Medical Management of BPH

Stephen Kraus MD, MSCI, FACS
Professor and Vice Chairman
Department of Urology
Goals and Objectives

- Is the disease process different in elderly?
  - Different pathology?
  - More severe?
- Is treatment different in the elderly?
  - Not respond to treatment as well?
  - Not tolerate treatment as well?
  - Is treatment different due to medical co-morbidities and/or other concomitant treatments that patient is on?
Goals and Objectives
What is BPH

- Technically, a histological diagnosis
- No bearing on patient symptoms or impact
- Incidence is age dependent
  - Typically NOT a young man’s disease
Alphabet Soup

- BPH
  - Histologic BPH
  - Macroscopic glandular enlargement
  - BPH related symptoms
- BPE
- BOO
- LUTS
- OAB
So what do we really mean when we say BPH?
<table>
<thead>
<tr>
<th>Storage</th>
<th>Voiding</th>
<th>Postmicturition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Hesitancy</td>
<td>Dribbling</td>
</tr>
<tr>
<td>Nocturia</td>
<td>Poor flow</td>
<td>Incomplete emptying</td>
</tr>
<tr>
<td>Urgency</td>
<td>Intermittency</td>
<td></td>
</tr>
<tr>
<td>Incontinence</td>
<td>Straining</td>
<td></td>
</tr>
</tbody>
</table>
## Male Lower Urinary Tract Symptoms (LUTS)

<table>
<thead>
<tr>
<th>Storage</th>
<th>Voiding</th>
<th>Postmicturition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Hesitancy</td>
<td>Dribbling</td>
</tr>
<tr>
<td>Nocturia</td>
<td>Poor flow</td>
<td>Incomplete emptying</td>
</tr>
<tr>
<td>Urgency</td>
<td>Intermittency</td>
<td></td>
</tr>
<tr>
<td>Incontinence</td>
<td>Straining</td>
<td></td>
</tr>
</tbody>
</table>

Obstructive
<table>
<thead>
<tr>
<th>Storage</th>
<th>Voiding</th>
<th>Postmicturition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Hesitancy</td>
<td>Dribbling</td>
</tr>
<tr>
<td>Nocturia</td>
<td>Poor flow</td>
<td>Incomplete emptying</td>
</tr>
<tr>
<td>Urgency</td>
<td>Intermittency</td>
<td></td>
</tr>
<tr>
<td>Incontinence</td>
<td>Straining</td>
<td></td>
</tr>
</tbody>
</table>

**Irritative**
Causes: **Lower Urinary Tract Symptoms**

- **Bladder outlet obstruction**
  - Benign prostatic enlargement
  - Prostate cancer
  - Urethral stricture

- **Bladder:**
  - Involuntary detrusor contraction (OAB)
  - Detrusor hypo- or areflexia
  - Intrinsic bladder wall disorder - poor ‘compliance’
  - Bacterial cystitis, Interstitial cystitis, Trigonitis
  - Bladder neoplasm
BPH

- First phase
  - Develop small hyperplastic nodules in peri-urethral area
  - Increase in number over years

- Second phase (typically >60 years old)
  - Dramatic and simultaneous increase in size of glandular nodules
  - Also with changes in stromal tissue
    » Resembles of developmental mesenchyme
  - Considered “distorted reawakening of embryonic process in adult life”

BPH

Causes and associations

- Age
- Systemic
  » Endocrine
  » Autonomic
  » Cardiovascular-Ex: prevalence/duration of HTN assoc with BPH
- Inflammatory
  » Neurogenic inflammation triggers prostatic inflammation
- Metabolic
  » Diabetes and metabolic syndrome
  » Obesity
  » BMI
- Erectile dysfunction
- Prostatitis

References:
McVary, BJU Int 2006;97(S2) 23-28
Parsons, J Clinical Endocrinology &Metabolism 91(7) 2562-68
Hammersten Blood Press 1999 8(1) 29-36
Male LUTS Increases with Age

Nordling, Exp Gerontol 2002;37(8–9):991–9;
Female LUTS Increases with Age

Nordling, Exp Gerontol 2002;37(8–9):991–9;
Age-related changes in prostate weight

