Special Considerations for the Evaluation & Management of Urinary Incontinence in the Geriatric Woman

Sarah E. McAchran, MD, FACS
Associate Professor, Urology and Obstetrics & Gynecology
Female Pelvic Medicine & Reconstructive Surgery
Co-Medical Director, Women’s Pelvic Wellness Clinic
November 20, 2019

Objectives

• Understand the demographic burden of urinary incontinence in the US
  — Review 2014 CDC report on Prevalence of Incontinence in Older Americans
• Understand the multifactorial nature of urinary incontinence in the geriatric female population
• Understand the evaluation and management of Urge and Stress incontinence in the elderly woman

THE DEMOGRAPHIC BURDEN
First report to look at incidence of incontinence by place of residence:
1) Community dwelling older adults
2) Residential care facilities
3) Nursing home residents
4) Hospice/home health

Data Sources

- National Health and Nutrition Examination Survey (NHANES)
  - non-institutionalized persons
- National Survey of Residential Care Facilities (NSRCF)
  - residents of care residential care facilities
- National Home and Hospice Care Survey (NHHCS)
  - home health and hospice
- Long Term Care Minimum Data Set (MDS)
  - nursing home patients
### NHANES
National Health and Nutrition Examination Survey

- 2625 face-to-face respondents
- Unique in that it combines interviews and physical exams
- Years 2007-2010 were combined
- All self-reported
- Bladder incontinence defined using the bladder Incontinence Severity Index

### Incontinence Severity Index

**Frequency of incontinence episodes**
- 0 = never
- 1 = less than once/month
- 2 = a few times a month
- 3 = a few times/week
- 4 = every day and/or night

**Amount of urine lost per episode**
- 1 = drops
- 2 = small splashes
- 3 = more

Introduced in 1993—validated against pad weight and correlated with impact.

**ISI values 0 – 12 are sub-divided into 5 categories**
- 0 = None
- 1-2 = Slight incontinence
- 3-6 = Moderate incontinence
- 8-9 = Severe
- 12 = Very Severe incontinence
ISI Severe Incontinence

3 x 3 = 9
(a few times a week) x (More than small splashes)

4 x 2 = 8
(every day and/or night) x (small splashes)

SUMMARY OF CDC REPORT

- If only Moderate, Severe, and Very Severe are considered:
  - 24% men and women
- If only Severe and Very Severe are considered:
  - 5% men and women

Irrespective of residence type, >70% of all home health/hospice care recipients either require a catheter or have incontinence

>70% of all home health/hospice care recipients either require a catheter or have incontinence

*Per International Continence Society; requires objective demonstrability and presence of hygienic or social problem for uncontrolled loss of urine to be acknowledged as UI.

**THE AGING LOWER URINARY TRACT**

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**Urinary Incontinence Is More Prevalent Than Other Chronic Diseases in Women**

- 26% Urinary Incontinence
- 21% Hypertension
- 20% Depression
- 8% Diabetes

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**Urinary Incontinence Expenditures Are Greater Than Other Women's Health Conditions**

- $24 in Urinary Incontinence
- $16 in Obstetrics
- $13 in Breast Cancer

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The Urinary Tract

Normal Bladder Function

- Normally urination doesn't require much thought.
- It's a combination of both voluntary (conscious) and involuntary (automatic) muscle actions that coordinate to hold and release urine.
Normal Bladder Function

- Over several hours the bladder fills with urine and the bladder muscle is relaxed and stretches.
- The sphincter stays tightly closed.
- When the bladder reaches 8-10 oz, the nerves along the bladder send a message to the brain. *This is an urge.*

- If it's not a convenient time to go the bathroom, you consciously tighten your sphincter.
- This signals the bladder to relax.
- It can then continue to fill and stretch.
When you decide it's a good time to urinate, your brain flips the switch from STORAGE MODE to EMPTY MODE.

You consciously relax your sphincter and the bladder muscle then contracts to squeeze out urine.

Geriatric LUT Physiology

- Widening of spaces between detrusor smooth muscle cells
- Within the smooth muscle sarcolemma:
  - Elongation of the dense band components
  - Depletion of caveolae (small invaginations in the sarcolemma involved in transport and signaling)
- Cell junction changes have been noted
- Age related changes to the urethra

Geriatric LUT Physiology

- Age related changes to the urethra
- Pronounced change in striated smooth muscle
- Decreased urethral closure pressure
Geriatric Bladder Function

- Involuntary or uninhibited detrusor contractions = urgency/urge incontinence
- Impaired contractility = incomplete bladder emptying or elevated post-void residuals
- Impaired urethral coaptation—stress urinary incontinence
- DHIC—detrusor hyperactivity with impaired contractility

Geriatric Genitourinary Function

Increased
- Post-void Residual (PVR)
- Detrusor overactivity
- Urine output later in the day
- Extravascular fluid shifts to legs upon arising
- Intravascular fluid shift from legs upon reclining

Decreased
- Ability to postpone voiding
- Total bladder capacity
- Detrusor contractility
- Immune function
- Anti-diuretic hormone (ADH) production
- Ability to concentrate urine because of apoptosis of long nephrons
- Vaginal and urethral epithelial thickness

