Association of BPH with OAB: 
The Plumbing or the Pump?

Ryan P. Terlecki, MD FACS
Associate Professor of Urology
Director, Men’s Health Clinic
Director, GURS Fellowship in Reconstructive Urology, Prosthetic Urology, and Infertility
Wake Forest Baptist Health
Disclosure of Financial Relationships

Ryan P Terlecki, MD, FACS

Has disclosed relationships with an entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients.

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**Research Grants/Contracts**
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Allergan
Department of Defense
Objectives (in 20 minutes)

- Summarize data on relationship between OAB, urodynamic parameters, and voiding symptomatology in men with LUTS
- Review outcomes data on concomitant pharmacological treatment of OAB and BPE (‘H’ is histological)
- Discuss rates of persistent dysfunction after surgical relief of BOO
Audience Response Question 1
Audience Response Question 2
Overactive Bladder (OAB)

- Urgency +/- UUI, usu w/frequency and nocturia in absence of UTI or obvious pathology (clear overlap with male LUTS in many cases)

- OAB affects about 12-14% men and women >40y (in 52-80% of men with BOO)

- Men more likely to have urgency, frequency, nocturia (women more UUI)
Overactive Bladder (OAB)

- LUTS: Storage, Voiding, Post-Void
- Storage: Frequency, Urgency, Nocturia, UI (seen in 51.3% men, 59.2% women)
- Voiding: Slow FOS, Split stream, Intermittency, Hesitancy, Straining (25.7% men, 19.5% women)
- Post-micturition: PVD (16.9% men, 14.2% women)

Moss et al. Curr Urol Rep 2017. 18:1
Male LUTS

- Male LUTS involve **detrusor and outlet**
- BPE +/- BPO managed w/alpha blockers/5ARIs still leaves some men w/bothersome LUTS
- OAB meds **used less in men** despite similar prevalence of storage LUTS as women
- Numerous PCRCTs show antimuscarinics and beta-3 agonists, alone or in combo, improve storage symptoms, **without negative impact** on Qm, PVR, or incidence of retention

Moss et al. Curr Urol Rep 2017. 18:1
Male LUTS

- LUTS/BPH both increase with age

- Voiding symptoms may be more common, Storage symptoms more bothersome/embarrassing

- Men often first receive alpha blockers to treat storage symptoms (i.e., urgency) due to perception that BPE is cause, but storage LUTS remain bothersome in 2/3 men

Lee et al. BJU Int 2004; 94:817-20
Obstructive Symptoms Are Most Prevalent in BOO/BPH

International Continence Society – Benign Prostatic Hyperplasia Study

- Reduced stream
- Terminal dribble
- Hesitancy
- Intermittency

Storage Symptoms Are Most Bothersome in BOO/BPH

International Continence Society – Benign Prostatic Hyperplasia Study

- Nocturia
- Frequency
- Urge incontinence
- Miscellaneous UI
- Nocturnal incontinence

Percent of Men (n = 662)

Prevalence
Bothersomeness felt

Urodynamics

- Not routine in male LUTS; no preop RCT
- Results *poorly correlate* with clinical OAB
- Shows DO in 50% of OAB cases (more when UUI present)
- Severe urgency appears to be a negative predictor for obstruction
- UDS appears indicated in setting of UUI, extreme ages (>80, <40), or possible neurological disease

Cornu and Grise. Curr Opin Urol 2016. 26:17-21
After TURP

- Old data suggests 20% persistence of OAB symptoms

- Recent data on 1y postop outcomes suggest worse outcomes in older patients, those with capacity <250 cc (>83% with persistent DO symptoms at 1 year)

- GOLIATH study showed similar improvement in OAB symptoms between PVP and TURP

Thomas et al. Eur Urol 2015
Pathophysiology

- Most data from animal studies

- Obstruction can lead to overactivity and/or decreased compliance

- Initial detrusor hypertrophy (smooth muscle)

- Later increases in ECM (collagen)

Li et al. BJU Int 2008; 101:1588-94
Kim et al. Can Urol Assoc J 2013. 7:E268-274
Pathophysiology

- Decrease in calcium-activated potassium channels (big potassium; BK)
- Some data suggests ischemic-induced changes in response to neurotransmitters
- Nitric oxide pathway also implicated
- Bladder histology compared between patients undergoing TURP vs controls
  - Significantly increased Collagen I and III
  - Significantly increased M2 and M3 (more so in patients with persistent DO)

Barbosa et al. Urology 2017. 106:167-72
Why is this important?

