding volume
    - voids small amounts, frequently
      - urologic function is more likely to be abnormal
    - voids normal amounts, frequently
      - Medical cause is more likely than a urologic cause
## LUTS; differential diagnosis and other causes

<table>
<thead>
<tr>
<th>Differential diagnosis</th>
<th>Medications</th>
<th>Other risk factors</th>
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<tbody>
<tr>
<td><strong>Consider</strong></td>
<td>May cause or exacerbate LUTS:</td>
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<tr>
<td>Bladder cancer</td>
<td>Tricyclic antidepressants</td>
<td>Obesity</td>
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<tr>
<td>Prostate cancer</td>
<td>Anticholinergic agents</td>
<td>Cigarette smoking</td>
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<tr>
<td>Prostatitis</td>
<td>Diuretics</td>
<td>Regular alcohol consumption</td>
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<tr>
<td>Bladder stones</td>
<td>Narcotics</td>
<td>Elevated blood pressure</td>
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<tr>
<td>Interstitial cystitis</td>
<td>First-generation antihistamines</td>
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<tr>
<td>Radiation cystitis</td>
<td>Decongestants</td>
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<tr>
<td>Urinary tract infection</td>
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<tr>
<td>Diabetes mellitus</td>
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<tr>
<td>Parkinson’s disease</td>
<td></td>
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<tr>
<td>Primary bladder neck hypertrophy</td>
<td></td>
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<tr>
<td>CHF</td>
<td></td>
<td></td>
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<tr>
<td>Multiple sclerosis</td>
<td></td>
<td>2007;61:1535-46</td>
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<tr>
<td>Nocturnal polyuria</td>
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<tr>
<td>CHF, congestive heart failure.</td>
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</table>
Focused physical examination

- Abdominal examination for tenderness, masses or an overdistended bladder
- Neurological examination with mental and ambulatory status and neuromuscular function

- Genitalial examination, meatus and testes
- DRE, rectal tone and prostate size, shape, consistency

Labaratory test

- Urinalysis by dipstick or microscopic
  - strongly recommended for blood, protein, glucose or any signs of infection
- PSA
- Blood sugar, either random or fasting
  - not included in AUA guidelines
- Urine cytology, optional
  - Haematuria with storage symptoms or at risk for bladder cancer
- Serum creatinine
  - no longer indicated

Is it OAB or BPH?

- Differentiate between storage and voiding issues

- Cannot make a definitive diagnosis of obstruction without advanced testing, such as urodynamics

- Storage issues affect the bladder
  - consider OAB

- Voiding issues relate to obstruction and urine expulsion
  - Focused on prostate

- Many patients exhibit both OAB and BPH
Provisional BPH and Provisional OAB

- Empiric medical therapy
- Behavioural modification

- Pressure-flow studies, PVR urine
  - Not necessary prior to medical therapy by AUA guidelines

- Bothersome LUTS
- Enlarged prostate (> 30 ml)
- PSA > 1.4 ng/ml
  - increased risk of acute urinary retention
  - dual therapy with an alpha blocker and a 5ARI 24,37


diagnosis of OAB as the cause of the LUTS

- Treatment for BPH proves ineffective
  - add treatment for OAB
  - risk of retention

- Small repeat the PVR (50 ml)
- Good flow rate (8 ml/s)
  - diagnosis of OAB as the cause of the LUTS
Treatment of OAB: behavioural and pharmacologic therapy

- Behavioural therapy
  - patient education
  - bladder retraining, urge suppression techniques
  - dietary alterations
  - changing the timing of medications (e.g. diuretics)
  - encouraging exercise and weight loss

- Pharmacologic therapy
  - antimuscarinic therapy
  - darifenacin, oxybutynin, solifenacin, tolterodine
trospium, transdermal form of oxybutynin

- Combination therapy
Place of anti-diuretic hormone for nocturia due to BPH

- Nocturia
  - polyuria, diabetes mellitus, neurological bladder, cardiac failure, polydipsia, reduced bladder capacity, insomnia or psychiatric problems

- Act on BOO, on bladder sensitivity by anti-cholinergic drugs, on sleepiness by hypnotic drugs, on urinary volume by anti-diuretics

- Desmopressin
  - number of nocturnal voids 3 -> 1.7 (43%)
  - duration of the first sleep period 61-> 269 min (59%)
  - total volume of urination 1.5-> 0.9 l

OAB with BPH

- 40–70% of BOO
  - OAB due to detrusor overactivity
    
    Hyman J Urol 2001;166(2):550–552

- ischemia
- cholinergic detrusor denervation
- increased detrusor collagen content
- Changes in the electrical properties of detrusor smooth muscle cells

Availables in OAB with BPH

- **Alpha-blockers**
  - promote relaxation of the bladder neck and prostate smooth muscle
  - limited success in OAB related symptoms

  Lee JY et al. BJU Int 2004; 94(6):817–820

- **5-alpha-reductase inhibitors**
  - Epithelial apoptosis and atrophy
  - reduce prostate size
  - few effects to attenuate OAB symptoms

  Chapple CR. BJU Int 2004;94(5):738–744
The paradox: anti-cholinergic drugs for BPH!