EVALUATION OF URINARY INCONTINENCE IN OLDER WOMEN
Under-Reported

• Most patients do not mention the problem to their doctor, some wait up to 3 years
  – Self-manage
  – 59% of patients do not seek help because they believe no effective treatment is available
  – 73% of patients who seek treatment are currently not on medication
• Most patients do not mention the problem to their friends
• Most people think incontinence is part of normal aging

Millsom et al. BJU Int. 2001; 87:760-766

Incontinence History

• Targeted to identify:
  – Type
  – Severity
  – Duration
  – Burden / Goals of Care
  – Potentially Modifiable Contributing Factors
• More useful than Physical Exam for initial assessment

ICIQ-UI Short Form

• How often do you leak urine?
• How much urine do you usually leak?
• Overall, how much does leaking urine interfere with your everyday life?
• When does urine leak? (self diagnosis items that discern urge incontinence from stress incontinence)

https://iciq.net/
ICIQ-UI Short Form

- Type of incontinence
- Severity
- Burden

Excellent sensitivity to change so you can use to evaluate improvement or worsening

Examination

- Assessment of mobility and cognitive function
- Pelvic examination
  - Evaluate for atrophy, prolapse beyond the introitus, prior surgery
- Assessment of post-void residual urine
- Cough stress test
- Urinalysis
  - hematuria, pyuria, bacteriuria, glucosuria

Physical Exam Findings: Prolapse

- Relaxation of the vaginal walls
- Varied symptoms
- May impact body image
- Sex still safe!
Physical Exam Findings: Atrophy

Age and Genitourinary Function

- Lower urinary tract (LUT) dysfunction in elderly women is *almost always multifactorial*
  - Mobility
  - Manual dexterity
  - Environment and access to toilets
  - Mentation
  - Medical conditions
  - Medications

Non-Urologic Factors Related to Urinary Incontinence

<table>
<thead>
<tr>
<th>Comorbid Disease</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>α-Adrenergics (blockers &amp; agonists)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>ACE-I</td>
</tr>
<tr>
<td>Degenerative joint disease</td>
<td>Calcium channel blockers</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>Diuretics</td>
</tr>
<tr>
<td>Severe constipation</td>
<td>Opiates</td>
</tr>
<tr>
<td></td>
<td>Anticholinergics (antidepressants, antipsychotics)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neurological/Psychiatric</th>
<th>Function &amp; Environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>Impaired Cognition</td>
</tr>
<tr>
<td>Parkinson's disease</td>
<td>Impaired Mobility</td>
</tr>
<tr>
<td>Normal pressure hydrocephalus</td>
<td>Inaccessible toilets</td>
</tr>
<tr>
<td>Dementia</td>
<td>Lack of caregivers</td>
</tr>
</tbody>
</table>
Acute Incontinence

- Delirium
- Infection
- Atrophic urethritis/vaginitis
- Pharmaceuticals
- Psychological (depression)
- Endocrine (hypercalcemia, hyperglycemia)
- Restricted mobility
- Stool impaction

Goode et al, JAMA. 2010;303(21):2172-2181
### Condition Mechanism Treatment Implications

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mechanism</th>
<th>Treatment Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary Tract Infection</td>
<td>Cystitis causes urgency &amp; frequency</td>
<td>Asymptomatic bacteriuria is more common in elderly patients and does not need treatment. However, consider treatment of bacteriuria when incontinence is new onset or with acute exacerbating. (DuBeau CE, et al. Incontinence in the Frail Elderly. In: Abrams P, Cardozo L, Khoury S, Wein A eds. 4th International Consultation on Incontinence, 2009)</td>
</tr>
<tr>
<td>Constipation</td>
<td>Postulated physical irritation of the bladder from rectal distention</td>
<td>Appropriate management with increased fluid intake, increased dietary fruit and fiber, stool softeners, and laxatives as needed. (DuBeau CE, et al. Incontinence in the Frail Elderly. In: Abrams P, Cardozo L, Khoury S, Wein A eds. 4th International Consultation on Incontinence, 2009)</td>
</tr>
</tbody>
</table>

### Condition Mechanism Treatment Implications

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mechanism</th>
<th>Treatment Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobility Impairment</td>
<td>Slowed mobility from any cause can precipitate urgency incontinence, pain with movement from DJD or other conditions can cause postponement of voiding with resultant incontinence</td>
<td>Physical therapy, assistive devices, or other interventions to improve mobility. Improved pain management and education concerning regular toileting.</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>Nocturnal diuresis due to production of atrial natriuretic peptide</td>
<td>Treatment decreases nocturnal diuresis and decreases nocturnal enuresis. (Fitzgerald MP et al, Am J Obstet Gynecol. 2006;194(5):1399-1403.)</td>
</tr>
<tr>
<td>Obesity</td>
<td>Pressure on the bladder from central obesity as well as stress on the pelvic floor musculature</td>
<td>In a randomized controlled trial, an average weight loss of 17 lb over 6 months reduced incontinence episodes by 47%. (Subak LL et al. N Engl J Med. 2009;360(5):481-490.)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Increased diuresis</td>
<td>Evaluate necessity. Loop diuretics moved to late in the afternoon to decrease day time frequency and diuresis before bed.</td>
</tr>
<tr>
<td>ACE-I</td>
<td>Cough can precipitate stress incontinence</td>
<td>Consider alternative medications.</td>
</tr>
<tr>
<td>Anticholinergics, sedatives, hypnotics</td>
<td>May cause incomplete bladder emptying and constipation. Also may cause cognitive impairment</td>
<td>Discontinue or reduce dose when possible.</td>
</tr>
</tbody>
</table>
OVERACTIVE BLADDER (OAB)
OAB Symptoms

