Updates in the non-pharmacological treatment on overactive bladder

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Overactive Bladder

- Also known as urgency-frequency syndrome
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgency</td>
<td>Sudden desire to pass urine that is difficult to hold</td>
</tr>
<tr>
<td>Daytime frequency</td>
<td>Frequent urination during daytime</td>
</tr>
<tr>
<td>Nocturia</td>
<td>Wake up at night one or more times to void</td>
</tr>
<tr>
<td>Urge urinary incontinence</td>
<td>Involuntary leakage of urine with or immediately after a sense of urgency</td>
</tr>
</tbody>
</table>
Treatment

**Behavioral therapy**
- Lifestyle guidance
- Bladder training
- Toileting assistance

**Drug therapy**
- Anticholinergic drugs

**#Physical therapy**
- PFX
- Biofeedback

**#neuromodulation**
- Electrical stimulation
- Magnetic stimulation
- Precutaneous PTN stimulation
- Implantable-type neuromodulation
Lifestyle Guidance
Bladder retraining
Toileting assistance

- elderly
Physical therapy

- Pfex
- Biofeedback
- Neuromodulation
Pelvic Floor Exercise

- Inhibit involuntary detrusor contraction
Mechanism

Voluntary contraction of PF

Inhibit parasympathetic excitatory pathway for micturition reflex & urge to void

Somatic motor efferents that contract striated external sphincter improve sphincter tone which prevent leakage during involuntary detrusor contraction

continence
Evidence

- Drug (oxybutynin & placebo) vs PFEx + biofeedback
- 197 women with urge/ mixed
- 80.7% reduction in exercise group + highest subjective improvement rate
- Significantly more effective than drug group
Evidence

- Bo and Berghams review: limited well controlled studies to come into conclusion
Biofeedback

- Patient awareness
- Adjunct to PFEx
Types of Biofeedback
Evidence

- 222 patients with self help booklet with or without biofeedback
- Improvement in all groups but no significant difference among groups
Evidence

- 12 week study of 103 patients
- PFEx at home and clinic based biofeedback
- Higher subjective improvement rate in biofeedback group
- Controversial
Evidence

Cochrane review 2011

“biofeedback may provide benefit in addition to pelvic floor training in women with incontinence. However, not clear whether it was the biofeedback that provided the additional benefit.”
Neuromodulation
Electrical stimulation

- Stress incontinence
- Transvaginal, transanal, precutaneous
- Inhibition of pelvic nerves by afferent stimulation of the pudendal nerve & hypogastric nerve
- Inhibition of bladder contraction by stimulation of efferent hypogastric nerve
Evidence

Cochrane Review 2006:

- Anticholinergic drugs vs non-drug active therapies for overactive bladder syndrome in adults without neurologic problems
- 23 trials with 3685 subjects
Cochrane review 2006

Bladder training alone

Anticholinergic drug*

Cochrane review 2006
Anticholinergic drug alone

Anticholinergic drug + bladder training*

Electrical stimulation (PTNS)*

Cochrane Review  2006
Precutaneous Posterior Tibial nerve stimulation
Randomised controlled trial

USA

Recruitment period: 2008-9

Study population: ambulatory adults with OAB symptoms

n = 220 (110 PTNS vs 110 sham)

Mean age (years): PTNS = 62.5, sham = 60.2
Sex: PTNS = 78% female, sham = 80% female

Patient selection criteria: ambulatory adults with OAB symptoms, age ≥ 18 years, score ≥ 4 on OAB-q short form for urgency, average urinary frequency ≥ 10 voids per day, bladder symptoms ≥ 3 months, self-reported failed conservative care, discontinued all antimuscarinics for ≥ 2 weeks. Exclusion criteria included pregnancy, neurogenic bladder, botulinum toxin in bladder or pelvic floor muscles within past year, pacemakers, current urinary tract or vaginal infection, use of sacral nerve stimulation, current use of TENS in pelvic region, back or legs, and previous PTNS treatment.

Technique: In the active treatment group, PTNS was delivered using the Urgent® PC neuromodulation system. Two inactive sham surface electrodes were also placed on the foot. In the sham group, a placebo needle was used (it gives the sensation of a slight prick but does not actually puncture the skin) and 2 active TENS surface electrodes were placed on the foot along with an inactive PTNS surface electrode.