- Muscarinic receptor antagonists in BPH
  - a precipitated factor of urinary retention

- Not routine use of anti-cholinergic agents as primary therapy for BPH/LUTS or combined with alpha-blockers

Chapple CR. BJU Int 2004;94(5):738–744

- OAB, failed in first line of treatment with alpha blocker,
  - anti-cholinergic drugs proposed
  - low risk of acute urinary retention Kaplan et al. reported

Inflammation and BPH

- MTOPS study
  - Inflammation could be a risk factor of BPH progression

- BPH with inflammation
  - older (64 vs. 62 years)
  - Higher PSA level (3.3 vs. 2.5 ng/ml)
  - higher prostatic volume (41 vs. 36 ml)
  - fourfold increased risk of AUR (2.4 vs. 0.6%)
  - risk of progression (21% Vs 13%)

- Inflammation plays a significant role in BPH symptoms

Roehrborn et al. J Urol 2005; AUA #1277
Diclofenac, ibuprofene, ketoprofen, loxoprofen,
- aspirin, cox-2 inhibitor

Mechanisms of action
- diuresis reduction by renal blood flow reduction
- sedative effect on the hypersensitivity of the bladder
- neuronal conduction change to the bladder sphincter
- improvement of the sleep cycles

Loxoprofen
- LUTS resistant to a first-line treatment
- improvement of the nocturia, 74%

Botulinum toxin and BPH; neurogenic bladder

- Bladder sphincter dyssynergia, non relaxing uretral sphincter,
  - cauda equina lesion or peripheral neuropathy
- Transperineal, intraurethral injection
- BT A (50 IU and 100 IU) general anesthesia
- Total success rate; 84.5%
- Indwelling catheters or CIC discontinue (87%)

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<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After treatment</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Mean maximum voiding pr (cm H$_2$O)</td>
<td>62 ± 40</td>
<td>43 ± 31</td>
<td>0.000</td>
</tr>
<tr>
<td>Maximal urethral closure pr (cm H$_2$O)</td>
<td>65 ± 36</td>
<td>48 ± 31</td>
<td>0.000</td>
</tr>
<tr>
<td>Post-void residual (ml)</td>
<td>1226 ± 165</td>
<td>89 ± 112</td>
<td>0.000</td>
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Botulinum toxin ; LUTS with BPH

- Randomized, placebo-controlled study
- Transperineal, no local anesthesia
- 200 IU of BT (Botox)
- Medium follow-up, 20 months
- Peak urinary flow 8 ->15 ml/s

Decline of value from baseline after 1 month treatment

<table>
<thead>
<tr>
<th>Metric</th>
<th>Decline</th>
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<tbody>
<tr>
<td>AUA SS</td>
<td>54%</td>
</tr>
<tr>
<td>PSA</td>
<td>42%</td>
</tr>
<tr>
<td>Post void residual</td>
<td>60%</td>
</tr>
<tr>
<td>Prostate volume</td>
<td>54%</td>
</tr>
</tbody>
</table>

Botulinum toxin and BPH ; urinary retention

- Symptomatic BPH with urinary retention and PVR
- Mean age, 75: prostatic volume, > 30 g
- Transurethrally on ten sites using rigid cystoscopy
- 200 IU of BT (Botox), general anaesthesia
- Excellent results, 80% (6 months)
- No side effect

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<thead>
<tr>
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<th>After 6 month treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVR (ml)</td>
<td>243</td>
<td>37</td>
</tr>
<tr>
<td>Peak urinary flow (ml/sec)</td>
<td>7.6</td>
<td>11.6</td>
</tr>
<tr>
<td>Prostatic volume (gm)</td>
<td>65</td>
<td>49</td>
</tr>
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</table>

Botulinum toxin and BPH; transrectal application

- 2005 AUA congress
- Multicentric study
- Transrectally inject using ultrasound scan
- 100 IU, 200 IU
- Without anaesthesia

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<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After 3month treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPSS</td>
<td>21</td>
<td>11</td>
</tr>
<tr>
<td>Peak urinary flow (ml/sec)</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Complication</td>
<td>One AUR</td>
<td>No fecal and urinary incontinence</td>
</tr>
</tbody>
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Botulinum toxin and BPH; prostate volume

- Inclusion
  - Prostate volume, 80 cc
  - Peak urinary flow < 10 ml/s
  - Medium age, 69
- 150 IU BT
- Follow up to 6 months

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<tr>
<td>IPSS</td>
<td>24</td>
<td>9</td>
</tr>
<tr>
<td>Post-void residual (ml)</td>
<td>295</td>
<td>85</td>
</tr>
<tr>
<td>Peak flow rate (ml/sec)</td>
<td>8.2</td>
<td>18.1</td>
</tr>
<tr>
<td>Prostate volume (gm)</td>
<td>106</td>
<td>53</td>
</tr>
</tbody>
</table>

Conclusion

- Usual treatment of BPH
  - alpha-blockers
  - 5-alpha-reductase inhibitors
  - phytotherapy

- New therapeutic possibilities
  - anti-diuretics
  - anti-cholinergic drugs
  - treatments in the decision, not clearly defined yet

- Should we use them as the second line or directly as a first-line treatment?
Conclusion

- Inflammation plays an important role in BPH
  - vary therapeutic efficiency
  - lack of clinical data

- Botulnum toxin
  - important tool of the neuro-urology management
  - hopeful treatment of BPH with real clinical improvements