Berry J Urology, 1984, 132(3) 474-9
Odds of Moderate/Severe Symptoms Increase with Prostate Size

- Community based study
- Odds for moderate or severe LUTS (age adjusted)
  - 1.2 x greater for prostates > 30 gm vs ≤ 30 gm
  - 3.0 x greater for prostates > 40 gm vs ≤ 40 gm
  - 3.5 x greater for prostates > 50 gm vs ≤ 50 gm

Girman, J Urol 1995: 153, 1510-15
BPH: Relationship Between Symptoms, Prostate Volume & Age

Prevalence of BPH

- 20% of men age 41-50
- 50% of men age 51-60
- 65% of men age 61-70
- 80% of men age 71-80
- 90% of men age 81-90

- 25-50% microscopic & macroscopic BPH will develop clinical BPH
- The prevalence of clinical BPH in men ages 55-74 years 5-30%

Berry J Urology, 1984, 132(3) 474-9
Prostate grows with age and time

Pressure on the urethra restricts urine flow
Bladder Neck

Proximal Prostatic Urethra
Components of Prostatic Enlargement: Epithelial & Stromal
31% of men with initial mild sx (IPSS<8) progressed to moderate (IPSS 8-18) or severe (IPSS 19-35) over 48 month
Potential Consequences of BPH

- Bothersome LUTS
- Urinary retention
- Urinary tract infection
- Renal impairment
- Bladder stones
- Bladder damage
  - Trabeculations
  - Diverticulum
- Incontinence
  - Overflow
  - OAB

Trabeculated Bladder
Risk of Acute Urinary Retention Related to Prostate Size


Risk of Urinary Retention &/or BPH Surgery Increases with Prostate Size

PLESS = Proscar Long-term Efficacy & Safety Study
Urology 53:473, 1999
BPH: Diagnosis and Treatment

- **Initial Evaluation**
  - History
  - PSA in selected patients
  - DRE and focused physical exam
  - Urinalysis

- **AUA/IPSS Symptom Index**
  - Assessment of Patient Bother

- **Presence of Refractory Retention or Any of the Following Clearly Related to BPH**
  - Persistent gross hematuria
  - Recurrent UTIs
  - Bladder stones
  - Renal insufficiency

- **Discussion of Treatment Options**

- **Mild Symptoms (AUA/IPSS ≤7) or No Bothersome Symptoms**
  - **Patient Chooses Noninvasive Therapy**
    - Watchful Waiting
    - Medical Therapy

- **Moderate/Severe Symptoms (AUA/IPSS ≥8)**
  - **Optional Diagnostic Tests**
    - Uroflow
    - Postvoid residual urine
  - **Patient Chooses Invasive Therapy**
    - Minimally Invasive Therapy
    - Surgery

- **Surgery**

DRE = digital rectal exam; IPSS = International Prostate Symptom Score; PSA = prostate specific antigen; UTI = urinary tract infection.

*Patients with a ≥10-year life expectancy for whom knowledge of the presence of prostate cancer would change management or patients for whom the PSA management may change the management of voiding symptoms.

Work-up

LUTS?

History:
AUA-SSI

Exam:
Abdomen (bladder, flanks, etc)
DRE (size, induration, nodules)

Labs:
UA, Urine C&S,
PSA
Creatinine

Other Testing:
Post-void residual
Uroflow
“Relax, Mr. Wilde, it's just a simple prostate examination!”
### AUA Symptom Score Index

- **7 questions**
  - Irritative
  - Obstructive
  - QOL

#### AUA SYMPTOM SCORE (AUASS)

<table>
<thead>
<tr>
<th>(Circle One Number on Each Line)</th>
<th>Not at All</th>
<th>Less Than 1 Time in 5</th>
<th>Less Than Half the Time</th>
<th>About Half the Time</th>
<th>More Than Half the Time</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past month or so, how often have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>During the past month or so, how often have you had to urinate again less than two hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>During the past month or so, how often have you found you stopped and started again several times when you urinated?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>During the past month or so, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>During the past month or so, how often have you had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>During the past month or so, how often have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Over the past month, how many times per night did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?</td>
<td>None</td>
<td>1 Time</td>
<td>2 Times</td>
<td>3 Times</td>
<td>4 Times</td>
<td>5 or More Times</td>
</tr>
</tbody>
</table>

Add the score for each number above and write the total in the space to the right.