- **Urgency**
  - Sudden, strong desire to urinate

- **Frequency**
  - 8+ visits to the toilet per 24 hours
  - 2+ visits to the toilet during sleeping hours (nocturia)

- **Urge Incontinence**
  - Sudden & involuntary loss of urine

Overactive Bladder Triggers

- Hearing or touching running water
- Seeing a bathroom
- Placing your feet on the floor when you first get out of bed
- Putting your key in the door when you get home
- Anxiety or stressful situations
- Exposure to cold

www.urolgyhealth.org

OAB Symptom Quiz
OAB is a bladder problem

- Leakage of larger volumes with overwhelming urgency – due to bladder contractions
- When I gotta go, I gotta go!

Normal Lower Urinary Tract (LUT) Function: Reciprocal Activities

Stress Urinary Incontinence Is the Most Common Type in Women

53

54
Prevalence of UI in Women

Stress is the most common type in women <60 years old

Women >60 years old

Stress

Urge

Mixed

55%

20%

25%

55%

35%

30%

35%


NOBLE Study

- National Overactive Bladder Evaluation
- Published 2002
- Questionnaire based study
  - OAB instruments, SF-36, Depression index, sleep instrument
- 5,204 US citizen sample
- To evaluate the prevalence and burden of OAB in the United States


Prevalence of OAB in the US

- Men 16% and Women 16.9%
- Prevalence of OAB increases with age

NOBLE Results

- Prevalence between men & women was roughly equal
- Severity of symptoms worse for women, with women having more OAB-wet and men more OAB-dry
- OAB with or without UI was associated with clinically and significantly:
  - lower SF-36 quality of life scores
  - higher CES-D depression scores
  - poorer quality of sleep

TREATMENT

AUA Guidelines on OAB, 2019

Diagnosis and Treatment of Non-Neurogenic Overactive Bladder (OAB) in Adults: an AUA/SUFU Guideline (2019)

Panel Members

- L. Aron Gondley, Deborah J. Lichten, Kathryn L. Kang, Tanya C. Chua, Jacqueline Chesebro, Daniel J. Collins, Anuag Kumar Day, Navneet Bhati, Peter X. Hanssens, Mike J. Stampers, Christopher D. Tse, Sandy Heiner Havaela

The Practice Guideline Committee would like to acknowledge the contributions of Dr. Alexander Gondley to the 2019 Guideline Amendment.
Conservative Therapy

- Lifestyle changes
  - Caffeine reduction
  - Fluid management
- Prevent constipation
- Maintain a healthy weight
- Re-train the bladder—Mind Over Bladder
  - Work with a pelvic floor physical therapist
  - There are home programs as well
- Pelvic Floor Physical Therapy
  - Strengthening, urge suppression
- Bladder diary—app or paper:
  - 24 hour record of volume in, out, leakage episodes, triggers

Treatment Algorithm for OAB

Conservative Therapy
- Diet Modification
- Pelvic Floor PT

Pharmacotherapy
- Neuromodulation
  - PTNS
- Sacral Neuromodulation
  - Botox (non-FDA Approved)

Surgical Intervention
- Urinary Diversion, Augmentation Cystoplasty
Voiding Diary

3-Day Voiding Diary

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Urination</th>
<th>Voided Volume</th>
<th>Amount of Fluid Intake</th>
<th>Activity at Time of Urination</th>
</tr>
</thead>
<tbody>
<tr>
<td>4:00 am</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5:30 am</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11:00 am</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

www.sufu.org

Education: www.iuga.org

• Website not user-friendly
• Download patient info for free
• Multiple languages

www.nafc.org
Treatment Algorithm for OAB

Conservative Therapy
- Behavioral
- Diet Modification
- Pelvic Floor PT

Pharmacotherapy
- Oxybutynin Chloride – Immediate Release
- Oxybutynin Chloride XL (Ditropan XL)
- Transdermal Oxybutynin Patch (Oxytrol)
- Oxybutynin Chloride Gel (Gelnique)
- Tolterodine – Immediate Release
- Tolterodine LA (Detrol LA)
- Fesoterodine fumarate (Toviaz)
- Trosiptum (Sanctura)
- Trosiptum Chloride XR (Sanctura XR)
- Solifenacin (Vesicare)
- Darifenacin (Enablex)

