Detrusor Overactivity

DR. NOOR ASHANI MD. YUSOFF
DEPT. OF UROLOGY
INSTITUTE UROLOGY AND NEPHROLOGY
HOSPITAL KUALA LUMPUR
Detrusor overactivity (involuntary detrusor contractions) may cause by:

- neurologic origin (detrusor hyperreflexia) of idiopathic origin or
- caused by a variety of non-neurogenic clinical conditions (detrusor instability)
• Demonstrated ultrastructural changes in patients with detrusor overactivity that are thought to result in:
  – diminished electrical resistance between detrusor muscle cells.
  – a hyperexcitable state results in involuntary detrusor contractions.
TREATMENT

• Eliminate the underlying cause:
  – Urinary tract infection
  – bladder stones,
  – foreign bodies, and
  – bladder cancer
  – Neurologic causes are rarely remediable,
    • some (multiple sclerosis, transverse myelitis), process itself may remit.
    • Rarely, herniated disc or tethered spinal cord respond to neurosurgical procedures.
Future approaches may include:

1. other types of systemic pharmacologic therapy;
2. intravesical administration of drugs, including blockers of afferent input;
3. intradetrusor injection of botulinum toxin;
4. the use of tissue engineering to simplify augmentation cystoplasty;
5. genetic interventions to reverse neuroplasticity changes; and
6. combinations of these approaches.
• Abolish involuntary detrusor contractions:
  – medications,
  – behavior modification,
  – electrical stimulation, and
  – biofeedback
• Neuromodulation:
  – Electrical stimulation of sacral or peripheral nerves
  – result in muscle contraction, activation of reflexes,
    and modulation of some central nervous system
    functions
• Intravesical instillation
• Intradetrusor injection
• Augmentation cystoplasty.
• Urinary diversion.
• In 1959, Ingelman-Sundberg described:
  – a transvaginal technique intended to accomplish partial denervation of the subtrigonal nerve supply to the bladder (1959, 1978)
  – Only patients with refractory detrusor instability who respond favorably to a temporary nerve block should be considered candidates for the Ingelman-Sundberg procedure.
  – Despite encouraging preliminary results, this procedure has never achieved widespread acceptance, and there have not been enough studies to determine its efficacy.
Intravesical Treatment

• Vanilloids drugs:
  – Capsaicin
  – Resiniferatoxin

• Capsaicin-sensitive bladder afferents contribute to hyperactivity of the bladder in neurogenic and nonneurogenic detrusor overactivity
Intravesical Treatment

• Capsaicin:
  – A specific neurotoxin that desensitizes afferent C-fibers that may be responsible for the signals that trigger detrusor overactivity.
  – Resiniferatoxin is a less pungent agent that desensitizes capsaicin afferent C-fibers but fails to depolarize nerves
  • Further injections may be required (every 3 months)
FIGURE 1. Changes in (A) first detrusor contraction (FDC) and (B) maximal cystometric capacity (MCC) in patients with neurogenic detrusor overactivity treated with intravesical resiniferatoxin (RTX) 50 nmol/L or its vehicle solution (10% ethanol). NS = not significant. (Adapted with permission from Neurourol Urodyn.11)
Detrusor myectomy (autoaugmentation)

• Incising and removing the bladder muscle to form a pseudodiverticulum with bladder mucosa
• Successful in a small number of both males and females.

Detrusor myectomy (autoaugmentation)

- Detrusor myomectomy:
  - The detrusor muscle is excised from the anterior, lateral, and superior surface of the bladder.
Enterocystoplasty

- Create a low-pressure, large-capacity reservoir with low-filling pressure
- Reservoir:
  - Protects the upper urinary tract reflux and infection
  - Improves urinary continence.
- De-tubularizing the intestine into a sphere
  - Reduces disruptive peristaltic contractions
  - Increases bladder capacity
Enterocystoplasty

• The rate of good outcomes (improvement or stabilization of continence and upper tract deterioration) varies from 58% to 92%.