Evidence

Number of patients analysed: 220 (110 vs 110)

Moderate or marked improvement in overall bladder symptoms at 13 weeks (global response assessment - intent to treat analysis)
- PTNS = 54.5% (60/110)
- Sham = 20.9% (23/110), p < 0.001

Global response assessment improvement at 13 weeks compared to baseline

<table>
<thead>
<tr>
<th></th>
<th>PTNS n (%)</th>
<th>Sham n (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary urgency</td>
<td>44/103 (42.7%)</td>
<td>24/105 (22.9%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Urinary frequency</td>
<td>49/103 (47.6%)</td>
<td>23/105 (21.9%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Urinary urge incontinence</td>
<td>39/103 (37.9%)</td>
<td>23/104 (22.1%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Voiding diary OAB symptom episode data (mean ±SD)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>13 weeks</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTNS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean voids/day</td>
<td>12.3 ± 3.2</td>
<td>9.8 ± 2.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Night time voids</td>
<td>2.9 ± 1.6</td>
<td>2.1 ± 1.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Voided volume (ml)</td>
<td>169.5 ± 78.9</td>
<td>183.0 ± 75.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Median number of urge incontinence episodes</td>
<td>3.0</td>
<td>0.3</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Moderate to severe urgency</td>
<td>8.3</td>
<td>3.7</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Treatment-related adverse events:
- Ankle bruising = 0.9% (1/110)
- Discomfort at needle site = 1.8% (2/110)
- Bleeding at needle site = 2.7% (3/110)
- Tingling in the leg = 0.9% (1/110)

No local treatment related adverse events were reported in the sham group.

No systemic adverse events were reported in either group.

Follow-up issues:
- 12 patients withdrew prior to 13-week follow-up. 5 patients withdrew consent (4 PTNS, 1 sham), 4 were lost to follow-up (2 in each group), and 3 withdrew for ‘other reasons’ (1 PTNS, 2 sham).

Study design issues:
- Patients were randomised using a random block design stratified by site.
- Subjects and study coordinators who administered questionnaires and reviewed voiding diary outcome measures were blinded to treatment assignment.
- Validated sham intervention.
- An intent to treat analysis was done, which counted any patient not assessed at 13 weeks as a failure.
- The OAB-q is validated for use in both continent and incontinent OAB patients. It consists of an 8-item symptom ‘bother’ scale (lower score means less symptoms) and 25 HRQL items, comprising 4 subscales (concern, coping, social interaction, sleep) and a total HRQL score. For the HRQL items, a higher score indicates better HRQL.

Study population issues:
- Baseline characteristics were homogenous across treatment groups.

Other issues:
- This study was published after the search date specified in the overview.
### Study details

**Peters KM (2009)**

**Randomised controlled trial**

USA

Recruitment period: 2006–8

Study population: ambulatory adults with OAB symptoms

\( n = 100 \) (50 PTNS vs 50 extended-release tolterodine)

Mean age (years): PTNS = 57.5, tolterodine = 58.2

Sex: PTNS = 96% female, tolterodine = 92% female

Patient selection criteria: ambulatory adults with OAB symptoms, with or without a history of previous anticholinergic drug use, with \( \geq 8 \) voids per 24 hours.

Exclusion criteria were OAB pharmacotherapy within the previous month, primary complaint of stress urinary incontinence, demonstrated sensitivity to tolterodine, pacemakers or implantable defibrillators, excessive bleeding, urinary or gastric retention, nerve damage or neuropathy, uncontrolled narrow angle glaucoma, positive urinalysis for infection or pregnancy.

**Technique**: PTNS was delivered using the Urgent® PC neuromodulation system. Parameters were maximised based on patient motor and sensory responses. Patients on tolterodine received a 90-day prescription for 4 mg daily with a subsequent decrease to 2 mg daily if the higher dose could not be tolerated.

**Follow-up**: 12 weeks

Conflict of interest/source of funding: supported by Uroplasty Inc.