TOTAL: ___________

**SYMPTOM SCORE:** 1-7 (Mild)  8-19 (Moderate)  20-35 (Severe)

#### QUALITY OF LIFE (QOL)

<table>
<thead>
<tr>
<th>Delighted</th>
<th>Pleased</th>
<th>Mostly Satisfied</th>
<th>Mixed</th>
<th>Mostly Dissatisfied</th>
<th>Unhappy</th>
<th>Terrible</th>
</tr>
</thead>
<tbody>
<tr>
<td>How would you feel if you had to live with your urinary condition the way it is now, no better, no worse, for the rest of your life?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
Uroflowmetry

A

![Graph A]

- \( Q_{\text{max}} = 31.4 \text{ mL/s} \)
- Average flow = 15.9 mL/s
- Flow time = 17.1 s
- Time to \( Q_{\text{max}} \) = 8.1 s
- Voided volume = 273 mL
- PVR = 50 mL

B

![Graph B]

- \( Q_{\text{max}} = 5.8 \text{ mL/s} \)
- Average flow = 1.5 mL/s
- Flow time = 153.6 s
- Time to \( Q_{\text{max}} \) = 72.1 s
- Voided volume = 148 mL
- PVR = 50 mL

Mild/Mod Obstructed

Grossly Abnormal
First choice of U.S. Urologists For the treatment of LUTS

<table>
<thead>
<tr>
<th>AUA score 0 to 7 (mild):</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watchful waiting</td>
<td>77</td>
</tr>
<tr>
<td>α-Blockers</td>
<td>17</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
</tr>
<tr>
<td>Finasteride</td>
<td>1</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AUA score 8 to 19 (moderate):</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Blockers</td>
<td>65</td>
</tr>
<tr>
<td>Other</td>
<td>15</td>
</tr>
<tr>
<td>Watchful waiting</td>
<td>6</td>
</tr>
<tr>
<td>Finasteride</td>
<td>6</td>
</tr>
<tr>
<td>Transurethral resection</td>
<td>4</td>
</tr>
<tr>
<td>Laser</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AUA score 20 to 35 (severe):</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transurethral resection</td>
<td>41</td>
</tr>
<tr>
<td>α-Blockers</td>
<td>31</td>
</tr>
<tr>
<td>Other</td>
<td>16</td>
</tr>
<tr>
<td>Laser</td>
<td>6</td>
</tr>
<tr>
<td>Finasteride</td>
<td>3</td>
</tr>
<tr>
<td>No response</td>
<td>3</td>
</tr>
</tbody>
</table>
Pharmacologic Agents

- **Alpha blocking**
  - Prazosin
  - Terazosin (Hytrin)
  - Doxazosin (Cardura)
  - Tamsulosin (Flomax)
  - Alfuzosin (Uroxatral)
  - Sildosin (Rapaflo)

- **5α reductase inhibition**
  - Finasteride (Proscar)
  - Dutasteride (Avodart)
Mechanism of Action of $\alpha$-Blockers

- Adrenergic sympathetic nervous system fibers are present on smooth muscle in the prostatic stroma, capsule, and bladder neck.
- Stimulation of $\alpha$-1 adrenoceptors on smooth muscle in these regions increases smooth muscle tone and may contribute to BPH symptoms.
- Blockade of $\alpha$-1 adrenoceptors has been shown to decrease urethral resistance and may relieve urinary obstruction and BPH symptoms.
Mechanism of Action of α-Blockers

- α adrenoceptors
  - α-2 located presynaptic (functions as negative feedback mechanism)
  - α-1 are post synaptic (3 sub types)
    » α-1a: prostate stroma
    » α-1b: prostate smooth muscle of arteries and veins
    » α-1d: prostate, bladder body and dome

- Blockade of α-1 adrenoceptors
  - α-1a: results in reduced prostatic tone and improved voiding
  - α-1b: results in venous and arterial dilation
  - α-1d: reduces in irritative voiding symptoms
  - Ideal blockage would target α-1a and α-1d