• The complication rate is 22%:
  – Urinary tract infections and mucus production can obstruct catheter or voiding (long-term care)
  – Urolithiasis and hydroelectrolytic abnormalities (hyperchloremic acidosis)
  – Long-term perforation ranged from 2% to 6%
  – Surgical revision ranges from 15% to 36%.
Enterocystoplasty

• Augmentation enterocystoplasty is effective, provided that these basic principles are followed:
  – the intestinal segment is detubularized by incising the antimesenteric border,
  – the segment is reconfigured into the approximate shape of a half-sphere,
  – a wide anastomosis between the reconfigured bowel and the bladder is performed, and
  – a large bladder capacity is achieved. Many patients, however, will require intermittent self-catheterization after augmentation.
Cutaneous diversion

• In some patients with severe refractory incontinence, a urinary diversion by ileal loop or continent reservoir may be indicated.
Cutaneous diversion

- A catheterizable stoma (umbilical site) linked to a reservoir (native or neo-bladder).
  - The reservoir can contain a large volume, under low pressure, without upper urinary tract flow back or absorption of urinary constituents.
  - The system can be continent (Mitrofanoff type) or not (Bricker type) and represents the last step procedure in the surgical management of an OAB.
Cutaneous diversion
Sacral root neuromodulation

- The **treatment is done in two steps:**
  - a **screening test** (percutaneous nerve evaluation):
    - a temporary wire electrode is inserted in the S3 foramen and an external pulse generator is used to identify patients who may benefit from the therapy;
  - **permanent neuroprosthesis implantation** in those who respond favorably to the percutaneous nerve evaluation.
Diagram of Brindley intervention.
The material is composed of an external block (stimulation box) that can deliver the current for acute stimulation (electromagnetic induction).
The implant is composed of cables (2) and internal electrodes (1) connected to a subcutaneous receiver block (}
Stimulation of Sacral Nerve Roots

Intradural device (Brindley technique).

Extradural device (Brindley technique).

Stimulation of Sacral Nerve Roots

Postoperative X-ray (Brindley technique).
The implant is composed of internal electrodes, cables, and the subcutaneous receiver block.
Sacral Neuromodulation

- Stimulation of the S3 nerve yields optimal results.
- Require testing prior to permanent device.
## Sacral Neuromodulation

<table>
<thead>
<tr>
<th>S3</th>
<th>contraction of the levator ani muscles, causing a “bellows” contraction of the perineum (deepening and flattening of the buttock groove); plantar flexion of the big toe (and sometimes other toes) related to sciatic nerve stimulation; and paresthesia in the rectum, perineum, scrotum, or vagina</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2</td>
<td>rotation of the leg or hip, plantar flexion of the entire foot, contraction of the calf, contraction of the superficial pelvic floor, and a pulling sensation in the genital area and in the leg</td>
</tr>
<tr>
<td>S4</td>
<td>activates the posterior levator ani muscles no motor response in the lower extremities, and pulling sensations involve only the rectum</td>
</tr>
</tbody>
</table>

Sacral Neuromodulation

• a long-term sacral neuromodulator was described by Schmidt and co-workers.
  – four electrodes and a larger stimulation zone than the temporary test stimulation lead
  – A 5-cm midline or paramedial incision made over the selected foramen.
  – distal end of the lead is inserted into the foramen and anchored to the lumbodorsal fascia

Sacral Neuromodulation

• Spinelli reported:
  – A new technique characterized by a percutaneous approach to the sacral nerves.
  – The procedure is minimally invasive and the patient can be awake during electrode placement.

Postoperative X-rays (sacral neuromodulation). The lead (implanted in the third sacral foramen) is connected to the neurostimulator placed in a subcutaneous pocket in the upper buttock. The neurostimulator generates current and must be changed every 7 years.
Sacral Neuromodulation

Puncture of the S3 foramen with Perc Nerve Evaluation needle at a 60° angle to the skin to follow the physiological path of the spinal nerve

Electrode fixation and final position of the electrodes and the impulse generator. The picture shows the final version with bilateral electrodes.
Two-stage implantation with permanent leads and external stimulator for extended subchronic testing.
Method of implantation for a peripheral N. pudendus
Sacral Neuromodulation

Fig. 3. Therapeutic results after permanent sacral neuromodulation with bilateral electrode implantation.
Efficacy and Safety of Sacral Nerve Stimulation for Urinary Urge Incontinence: A Systematic Review

Miriam Brazzelli,* Alison Murray and Cynthia Fraser

From the Department of Clinical Neurosciences, University of Edinburgh, Edinburgh and Health Services Research Unit, University of Aberdeen, Aberdeen, United Kingdom