- Only 50% of men with preop DO have resolution after TURP (20-30% after simple prostatectomy)

Traditional medical therapy (BPE)

- Alpha blockers (tone)
- 5ARIs (size)
- PDE5i (voiding LUTS, not well studied for storage LUTS)
- MTOPS didn’t separate AUASS improvement by voiding vs storage
Medical therapy for OAB

- Antimuscarinics
- Beta-3 agonists
- Botox (hybrid medicosurgical)
Antimuscarinic monotherapy for BOO

- Blasphemous in past
- Tim Boone’s $20 bill
- Tolterodine in UDS-proven BOO didn’t significantly alter Qm or voiding pressure compared to placebo; Volume to first contraction and capacity significantly improved
- PVR went up (25 cc vs 0 cc); not meaningful. Only retention case was in placebo arm.

Herschorn et al. Urology 2010. 75:1149-55
Tolterodine Did Not Increase the Incidence of Urinary Retention in Men With OAB and BOO

<table>
<thead>
<tr>
<th>Urinary Symptom Adverse Events</th>
<th>Placebo (n = 72)</th>
<th>Tolterodine (n = 149)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Micturition disorder</td>
<td>2</td>
<td>2.8</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>3</td>
<td>4.2</td>
</tr>
<tr>
<td>Dysuria</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>Micturition frequency</td>
<td>2</td>
<td>2.8</td>
</tr>
<tr>
<td>Micturition urgency</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>Strangury</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>Bladder discomfort</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Urethral disorder</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>2</td>
<td>2.8</td>
</tr>
<tr>
<td>Overall</td>
<td>9</td>
<td>12.5</td>
</tr>
</tbody>
</table>

OAB/BOO: Abrams et al

Antimuscarinic monotherapy for BOO

- Risk of retention from ACs in men is < 1%
- Most commonly prescribed drug is oxybutynin, likely due to cost/coverage

Kaplan et al. BJU Int 2008;102:1133-39
Beta-3 agonist monotherapy

- Nitti looked at studies showing improvement but not stratified by gender
- He performed a PCRCT in 200 men looking at UDS, and non-inferior to placebo, but storage LUTS not evaluated (certainly not a home-run treatment yet)
- Recent analysis of 5 phase III studies showed that mirabegron 50 mg was better than placebo for frequency (BEYOND trial). Similar improvement in urgency, frequency, and UUI as solifenacin 5 mg.

Antimuscarinics + Alpha Blockers

- Several published studies looking at adding tolterodine to alpha blocker

- Improvements in QOL (not seen with tamsulosin alone), Qm, voiding pressures, and AUASS reported with little to no incidence of retention

- Similar findings with tamsulosin in combo with solifenacin or darifenacin

Lee et al. BJU Int. 2004; 94:817-20
Drake et al. BJU Int 2016; 117:165-72
Tolterodine and Tamsulosin Combination Therapy in Men With BOO: Effects on QoL

OAB/BOO: Athanasopoulos et al

Mean Score (QoL9 UROLIFE)

Baseline

12 Weeks

Tamsulosin
(n = 25)

Tamsulosin + tolterodine
(n = 25)

P = 0.0003

P = NS

542.2

548.2

525.0

628.4

460

480

500

520

540

560

580

600

620

640

Improved QoL

Meta-analyses (combo therapy)

- Hao et al reviewed 18 RCTs (1978 men alpha blocker only, 2106 combo w/antimuscarinic). **Combo tx** noted significant improvement in storage IPSS, QoL score, voids/24h, and urgency episodes/24h. No sig diff in Qm, total IPSS, and voiding IPSS

- Gong et al. meta-analysis of studies comparing tamsulosin alone vs combo with solifenacin (7 studies, 3063 men). **Combo** w/sig improvement in storage IPSS, QoL, voids/24h, and urgency episodes/24h. Similar AEs, rare AUR, and no clinically significant change in Qm
Who is a good candidate?

- Some suggest those with good Qm, predominantly storage LUTS, PVR $\leq 50$ cc
- Caution w/antimuscarinics in elderly; beta-3 may be better but more data needed (still not recommended with severe uncontrolled HTN)
- Other options
  - Botox
  - Neuromodulation (results somewhat disappointing in men)
  - NSAIDs/Analgesics (select cases)
Audience Response Question 1
Audience Response Question 2
Conclusions

- Treat most bothersome symptoms first

- Alpha blockers are good first choice for voiding symptoms, but antimuscarinics should be considered when storage symptoms predominate (EAU Guidelines 2013)

- Both mono and combo tx with antimuscarinics are accepted options in men with storage LUTS

Oelke et al. Eur Urol 2013; 64:118-140
Conclusions

- AE rate (esp AUR) of using anticholinergics in BPH is low and there is minimal negative impact on UDS parameters (PVR, Qm)

- More research is need on beta-3 agonists in men

- Don’t be afraid to try and take men off alpha blockers and 5ARIs if eligible (tx polypharmacy)