### Key efficacy findings

<table>
<thead>
<tr>
<th>Subject assessment</th>
<th>PTNS (n = 44)</th>
<th>Tolterodine (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cured</td>
<td>1 (2.3)</td>
<td>2 (4.8)</td>
</tr>
<tr>
<td>Improved</td>
<td>34 (77.3)</td>
<td>21 (50)</td>
</tr>
<tr>
<td>Cured or improved*</td>
<td>35 (79.5)</td>
<td>23 (54.8)</td>
</tr>
<tr>
<td>No improvement/worsening</td>
<td>9 (20.5)</td>
<td>19 (45.2)</td>
</tr>
</tbody>
</table>

**Investigator assessment**

<table>
<thead>
<tr>
<th>Investigator assessment</th>
<th>PTNS (n = 44)</th>
<th>Tolterodine (n = 43)</th>
</tr>
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<tbody>
<tr>
<td>Cured</td>
<td>2 (4.5)</td>
<td>2 (4.7)</td>
</tr>
<tr>
<td>Improved</td>
<td>33 (75)</td>
<td>24 (56.8)</td>
</tr>
<tr>
<td>Cured or improved**</td>
<td>35 (79.5)</td>
<td>26 (60.5)</td>
</tr>
<tr>
<td>No improvement/worsening</td>
<td>9 (20.5)</td>
<td>17 (39.5)</td>
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</table>

**p = 0.01,** **p = 0.05**

### Voiding diary OAB symptom episode data (mean ± SD)

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<th>Baseline</th>
<th>12 weeks</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTNS (n = 41)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voids/day</td>
<td>12.1 ± 3.1</td>
<td>9.8 ± 3.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Nocturia</td>
<td>2.5 ± 1.2</td>
<td>1.7 ± 1.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Urge incontinence</td>
<td>2.2 ± 2.3</td>
<td>1.2 ± 1.6</td>
<td>0.007</td>
</tr>
<tr>
<td>Moderate to severe urgency episodes/day</td>
<td>6.0 ± 4.1</td>
<td>3.9 ± 2.8</td>
<td>0.002</td>
</tr>
</tbody>
</table>

### Key safety findings

Proportion of patients with at least 1 moderate adverse event reported to be related to the treatment:

- PTNS = 16.3% (8/49)
- Tolterodine = 14.3% (7/49)

In the PTNS arm, there was 1 report each of generalised swelling, worsening of incontinence, headache, haematuria, inability to tolerate stimulation, leg cramps, intermittent foot/toe pain and vasovagal response to needle placement.

Adverse events in the tolterodine arm included constipation, infection, dizziness, headache, vision disturbance, diarrhoea, increased frequency, fatigue, ear pain and abdominal pain.

In a repeated measures regression analysis during 12 weeks, constipation and dry mouth were reported less frequently in the PTNS arm compared to the tolterodine arm (\( p < 0.05 \)).

### Study design issues:

- Patients were randomised using a random block design stratified by site.
- The primary endpoint was mean reduction in number of voids per 24 hours (1-sided t test used with a non-inferiority margin of 20%).
- Secondary endpoints were analysed with 2-sided t tests.
- Two-day voiding diaries were collected at baseline and at 12 weeks, and were analysed by an independent biostatistician.
- The OAB-q is validated for use in both continent and incontinent OAB patients. It consists of an 8-item symptom ‘bother’ scale and 25 HRQL items, comprising 4 subscales (concern, coping, social interaction, sleep) and a total HRQL score. For the HRQL items, a higher score indicates better HRQL.

### Study population issues:

- Baseline characteristics were homogenous across treatment groups.
Long term effect
PTNS.....24 months

- 12 weekly 30 mins session program with 50 subjects
- RCT, 2 treatment session at 14-day interval, 2 treatments at 21-day interval, once in 28 day
- 110 subjects; 50 in study
Long term effect.....

- Sustained effect demonstrated

- Followed by a 14 week prescribed tapering protocol & a Personalized Treatment Plan with an average of 1.3 treatments per month.
Systematic review...PTNS

- Four RCT & 6 prospective observational cohort studies
- Strong evidence of efficacy vs sham
- Limited evidence the use of PTNS & tolterodine is equally effective
- 6-12 weeks – treatment period

Steinhauser & Berghmans 2013
Reference