Mechanism of Action of $\alpha$-Blockers

<table>
<thead>
<tr>
<th>Receptor Agonist</th>
<th>Rank Order of Receptor Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prazosin</td>
<td>$\alpha_{1A} = \alpha_{1B} = \alpha_{1D}$</td>
</tr>
<tr>
<td>Doxazosin</td>
<td>$\alpha_{1A} = \alpha_{1B} = \alpha_{1D}$</td>
</tr>
<tr>
<td>Terazosin</td>
<td>$\alpha_{1B} = \alpha_{1D} &gt; \alpha_{1A}$</td>
</tr>
<tr>
<td>Alfuzosin</td>
<td>$\alpha_{1A} = \alpha_{1B} = \alpha_{1D}$</td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>$\alpha_{1A} = \alpha_{1D} &gt; \alpha_{1B}$</td>
</tr>
<tr>
<td>Silodosin</td>
<td>$\alpha_{1A} &gt; \alpha_{1D} &gt;&gt; \alpha_{1B}$</td>
</tr>
</tbody>
</table>

Shibata, Mol Pharmacol, 1995;48(2):250–8;
Tamsulosin Effects AUA Sx Score

![Graph showing mean change in AUA Sx Score over duration of treatment] (Placebo □ 0.4 mg ▲ 0.8 mg)

*Indicates significant difference from placebo ($P \leq 0.05$).

Tamsulosin Effects on Flow rate

Lepor H et al Urology. 1998;51:892-900

*Indicates significant difference from placebo (P ≤ 0.05).
## Adverse Events of $\alpha$-Blockers

<table>
<thead>
<tr>
<th>Effect</th>
<th>Phenoxybenzamine (%)</th>
<th>Prazosin (%)</th>
<th>Terazosin (%)</th>
<th>Doxazosin (%)</th>
<th>Tamsulosin (%)</th>
<th>Alfuzosin (%)</th>
<th>Silodosin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>15–20</td>
<td>10–15</td>
<td>2–8</td>
<td>1–2</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Dizziness</td>
<td>10–14</td>
<td>15–17</td>
<td>7–14</td>
<td>10–15</td>
<td>15</td>
<td>6–9</td>
<td>5</td>
</tr>
<tr>
<td>Headache</td>
<td>4–15</td>
<td>13–15</td>
<td>4–10</td>
<td>9–10</td>
<td>19</td>
<td>8–14</td>
<td>NR</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>5–8</td>
<td>NR</td>
<td>2–7</td>
<td>NR</td>
<td>8</td>
<td>1–2</td>
<td>22</td>
</tr>
<tr>
<td>Fatigue</td>
<td>10–15</td>
<td>10</td>
<td>4–8</td>
<td>1–2</td>
<td>8</td>
<td>1–7</td>
<td>NR</td>
</tr>
<tr>
<td>Syncope</td>
<td>NR</td>
<td>NR</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>NR</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>8</td>
<td>NR</td>
<td>2</td>
<td>NR</td>
<td>13</td>
<td>5–6</td>
<td>NR</td>
</tr>
</tbody>
</table>

## Tamsulosin and Age

<table>
<thead>
<tr>
<th>Reference (study duration)</th>
<th>Entry criteria</th>
<th>No. of evaluable patients</th>
<th>Mean baseline IPSS</th>
<th>Mean reduction in IPSS from</th>
<th>No. of evaluable patients</th>
<th>Baseline $Q_{\text{max}}$ (ml/sec)</th>
<th>Mean change in $Q_{\text{max}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michel et al. [74] study A (4wk)</td>
<td>Age &lt;61y</td>
<td>2150</td>
<td>17.1</td>
<td>8.9</td>
<td>725</td>
<td>12.9</td>
<td>5.1</td>
</tr>
<tr>
<td></td>
<td>Age 61-70y</td>
<td>3654</td>
<td>18.4</td>
<td>8.9</td>
<td>1240</td>
<td>11.7</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>Age &gt;70y</td>
<td>2478</td>
<td>20.0</td>
<td>9.0</td>
<td>832</td>
<td>10.5</td>
<td>4.3</td>
</tr>
<tr>
<td>study B (12wk)</td>
<td>Age &lt;61y</td>
<td>2573</td>
<td>17.4</td>
<td>10.5</td>
<td>1777</td>
<td>12.5</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>Age 61-70y</td>
<td>3796</td>
<td>18.7</td>
<td>10.6</td>
<td>2709</td>
<td>11.4</td>
<td>4.6</td>
</tr>
<tr>
<td></td>
<td>Age &gt;70y</td>
<td>2433</td>
<td>20.4</td>
<td>13.5</td>
<td>1610</td>
<td>10.2</td>
<td>4.3</td>
</tr>
</tbody>
</table>
Mechanism of Action of 5α-Reductase Inhibitors