Table 2. Success rates at 6 months in randomized, controlled trials

<table>
<thead>
<tr>
<th>References</th>
<th>Cured</th>
<th>Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stimulation group:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weil et al⁷</td>
<td>9/16 (56)</td>
<td>Not reported (29)</td>
</tr>
<tr>
<td>Schmidt et al⁵</td>
<td>16/34 (47)</td>
<td>10/34 (29)</td>
</tr>
<tr>
<td>Weil et al⁶</td>
<td>Not reported</td>
<td>5/5 (100)</td>
</tr>
<tr>
<td><strong>Delay group:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weil et al⁷</td>
<td>1/22 (5)</td>
<td>0/22</td>
</tr>
<tr>
<td>Schmidt et al⁵</td>
<td>0/42</td>
<td>2/42 (5)</td>
</tr>
<tr>
<td>Weil et al⁶</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

Cured—greater than 90% and improved—greater than 50% symptom decrease.
Botulinum Toxin

- Patients with idiopathic detrusor overactivity (IDO), with response rates ranging from 65% to 94%.
- Improvements seen typically last for approximately 9 mo.
- Injections have been repeated up to six times.
Botulinum Toxin

• 20 studies in subjects with IDO showed improvements in symptoms and/or urodynamic variables for most patients after treatment with BTX-A.

• There were significant overall improvements in:
  – urinary frequency,
  – voided volume,
  – urge urinary incontinence,
  – number of leakage episodes,
  – pad usage,
  – bladder capacity,
  – and quality of life.
Botulinum Toxin

- Continence was regained in 33–91% of patients with a duration of effect of 5–9 months.
- In 14 studies, the dose of Botox in adults was 300 U.
Botulinum Toxin: Adverse events

- Procedure related UTI:
  - The most common side-effect
  - 39 of the 791 adults or children, 4.9%
- Haematuria (13/791, 1.6%)
- Transient urinary retention (eight of 791, 1%, all with IDO).
  - Several patients (24, 3.0%, across all studies) required CIC for several weeks
Botulinum Toxin