Surgical Intervention
- Urinary Diversion
- Augmentation Cystoplasty

Neuromodulation
- PTNS
- Sacral Neuromodulation
- Botox (non-FDA Approved)

Anticholinergics
- Introduced 2009
- OTC since 2013
Anticholinergics: 
Mechanism of Action

- Detrusor (bladder) muscle rich in cholinergic/muscarinic receptors
- Medications block muscarinic receptors in detrusor — stabilize bladder muscle
- Influence suburothelial receptors as well
  - Mediate urgency
- Multiple muscarinic subtypes have been identified

Comparative Receptor Presence in Detrusor Wall

Distribution of Muscarinic Receptors Through the Body
Efficacy

- Efficacy—demonstrated in randomized controlled trials for:
  - Oxybutynin
  - Tolterodine
  - Trospium
  - Darifenacin
  - Solifenacin
  - Fesoterodine

- Given Grade A recommendations by the International Continence Society

Antimuscarinic Class

Side Effects

- Dry mouth
- Constipation
- Blurred vision
- Headache

Oxybutynin

- Some selectivity for M3 and M1 receptors
- Other bladder activity
  - Direct smooth muscle relaxation
  - Local anesthesia
- Active metabolite: N-Desethyloxybutynin (N-DEO)
  - Potent antimuscarinic
  - Responsible for significant side effects
- Used for decades
- Side effects limit use
- May cause cognitive dysfunction
Long-term Evaluation of Oxybutynin IR for OAB

- Prospective randomized trial to compare oxybutynin 2.5 mg bid or 5 mg qhs
- Titrate doses up
- 53% overall reported improvement or cure
- 2/3 stopped medication within 4 months


Oxybutynin Extended Release

- Oxybutynin placed in slow-release vehicle
- Release of all medication takes 24 hours
- More released in distal GI tract with less metabolism
- Better efficacy, fewer side effects
- Available in 3 doses: 5, 10,15 mg
  - Can be titrated
- Approved at doses up to 30 mg
  - Usually for patients with neurogenic overactivity

Tolterodine (Detrol)

- First drug developed to specifically treat OAB
  - Greater selectivity for bladder
- Low potential to cross blood-brain barrier
  - Thought to have fewer cognitive side effects
- Extended-release form found to have increased efficacy with fewer side effects
**Trospium (Sanctura)**

- Nonselective quaternary amine
  - More highly charged and hydrophilic
  - Should not cross blood brain barrier
- Minimal metabolism—most drug renally excreted unchanged
  - Does not interact with drugs metabolized by cytochrome P450 system
- Available in Europe for 10 years
- Available in once/day dosing; must be taken on an empty stomach

**Solifenacin (Vesicare)**

- M3 selective antimuscarinic
- Available in 2 doses: 5 and 10 mg
  - Can be titrated
- Long half-life = 50 hours

**Darifenacin (Enablex)**

- Relatively M3 selective
- Low affinity for M1 receptor
  - Much of CNS cholinergic activity involves M1 receptors
  - Few CNS side effects
  - No QT interval prolongation
- Available in 2 doses: 7.5 and 15 mg
  - Can titrate
Oxybutinin Transdermal System (Oxytrol)

- Apply every fourth day
- Avoids first-pass metabolism, therefore lower N-DODE metabolite
- Fewer systemic side effects
  - Dry mouth and constipation = placebo
  - 17% incidence of skin reactions
    - Contact dermatitis
    - Erythema resolves
    - Pruritus - moisturizer and rotate location

Oxytrol

$30.09 for a one month supply at HealthWarehouse.com

Oxybutinin Topical Chloride Gel (Gelnique)

- Once daily gel formulation
- Similar systemic side effect profile to patch
- Less local skin reaction
Fesoterodine (Toviaz)

- Pro-drug, rapidly metabolized to 5-HMT, the major active metabolite of tolterodine
- Available as 4mg and 8mg once daily doses

### Anticholinergic Side Effects

<table>
<thead>
<tr>
<th>Agent</th>
<th>Chemical Structure</th>
<th>Dry Mouth (%)</th>
<th>Constipation</th>
<th>Cognitive</th>
<th>Sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxybutynin (IR)</td>
<td>Tertiary amine</td>
<td>93%</td>
<td>50%</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tolterodine (LA)</td>
<td>Tertiary amine</td>
<td>24.3%</td>
<td>6.1%</td>
<td>Minimal effects on EEG, case reports of nightmares, hallucinations</td>
<td>No reported</td>
</tr>
<tr>
<td>Darifenacin</td>
<td>Tertiary amine</td>
<td>20-31%</td>
<td>19-24%</td>
<td>None reported</td>
<td>None reported</td>
</tr>
<tr>
<td>Solifenacin</td>
<td>Tertiary amine</td>
<td>14-21%</td>
<td>7%</td>
<td>None reported</td>
<td>None reported</td>
</tr>
<tr>
<td>Trospium chloride</td>
<td>Quaternary amine</td>
<td>22%</td>
<td>9.5%</td>
<td>No, minimal effects on quantitative EEG</td>
<td>None reported</td>
</tr>
</tbody>
</table>