- Testosterone is converted to DHT by the enzyme 5α-reductase.
- DHT is primary androgen responsible for prostate enlargement.
- 5α-reductase inhibitors decrease DHT levels in serum and prostate.

Effect of Finasteride on Prostate Volume

![Graph showing the effect of Finasteride on prostate volume over 4 years compared to placebo. The graph indicates a significant decrease in prostate volume with Finasteride treatment.]

**Placebo**
- N = 155
- 136
- 119
- 98
- 85

**Finasteride**
- N = 157
- 144
- 130
- 116
- 102

Effect of Finasteride on BPH Symptoms

Impact of Medical Therapy on Clinical Progression of BPH

Cumulative incidence of BPH progression

- Placebo (n=737)
- Finasteride (n=768)
- Doxazosin (n=756)
- Combination (finasteride + doxazosin) (n=786)

66% risk reduction (p<0.001)

Most BPH Progression Was Due to Symptom Progression

- Distribution of BPH progression events
  - >4-point AUA-SI increase 80%
  - AUR 12%
  - Incontinence 7%
  - UTI/urosepsis 1%
  - Renal insufficiency 0%

Impact of Medical Therapy on Symptom Control

Cumulative incidence of ≥4-point increase in symptom

- Placebo (n=737)
- Finasteride (n=768)
- Doxazosin (n=756)
- Combination (Finasteride + doxazosin) (n=786)

64% risk reduction (p<0.0001)

McConnell JD. AUA Annual Meeting, May 2002
Impact of Medical Therapy on the Risk of Urinary Retention

Impact of Medical Therapy on Need for Invasive BPH Therapy

Cumulative incidence of BPH-related surgery

- Placebo (n=737)
- Finasteride™ (n=768)
- Doxazosin (n=756)
- Combination (finasteride + doxazosin) (n=786)

67% risk reduction (p<0.001)

Effect of Medical Therapy on Prostate Volume

Change from baseline in prostate volume

-13%*  Combination (Finasteride + doxazosin) (n=786)
-16%*  Finasteride (n=768)
Doxazosin (n=756)
Placebo (n=737)

+18%  +18%

Median % change from baseline

*p<0.001 vs. baseline

McConnell JD. AUA Annual Meeting, May 2002
Conclusions

- Combination therapy is the most effective form of medical therapy for BPH
  - 66% reduction in risk of BPH progression (p<0.001*)
  - 64% reduction in worsening symptoms (p<0.001*)
  - 81% reduction in risk of AUR (p<0.001*)
  - 67% reduction in need for invasive BPH therapy (p<0.001*)

### CombAT: Combination of Dutasteride and Tamsulosin at 2 years

<table>
<thead>
<tr>
<th></th>
<th>Δ AUA-IPSS</th>
<th>&gt;25%</th>
<th>≥2 pts</th>
<th>≥3 pts</th>
<th>Δ Qmax (mL/s)</th>
<th>Δ Prostate VOLUME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dutasteride</td>
<td>−4.9</td>
<td>59%</td>
<td>70%</td>
<td>65%</td>
<td>1.9</td>
<td>−28%a</td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>−4.3</td>
<td>55%</td>
<td>68%</td>
<td>62%</td>
<td>0.9</td>
<td>0%</td>
</tr>
<tr>
<td>Combination</td>
<td>−6.2</td>
<td>67%</td>
<td>77%</td>
<td>75%</td>
<td>2.4</td>
<td>−27%</td>
</tr>
</tbody>
</table>

Roehrborn, J Urol 2008;179(2):616–21
CombAT: Combination of Dutasteride and Tamsulosin at 4 years

Roehrborn, European Urology, 2010, 57(1) 123-131
CombAT: Combination of Dutasteride and Tamsulosin at 4 years
Whats New in Medical Therapy?