• Many studies have used:
  – 300 U Botox diluted in 30 mL saline
  – injected at 30 sites (i.e. the dose per site being =10 U/mL),
  – both injection and dilution protocols have varied widely.
FIG. 1. Continence rates according to diluent volume across selected Botox studies (NDO patients).
<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Study design</th>
<th>BOTOX® dose</th>
<th>Efficacy</th>
<th>Adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chancellor 2003 (abstract)</td>
<td>10</td>
<td>Prospective</td>
<td>BOTOX® 100–300 U in 20–30 mL saline at 20–30 sites, including trigone</td>
<td>Decreased voiding frequency and decrease or absence of incontinence was reported by 90% of 100 pts. The duration of effect was ≥6 months in some pts.</td>
<td>None observed</td>
</tr>
<tr>
<td>Kessler 2005 [26]</td>
<td>11</td>
<td>Prospective</td>
<td>BOTOX® 300 U in 30 mL saline at 30 sites, trigone sparing</td>
<td>Complete continence was achieved in 10/11 (91%) pts. Treatment significantly reduced daytime frequency, nocturia, number of pads required and improved most urodynamic parameters. The median duration of response was 5 months.</td>
<td>4 pts had PVRs &gt;150 mL following treatment and required de novo CIC.</td>
</tr>
<tr>
<td>Kuo 2004 [30]</td>
<td>11</td>
<td>Prospective</td>
<td>BOTOX® 200 U in 8 mL saline at 40 sites, trigone sparing</td>
<td>Symptoms improved in 79% of 100 pts. The duration of the effect was 3–9 (mean 5.5) months.</td>
<td>Not separately stated for IDO and NDD pts.</td>
</tr>
<tr>
<td>Kuo 2005 [49]</td>
<td>9</td>
<td>Prospective</td>
<td>BOTOX® 200 U in 20 mL saline into the suburothelial space at 43 sites, trigone sparing</td>
<td>At 3 months, 9 pts were continent, 8 had improved and treatment had failed in 1. Corresponding figures at 6 months were 7, 8 and 5, respectively. 4 pts remained continent at 12 months.</td>
<td>1 pt hematuria, 6 transient urinary retention, 7 UTI, 10 elevated PVR.</td>
</tr>
<tr>
<td>Peeran 2005 (abstract) [50]</td>
<td>15</td>
<td>Retrospective</td>
<td>BOTOX® 50–100 U</td>
<td>After 18 months, 33% had symptom control after a single injection. 47% required a 2nd injection after a mean 7 months to sustain symptom control and 20% required a 3rd injection to sustain symptom control.</td>
<td>No postoperative complications reported.</td>
</tr>
<tr>
<td>Popat 2005 [34,51,79]</td>
<td>31</td>
<td>Prospective</td>
<td>BOTOX® 200 U in 20 mL saline at 20 sites, trigone sparing</td>
<td>All 100 pts who underwent follow-up at 4 (n = 26) and 18 (n = 17) weeks achieved predefined clinical response and experienced significant improvement of urodynamic parameters. Full continence was achieved by 13/24 pts (54%) at 4 weeks and 8/14 pts (57%) at 16 weeks.</td>
<td>No pts were initially receiving CIC. 1/31 pts (3%) required CIC following treatment. 2 pts developed UTI and 1 had flu-like symptoms.</td>
</tr>
<tr>
<td>Rapp 2004 [52]</td>
<td>35</td>
<td>Prospective</td>
<td>BOTOX® 100 U in 3 mL saline at 30 sites, including trigone</td>
<td>Complete continence was achieved in 54% of pts; 26% showed slight improvement and 40% showed no improvement. Significant improvements from baseline were still seen at 6 months.</td>
<td>Mild hematuria, pelvic pain and dysuria were reported by 7 pts for &lt;3 days.</td>
</tr>
<tr>
<td>Schmid 2004 (abstract) [56]</td>
<td>50</td>
<td>Prospective</td>
<td>BOTOX® 100–200 U at 10–20 sites</td>
<td>30% of pts showed significant improvement in symptoms and urodynamic parameters; mean duration 7 months.</td>
<td>2 pts had transitional urinary retention.</td>
</tr>
<tr>
<td>Author</td>
<td>N</td>
<td>Study design</td>
<td>BoNT-A dose</td>
<td>Efficacy</td>
<td>Adverse events</td>
</tr>
<tr>
<td>-----------------------</td>
<td>-----</td>
<td>----------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------</td>
</tr>
<tr>
<td>Schulte-Bacaklo 2005</td>
<td>44</td>
<td>Prospective</td>
<td>BoTOX® 200–300 U in 20 mL saline at 40–50 sites, including trigone. Pts with residues ≥15 mL also received an injection into the external sphincter.</td>
<td>Daytime frequency, pad usage and urodynamics parameters were significantly improved for up to 8 months, but were off by 9 months. A subjective response was achieved in 89% of pts. Pad usage was reduced to a lesser extent in pts receiving sphincter injections.</td>
<td>Sphincter injections were associated with a slightly higher incidence of stress incontinence. No treatment-related systemic or local events were reported.</td>
</tr>
<tr>
<td>Smith 2005 [56]</td>
<td>10</td>
<td>Prospective</td>
<td>BoTOX® 100 U in 10 mL saline at 10 sites, including trigone.</td>
<td>Subjective improvement rates were similar to those observed with a more common 30-site injection procedure (i.e. 90%). Responses lasted 3–6 months.</td>
<td>No urinary retention or increased PVR</td>
</tr>
<tr>
<td>Verleye n 2004 (abstract) [56]</td>
<td>11 children</td>
<td>Prospective</td>
<td>BoTOX® 125 or 250 U</td>