Staskin DR, Drugs Aging 2005: 22(12): 1013-1028

Table 1. Incidence Rates of Adverse Events.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dry Mouth (%)</th>
<th>Constipation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fesoterodine</td>
<td>4mg 19%</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>8mg 35%</td>
<td>6%</td>
</tr>
<tr>
<td>Darifenacin</td>
<td>7.5mg 20%</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td>15mg 11%</td>
<td>15%</td>
</tr>
<tr>
<td>Solifenacin</td>
<td>5mg 11%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>10mg 28%</td>
<td>15%</td>
</tr>
<tr>
<td>Trospium</td>
<td>20mg/30mg ER</td>
<td>20%</td>
</tr>
<tr>
<td></td>
<td>60mg BID</td>
<td>11%</td>
</tr>
<tr>
<td>Tolterodine</td>
<td>4mg 23%</td>
<td>6%</td>
</tr>
<tr>
<td>Oxybutynin</td>
<td>5-20mg/day</td>
<td>71%</td>
</tr>
<tr>
<td></td>
<td>Gel 7%</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>20mg 8%</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td>35mg 1%</td>
<td>1%</td>
</tr>
</tbody>
</table>
Anticholinergic Discontinuation

- Database Study from UK (1991-2005)
  - 49,419 episodes of anticholinergic therapy
  - Overall discontinuation rate
  - Drug specific discontinuation rate

Gopal et al, Obstet Gynecol 2008; 112:1311-8

Anticholinergic Discontinuation

- Median time to discontinuation = 4.76 months (all drugs)
- 50% of women prescribed anticholinergics discontinue the medication at 6 months
  - 75% by 1 year
- Rates of discontinuation increase with duration of use

Gopal et al, Obstet Gynecol 2008; 112:1311-8

Anticholinergic (Ach) and Cognitive Impairment

- Acute impairment in:
  - Working memory
  - Attention
  - Psychomotor speed
  - Global cognitive impairment
- Elderly patients are more susceptible due to age-related changes of pharmacokinetics.
- Cholinesterase inhibitors may precipitate incontinence and pharmacologically directly oppose the action of Ach

Boudreau et al, JAGS 59:2069-2076
• Cognitive effects thought to be reversible upon discontinuation.
• Longitudinal study followed patients from 1994-2004.
• 10 year cumulative dose-response relationship was observed for dementia (0.9 vs. 1.54) and Alzheimer disease.

• Longitudinal study of 2 cohorts of cognitively normal adults.
• Use of anticholinergics was assessed.

• Use of medications with medium or high anticholinergic activity was associated with poorer memory, executive function, brain hypometabolism, brain atrophy, and increased risk of clinical conversion to cognitive impairment.
• Study concludes: “Use of medication with significant anticholinergic activity should likely be discouraged in older adults if alternative therapies are available.”
NEW TARGET:
BETA 3 RECEPTOR AGONISTS

Beta 3 Receptor Agonist (Mirabegron)

- Novel Target for OAB
- Introduced October 22, 2012
- Brand name = Myrbetriq

How it Works

U.S. Phase III Trial

- Nitti et al, Results of a Randomized Phase III Trial of Mirabegron in Patients with OAB, J Urol, Accepted Manuscript 2012

<table>
<thead>
<tr>
<th>Placebo</th>
<th>50mg</th>
<th>100mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean decrease in incontinence episodes/24h</td>
<td>-1.13</td>
<td>-1.47</td>
</tr>
<tr>
<td>Mean decrease in micturition/24 h</td>
<td>-1.05</td>
<td>-1.66</td>
</tr>
</tbody>
</table>

- Magnitude of improvement is similar to that of anticholinergic medication

European-Australian Phase III Trial

- Compared placebo, 50mg, 100mg, & tolterodine ER 4mg
- 1,978 patients randomized
  - 549 men & 1,429 women
- Primary endpoints
  - Assess safety and tolerability
  - Compare efficacy and safety with once daily tolterodine

Khullar et al, Abstract Annual Congress of EAU, 2011, Vienna

Mean change from baseline in Number of incontinence episodes
European-Australian Phase III Trial

<table>
<thead>
<tr>
<th>Adverse Events (%)</th>
<th>Placebo (n=494)</th>
<th>50mg (n=493)</th>
<th>100mg (n=496)</th>
<th>Detrol (n=495)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>7.7</td>
<td>6.9</td>
<td>6.4</td>
<td>8.1</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>1.6</td>
<td>2.8</td>
<td>2.8</td>
<td>2.8</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>2.6</td>
<td>2.8</td>
<td>2.8</td>
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<td>Headache</td>
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<td>3.7</td>
<td>1.8</td>
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<td>Influenza</td>
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<td>2.2</td>
<td>2.0</td>
<td>1.4</td>
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<tr>
<td>UTI</td>
<td>1.4</td>
<td>1.4</td>
<td>1.8</td>
<td>2.6</td>
</tr>
<tr>
<td>Constipation</td>
<td>1.4</td>
<td>1.6</td>
<td>1.6</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Khullar et al, Abstract Annual Congress of EUA, 2011, Vienna