- Antimuscarinics (LUTS due male OAB)
  - Tolterodine (Detrol)
  - Oxybutynin (Ditropan)
  - Solifenacin (Vesicare)
  - Darifenacin (Enablex)
  - Trospium (Sanctura)
  - Fesoterodine (Toviaz)

- PD5 Inhibitors ???
### Muscarinic Receptor Antagonist as Monotherapy in Male LUTS: Results

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Sx</th>
<th>$Q_{\text{max}}$ mL/s</th>
<th>PVR mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>43</td>
<td>17.3</td>
<td>9.8</td>
<td>97</td>
</tr>
<tr>
<td>1 mos</td>
<td>43</td>
<td>11.3</td>
<td>11.4</td>
<td>79</td>
</tr>
<tr>
<td>3 mos</td>
<td>39</td>
<td>10.7</td>
<td>10.9</td>
<td>72</td>
</tr>
<tr>
<td>6 mos</td>
<td>39</td>
<td>11.2</td>
<td>11.7</td>
<td>75</td>
</tr>
</tbody>
</table>

Muscarinic antagonist: Tolterodine Extended release
N=39

Kaplan, *J Urol.* 2005 174(6), 2273-76
Muscarinic Receptor Antagonist as Monotherapy in Male LUTS: Results

- Frequency decreased from 9.8 to 6.3/day
- Nocturia decreased from 4.1 to 2.9
- 4 men (9%) discontinued due to dry mouth
- No patients went into urinary retention
- 1 patient had a urinary tract infection
- 27 (63%) were potent at baseline, 29 (67%) were potent at 6 months

Kaplan, J Urol. 2005 174(6), 2273-76
Increased Treatment Benefit With Combination Therapy

Post-Hoc Intention-to-Treat Analysis

- Placebo: Benefit 59.5%, No benefit 40.5% (n = 222)
- Tolterodine ER: Benefit 62.7%, No benefit 37.3% (n = 217)
- Tamsulosin: Benefit 67.9%, No benefit 32.1% (n = 215)
- Tolterodine ER + tamsulosin: Benefit 76.4%, P<.001, No benefit 23.6% (n = 225)

New uses for PD51
Incidental Improvement

Mulhall 2006: Sildenafil

- Men presenting with ED
  - Excluded IPSS <10
  - Not randomized, prospective or placebo controlled
- 48 men, mean age 62
- Sildenafil 2x/week-mean usage
  - IPSS improvement of 4.6 points (p=.013)
  - QOL improvement of 1.4 points (p=.025)

Mulhall et al Journal of Sexual Medicine 2006
Incidental Improvement

- Daily Sildenafil 50mg vs placebo
  - 369 men with both ED & BPH, 12 wks
  - IPSS 6.3 vs. 1.9 (p<0.0001)
  - Also improvements:
    » IPSS QOL
    » BPH Impact score
  - No change in Qmax

Clinical Improvement

Roehrborn 2008 (Tadalafil dosing study)
- Tadalafil (mg) 2.5, 5, 10, 20 daily vs. placebo
- 1058 men with BPH-LUTS, 12 weeks

Results:
- IPSS improvement: -3.9 -4.9 -5.2 -5.2 -2.3 (<0.001)
- Also improvements in:
  » IPSS QOL
  » IPSS Domains
  » BPH Impact Index
  » All baseline severities
- No change in:
  » Qmax
  » PVR

Roehrborn et al Journal of Urology 2006
Alternative to Medical Therapy
Prostatectomy 1980 to 1994

Future: Medical Mgmt of BPH in Elderly Men

- Comparison of phytotherapies with established medical therapies (*Griebling, New Frontiers in Geriatric Research, 2004*)
- Do established medical therapies work as well in the elderly
  - Can tx slow progression in older populations?
  - Do older men respond the same when compared to younger men?
  - Do older men tolerate medical therapies as well as younger men?
  - Existing data sets