<td>Increase in functional bladder capacity, decrease in OAB contractions and urgency symptoms. 69% of pts were subjectively free of urge incontinence at 4 weeks, 83% at 12 weeks and 20% at 36 weeks. MCC and bladder compliance were significantly increased at 4 and 12 weeks.</td>
<td>1 pt required CIC for 2 weeks. 2 pts had elevated PVR requiring CIC for 1 week. 8 pts had UTI; no pt had acute urinary retention.</td>
</tr>
<tr>
<td>Wemer 2005 [60]</td>
<td>26</td>
<td>Prospective</td>
<td>BoTOX® 100 U in 30 mL saline at 30 sites, trigone sparing</td>
<td></td>
<td>4/7 pts reported improved symptoms; 3 pts did not respond. Improvements lasted for 3–20 weeks. No complications.</td>
</tr>
<tr>
<td>Zemmern 2001 (abstract) [11]</td>
<td>7</td>
<td>Prospective</td>
<td>5–7 BoTOX® injections of 50, 100 or 200 U, including trigone.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysport®</td>
<td></td>
<td></td>
<td>BoNT-A 200 U in 3 mL saline at 7 sites, trigone sparing</td>
<td>By 1 month, all 7 pts were continent.</td>
<td>No acute urinary retention or UTI</td>
</tr>
<tr>
<td>Radelewski 2001 (abstract) [10]</td>
<td>7</td>
<td>Prospective</td>
<td>BoNT-A 200 U in 3 mL saline at 10–15 sites, trigone sparing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Botox or Dysport® (results not separated)</td>
<td>15</td>
<td>Prospective</td>
<td>BoNT-A 100 U in 10 mL saline at 10 sites, trigone sparing. Dysport® 250 U in 10 mL saline at 10 sites, trigone sparing</td>
<td>5 pts (33%) required cisternice and 8 pts had a reduction in OAB symptoms. 75% of pts were very satisfied with treatment. The duration of efficacy was approximately 6 months.</td>
<td>Not reported.</td>
</tr>
<tr>
<td>Botulinum toxin type A (formulation not stated)</td>
<td>20</td>
<td>Prospective, randomized, drug dosage comparison</td>
<td>BoNT-A 100 U (n = 10) in 10 mL saline, trigone sparing. BoNT-A 150 U (n = 10) in 15 mL saline, trigone sparing</td>
<td>Efficacy outcomes were not significantly different between treatment groups. BoNT-A 100 and 150 U reduced urinary frequency ≤24 h by 63 and 12%, respectively. Both treatments increased total urinal volume by 144 mL.</td>
<td>No toxicity or hematuria. 1 pt had cystitis and a transient rise in PVR.</td>
</tr>
<tr>
<td>Gousse 2005 (abstract) [48]</td>
<td>20</td>
<td>Prospective</td>
<td>BoNT-A 100 U in 10 mL saline, trigone sparing.</td>
<td>Efficacy outcomes were not significantly different between treatment groups. BoNT-A 100 and 150 U reduced urinary frequency ≤24 h by 63 and 12%, respectively. Both treatments increased total urinal volume by 144 mL.</td>
<td>No toxicity or hematuria. 1 pt had cystitis and a transient rise in PVR.</td>
</tr>
<tr>
<td>Hampel 2005 (abstract) [47]</td>
<td>42</td>
<td>Prospective</td>
<td>BoNT-A 200–300 U at 20–30 sites</td>
<td>Median diurnal voiding frequency decreased from 16 to 8 (p &lt; 0.05) and mean MCC increased from 147 to 322 mL (p &lt; 0.001).</td>
<td>Not reported.</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Design</td>
<td>Intervention</td>
<td>Outcomes</td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>------</td>
<td>--------</td>
<td>--------------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>Rajkumar 2005 [52]</td>
<td>15</td>
<td>Prospective</td>
<td>BoNT-A 300 U in 30 mL saline at 30 sites, trigone sparing</td>
<td>Detrusor overactivity was eliminated in 6/15 pts (40%); 14/15 pts (93%) had improvement in urgency and frequency immediately after treatment. No acute urinary retention. No major adverse events were reported.</td>
<td></td>
</tr>
<tr>
<td>Sahai 2005 (abstract) [54]</td>
<td>18</td>
<td>Randomized, double-blind, placebo comparison</td>
<td>BoNT-A 200 U</td>
<td>BoNT-A significantly reduced urinary frequency and urge incontinence episodes compared with placebo for &gt;12 weeks. MCC was significantly reduced and QoL was significantly improved compared with placebo. Not reported</td>
<td></td>
</tr>
<tr>
<td>Schmid 2004 (abstract) [56]</td>
<td>50</td>
<td>Prospective</td>
<td>BoNT-A 100–200 U at 10–20 sites</td>
<td>40 pts (80%) showed significant improvement in symptoms and urodynamical parameters. Effects were apparent within 1–2 weeks, and mean efficacy duration was 7 months. Transient urinary retention in 2 pts</td>
<td></td>
</tr>
<tr>
<td>Schmid 2005 (abstract) [55]</td>
<td>100</td>
<td>Prospective</td>
<td>BoNT-A 100 U at 20 sites</td>
<td>88% of pts had significant improvements in symptoms and urodynamical parameters. Urinary completely resolved in 78% of pts and incontinence was resolved in 89%. The mean efficacy duration was 9 months. 3 pts had temporary urine retention; no severe adverse events occurred.</td>
<td></td>
</tr>
</tbody>
</table>

*Only the most recent results from this study have been tabulated. Study also included pts with NDO (see Table 1). CIC = clean intermittent catheterization; IDO = idiopathic detrusor overactivity; MCC = maximum cystometric capacity; NDO = neurogenic detrusor overactivity; PH = prostatic hyperplasia; PVR = postvoid residual volume; pt = patient; QoL = quality of life; UI = urinary tract infection.