Prescribing Issues

- Beta receptors
  - B1 Heart muscle contraction
  - B2 Smooth muscle relaxation
  - B3 Enhance lipolysis, Promotes relaxation of detrusor muscle in the bladder

Small increase in BP
- At 50mg dose in healthy volunteers, the maximum increase in SBP/DBP = 4.0/1.6 mmHg greater than placebo
- Dose dependent
- Reversible upon discontinuation
Prescribing Issues

- Inhibitor of CYP2D6
- Can increase systemic exposure to:
  - Metoprolol
  - Desipramine
- Use caution when prescribed with:
  - Thioridazine
  - Flecainide
  - Propafenone
Role in Therapy of OAB

- Patients who cannot tolerate anti-muscarinic side effects
- Patients with cognitive impairment
- *Patients who failed anti-muscarinics?*

NEUROMODULATION
ELECTRICAL & CHEMICAL

Treatment Algorithm for OAB
Sacral Neuromodulation (Interstim)

- FDA approved in 1997 for refractory:
  - Urgency/frequency
  - Urge incontinence
  - Idiopathic urinary retention

Neuromodulation of sacral nerves

Mechanism not fully understood

Theory:
- Alters the nerve signals going from the bladder back to the spinal cord ultimately leading to less frequent bladder contractions
Interstim–Medtronic


**InterStim Test Stimulation Procedure**

Simple outpatient procedure
Done under local anesthetic

**Staged Implant Procedure**

- In the OR, the permanent lead is implanted and connected to a percutaneous extension for the home test stimulation.
Implant Procedure

- Patients with a successful test stimulation go on to implantation of neurostimulator.

Current Literature: Systematic Review: Urge Incontinence

Randomized Controlled Trials vs. Case Series Reports

- In an independent investigation of 1,827 implants from 34 clinical trials, InterStim Therapy was shown to be an effective treatment option for the treatment of urinary urge incontinence.

Urgency-Frequency 6 Month SF-36 Scores
**Implantation:**

**Ranking of Adverse Events in first 12 Months Post-implant**

- Pain at neurostimulator site: 15.3%
- New pain: 9.0%
- Suspected lead migration: 8.4%
- Infection: 6.1%
- Transient electric shock: 5.5%
- Pain at lead site: 5.4%
- Adverse change in bowel function: 3.0%

Note: Additional events occurred - each less than 2.0%

**Contraindications to Interstim**

- Bony sacral abnormality
- Cognitive impairment: Can’t operate the device
- Can’t provide appropriate feedback about stimulation
- Non-compliant patients
- Patients with functional incontinence
- Patients with known need for future MRI (below neck)

**Sacral Neuromodulation in Elderly Patients**

- 2002 Study by Amundsen evaluated SNS in elderly patients
  - 25 patients > 55 years underwent test implantation
    - 12 responded and were implanted
    - Low morbidity, comparable to younger patients
    - Lower complete dry rate (17% vs 40%)

Sacral Neuromodulation in Elderly Patients

- Prospective evaluation of pre-operative risk factors for failure of neuromodulation found the following associated with failure:
  - Age > 55 years (cure rate of 37% vs. 65%)
  - 3 or more chronic conditions
  - Neurologic conditions


Percutaneous Tibial Nerve Stimulation (PTNS)

- Based on translational findings of traditional Chinese acupuncture techniques
- First described by Dr. Ed McGuire in 1983

PTNS

- Posterior Tibial Nerve
  - Mixed sensory and motor nerve
  - Fibers originating from spinal roots L4-53
  - Modulate the somatic and autonomic nerves to the pelvic floor muscles, bladder and urinary sphincter.
PTNS: SUmiT Trial

- Multicenter, double blinded, randomized controlled trial comparing the efficacy of PTNS to sham through 12 weeks of therapy
- 220 patients not on OAB drugs during study


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PTNS: OrBIT Trial

- Phase 1 compared PTNS to tolterodine
  - 79.5% improvement in OAB symptoms PTNS
  - 54.8% improvement for Tolterodine
- Phase 2 evaluated sustained efficacy at 12 months
  - Initial 12 week course
  - Ongoing therapy at tapering intervals
    - Avg of 12 ± 4.9 further treatments over 9 months

MacDonald et al, J. Urol 183, 234-240, 2010
PTNS: OrBIT Trial Results, Long Term

PTNS Risks of Treatment
- Transient pain at/near the stimulation site
- Transient mild pain or skin inflammation at or near the stimulation site
- Transient mild bleeding at needle insertion site.
Botulinum Toxin - Botox

- Decreases bladder muscle's ability to contract.
  - Inhibits acetylcholine release at presynaptic cholinergic junction.
  - Regional decreased muscle contractility and atrophy.
- Can be done in the office with local anesthetic or in the OR with sedation.
- Reversible in 5-8 months (detrusor).

Trials of Botox for Idiopathic OAB

- 4 Randomized, placebo controlled
  - Brubaker et al, 2008
  - Dmochowski et al, 2010
  - Pimenta et al, 2008
- 2 Randomized, without placebo control
- 15 Observational studies
  - Without control groups
- Significant reductions in incontinence episodes and in urgency were reported in all active treatment groups.

Botox for Refractory Idiopathic OAB

- 28 patients 200 units BoNT-A
- 15 patients placebo injections
- 60% BoNT-A documented improvement (questionnaire)
- Median response duration = 373 days.
- Trial placed on clinical hold
  - 43% women had post-void residual >200mL requiring CIC
  - Mean duration of CIC = 62 days.

Brubaker et al. J. Urol 2008 180(1) 217-222
Botox In Older Women

- Limited Data
- 21 patients aged 75-92 were assessed one month after Botox injection (200 units)
  - 16/21 patients (76%) reported greater than 50% improvement in symptoms
  - Frequency decreased from 11-5 voids/day
  - Pad use decreased from 4-1 pad/day
  - No complications reported

White et al, J Urol, 2008; 180(6): 2522-6

AUA OAB Guidelines on Botox

- FDA-approved for Idiopathic OAB (1/18/13)
- Symptoms improve
- Risk of adverse events requiring secondary interventions is substantial (UTI, retention)
- Patients must be willing to perform self-catheterization for long periods
- Clinician must be able to measure PVR
- Repeat injections are necessary to maintain improvement

Comparisons of Neuromodulation Therapies

<table>
<thead>
<tr>
<th>Sacral Neuromodulation</th>
<th>Botulinum Toxin Injections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restores function</td>
<td>Takes away function</td>
</tr>
<tr>
<td>Non NOAB</td>
<td>ALL OAB pts</td>
</tr>
<tr>
<td>Treats retention</td>
<td>Potential to cause retention</td>
</tr>
<tr>
<td>Helps GI conditions</td>
<td>No GI benefit</td>
</tr>
<tr>
<td>One Treatment</td>
<td>Need repeat rx</td>
</tr>
<tr>
<td>No carry over effect</td>
<td>30% have a permanent carry over effect</td>
</tr>
<tr>
<td>Immediate use of BTV if fails</td>
<td>Wait 3-6 months for adjvant rx</td>
</tr>
<tr>
<td>Long term benefit</td>
<td>Temporary</td>
</tr>
<tr>
<td>Safety: proven</td>
<td>Safety: proven</td>
</tr>
<tr>
<td>Revision: 25-50% over 2-10y</td>
<td>Frequent retreatment &lt;6 months</td>
</tr>
<tr>
<td>MRI compatible</td>
<td>MRI compatible</td>
</tr>
<tr>
<td>Simple: not totally office based yet</td>
<td>Simpler: office based (sometimes)</td>
</tr>
<tr>
<td>Time Consuming</td>
<td>Less time consuming</td>
</tr>
<tr>
<td>FDA Approved</td>
<td>FDA Approved</td>
</tr>
</tbody>
</table>
Treatment Algorithm for OAB

Conservative Therapy
Behavioral
- Cen-Meditation
- Pelvic PT
Pharmacotherapy
Neuromodulation
- Sacral Neuromodulation
- PTNS
- Botox (non-FDA Approved)
Surgical Intervention
Urinary Diversion
- Cystoplasty

STRESS URINARY INCONTINENCE

Stress Urinary Incontinence
Stress Urinary Incontinence

- 1 in 3 women will experience stress urinary incontinence (SUI) in their lifetime.

- It occurs when activity such as laughing or coughing or bending causes urine to leak out.

- The amount of urine that is lost can be a few drops to tablespoons or more.

Stress Incontinence is a Urethra Problem

Resting  Coughing

- Problem with the urethra (not the bladder)
  - Weakness of the tissue and muscles under/around the urethra
  - Urethra is too mobile
  - Urethra is not mobile enough
SUI Risk Factors

- Caucasian or Hispanic race
- Overweight or Obesity
- Smoking
- Chronic coughing (asthma, GERD)
- Pregnancy and childbirth
- Nerve injuries to the lower back
- Pelvic Surgery

Treatments—Stress Incontinence
Goal: Improve Quality of Life

- Physical therapy:
  - Exercises to help strengthen and control the pelvic floor muscles.
  - Biofeedback.
- Pessary:
  - Treats incontinence and prolapse.
  - Different shapes and sizes.
  - Sized to fit each patient.
- Surgery:
  - Slings and bulking agents.

Weight Loss

- Being overweight or obese leads to more chronic pressure on the pelvic floor
- 5-10% reduction in total body weight results in 50-70% reduction in SUI in women
- This doesn’t mean that everyone has to reach their ideal weight, but maintaining a healthy weight can be preventative

Subak et al, NEJM, 2009: 360:481-90
Pelvic Floor Physical Therapy

- Consider working with a specialty-trained Pelvic Floor Physical Therapist
- In appropriately selected women, Pelvic Floor PT reduced SUI by 33%

Pelvic Floor Physical Therapy: www.apta.org to find PT’s near you
Pelvic Floor Physical Therapy

• Initial evaluation:
  – Extensive history interview
  – examination of the spine and lower extremities
  – biofeedback assessment of the pelvic floor muscles and abdominal muscles
  – an internal pelvic floor assessment
  – education and initiation of a home program of exercises.

• Support usually improves at 6 weeks
• Three months brings even more significant results

Devices-Pessary

60% of women with stress incontinence were dry

Knob sits under urethra to increase urethral support

Pessaries

• Even frail older women can do well with pessaries because they can be removed, cleaned, and reinserted every 4-6 weeks in clinic
• Contraindicated in women with dementia who might be easily lost to follow-up
  – Neglected pessaries can lead to vaginal wall erosion and vesicovaginal or rectovaginal fistula formation

Knob sits under urethra to increase urethral support
Surgery for SUI

- Urethral bulking agent
  - A synthetic material is injected into the layers of the urethra to "bulk" it up and increase outlet resistance
  - Cure + Improvement rates = 60%
  - Can be done without anesthesia
  - 10-15% chance of de novo urge incontinence
  - Small risk of urinary retention

Surgery for SUI

- Slings
  - Most common surgery for SUI
  - Support is placed beneath the bladder neck or urethra to support and close the opening when abdominal stressors increase pelvic floor pressure
  - Woman’s own tissue (fascia)
  - Synthetic polypropylene mesh
Fascial Slings SUI (Pubovaginal Sling)

- Two incisions
  - Bikini line or outer thigh
  - Vaginal
- Overnight hospitalization
- Patients can resume normal, non-strenuous activities 6 weeks after the procedure.

Mesh Slings SUI

- Minimally invasive
  - Incisions are very small
  - Procedural pain is minimal
- Outpatient surgery
- Designed to reduce recovery time
- Patients can resume normal, non-strenuous activities 4-6 weeks after the procedure.

Mesh Slings SUI

- Long term durability, safety, and efficacy up to 17 years
- 2,000 publications in the scientific literature
- The mid-urethral (mesh) sling is associated with less pain, shorter hospitalization, faster return to work, and reduced cost
- Over 3 million have been placed worldwide
- FDA: “The safety and efficacy of multi-incision slings is well-established in clinical trials that followed patients for up to one year”
- Position Statement on Mesh Midurethral Sling for Stress Urinary Incontinence, AUGS SUFU
Mesh Sling Outcomes in Elderly

• In a study evaluating for risk factors for failure of MUS, both age and menopausal status were evaluated
  – <50 (n=134), 51-60 (n=144), 61-70 (n=68), 71-80+ (n=52)
  – Increasing age is an independent RF for failure of both transobturator and retropubic midurethral slings.
  – Both sling approaches were significantly less efficacious in post-menopausal compared to pre-menopausal women

Rechberger T et al, Int Urogynecol J Pelvic Floor Dysfunct. Published online: 24 February 2010.

Mesh Sling Outcomes in Elderly

• Sevestre et al reported outcomes after mesh sling at mean 2 year follow-up in 76 women older than 70
  – 67% cure (questionnaires)
  – 21% de novo urgency, 5% de novo urge urinary incontinence
  – Cure rate is lower because of the increased risk of post-operative urgency.

• Hellberg et al also found that there was a significantly higher rate of de novo urgency in older women (20.9% vs. 13.8%)

Sevestre et al, Eur Urol 2003; 44:128-31
Hellberg et al, Int Urogynecol J 2007; 18:423-9
TAKE-HOME MESSAGES

THE DEMOGRAPHIC BURDEN

- If only Moderate, Severe, and Very Severe are considered
  - 24% men and women
- If only Severe and Very Severe are considered
  - 8% men and women

Irrespective of residence type, >70% of all home health/palliative care recipients either require a catheter or have incontinence.

70.3% long term residents

THE FISCAL BURDEN

- Surgery for SUI
- Cost of OAB-UUI
THE PERSONAL BURDEN

The health-related QOL impact of incontinence is similar to that observed with other chronic conditions such as OA, COPD, and stroke.

Take Home Messages

• Lower urinary tract (LUT) dysfunction in elderly women is almost always multifactorial
  – Identify risk factors and treat modifiable factors
• Overactive Bladder prevalence increases with age
  – Treatment benefits must be carefully weighed against adverse effects
• Surgical treatment of stress incontinence in elderly patients is less successful with higher rates of de novo urgency and urge incontinence

Goode et al, JAMA. 2010;303(21):2172-2181

References

Incontinence in Older Women

Goode et al, JAMA. 2010;303(21):2172-2181
Online Resources

- The Simon Foundation for Continence [www.SimonFoundation.org](http://www.SimonFoundation.org)
- Society of Urodynamics Female Pelvic Medicine and Urogenital Reconstruction (SUFU) [www.sufu.org](http://www.sufu.org)
- American Urogynecologic Society (AUGS) [www.VoicesForPFD.org](http://www.VoicesForPFD.org)
- National Association for Continence (NAFC) [www.NAFC.org](http://www.NAFC.org)