Neurogenic detrusor overactivity: How to optimize treatment across different diseases

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Objectives

1. Define neurogenic detrusor overactivity (NDO) and identify its consequences

2. Discuss the considerations for treating NDO associated with:
   - Spinal cord injury
   - Multiple Sclerosis
   - Parkinson’s disease
   - Dementia
What is NDO?

“Involuntary detrusor muscle contractions occur during filling cystometry in the setting of a clinically relevant neurologic disease.”

Clinical relevance

Pathophysiology
- Suprapontine: loss of cerebral control of the micturition reflex
- Suprasacral: emergence of spinal reflex pathways mediated by c-fibers

Usually associated with storage symptoms (urgency, frequency, nocturia).
A common cause of incontinence in people with neurologic disease.
Is associated with renal dysfunction in some neurologic diseases.
NDO with incontinence significantly impairs quality of life and daily activities.
Urgency ≠ NDO all the time.

Chapple, NAU, 2014
Tang, BMC Neuro, 2014
## Treatment options

<table>
<thead>
<tr>
<th>Bladder Augmentation</th>
<th>Catheters</th>
<th>Anticholinergics</th>
<th>Intradetrusor Ona-botulinum toxin</th>
<th>Neuromodulation</th>
</tr>
</thead>
</table>

Each treatment has unique limitations

**Anticholinergics**
- Improves capacity by 50mL, decreased detrusor pressure by 40cmH₂O.
- Side effect profile
- Often need to use higher than labelled doses
- Cognitive changes
- Only a few high quality randomized studies have actually be done!

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**Anticholinergic Drug Exposure and the Risk of Dementia**

A Nested Case-Control Study

Carol A. Coupland, PhD; Three Hill, MS; Tom Owen, MD; Richard Morris, MD; Michael Murray, MS; Jill Hyslop, MD

**Original Investigation**

**Association Between Anticholinergic Medication Use and Cognition, Brain Metabolism, and Brain Atrophy in Cognitively Normal Older Adults**

Shannon L. Reisch, PhD; Beverly C. McDonald, PsyD; MBA; Allen F. Talamo, BS; John D. West, MD; Mantell Faliva, MD; Frederick M. Unverzagt, PhD; Sigurd Gus, PhD; Wille Hartaard, MD; MPh; Paul R. Giese, MD; MPh; Ronald C. Petersen, MD, PhD; Clifford R. Jack Jr., MD; William J. Jagust, MD; Paul C. Aisen, MD; Michael W. Weiner, MD; Andrew J. Saykin, PsyD; for the Alzheimer's Disease Neuroimaging Initiative

Madhuvrata, E Urol, 2012
Each treatment has unique limitations

Intrathecal ona-botulinum toxin
- May loss the ability to void spontaneously
- Expensive
- Limited duration of action
- 40% of neurogenic patients stop using it over time

Leitner, E Urol, 2016

Each treatment has unique limitations

Augmentation cystoplasty
- Major surgical undertaking
- 30 day readmission rate of 20-30%
- Followup surgery rate of 40%
- Must be willing to do catheters
- Life-long management of complications is required: stones, infections, renal dysfunction, metabolic changes, cancer, bladder perforation, bowel complications.

Cheng, W J Urol, 2019
Other treatment options

Beta-3 agonists
- Two small RCTs cautiously support their use for neurogenic detrusor overactivity

Neuromodulation
- Several case series suggest there may be a benefit, but limited quality and lack of randomized clinical trials.
- Costly

Spinal cord injury

Anticholinergics
- Randomized trials support urodynamic improvement
- Often can use at higher doses
- Often more tolerant of side effects
- 3-month study did not show cognitive changes in small population of SCI patients
- Oxybutinin vs newer agents

Intradetrusor ona-botulinum
- Randomized trials support urodynamic & QOL improvement
- Often already using catheters

Bladder augmentation
- Know when it is time!

The population most at risk of renal dysfunction!
### Multiple sclerosis

**Anticholinergics**
- Randomized trials support urodynamic improvement
- Consider newer agents
- May worsen underlying cognitive impairment

**Intradetrusor ona-botulinum**
- Randomized trials support urodynamic & QOL improvement
- But they often have to initiate CIC
- Consider a low dose

**Beta-3 agonists**
- Preliminary studies are promising
- Limited side effects

**Neuromodulation**
- Tibial or central

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### Parkinsons

**Anticholinergics**
- Small studies support symptom improvement
- Consider tolterodine (most studied)

**Intradetrusor ona-botulinum**
- Small studies (<25 patients) support symptom improvement
- PVR often rises, but CIC is uncommon (0-20%)

**Beta-3 agonists**
- Limited side effects

**Neuromodulation**
- Tibial or central

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Dementia

**Anticholinergics**
- Can be used with caution, but cognitive side effects are worrisome

**Intradetrusor ona-botulinum**
- Small studies support symptom improvement
- PVR higher in 60%, and CIC in 10%

**Beta-3 agonists**
- Limited side effects

**Neuromodulation**
- Tibial or central

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**Summary**

<table>
<thead>
<tr>
<th></th>
<th>SCI</th>
<th>MS</th>
<th>Parkinson’s</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergics</td>
<td>+++</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Beta 3 agonists</td>
<td>+/-?</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Intravesical Ona-botulinum</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Neuromodulation</td>
<td>-</td>
<td>++ (Tibial&gt;Central)</td>
<td>+ (Tibial/Central)</td>
<td>+ (Tibial)</td>
</tr>
<tr>
<td>Bladder augmentation</td>
<td>+++</td>
<td>+</td>
<td>Rare</td>
<td>Rare</td>
</tr>
</tbody>
</table>

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Brain Over Bladder: A Systematic Review of Dual Cholinesterase Inhibitor and Urinary Anticholinergic Use
Laura R. Vranghulda, Jamie A. Glazner, Emily F. Pera, Julie Rusher, Kevin M. Hamner<br>

Review
Intravesical OnabotulinumtoxinA Injection for Overactive Bladder Patients with Frailty, Medical Comorbidities or Prior Lower Urinary Tract Surgery
Chun-Hee Liao, Ching-Cheng Wang, and Yuan-Hong Jang
Conclusion

Always personalize the treatment to the patient; there are exceptions to all the rules in neurogenic bladder!

Don’t underestimate the negative impact on QOL if your treatment necessitates CIC.

With 2 oral medication classes, botulinum toxin and neuromodulation there are many different combination options available.

Aggressive treatment of NDO is necessary in SCI patients, as that is the primary population that is at risk for renal deterioration, and one of the risk factors is NDO.

An invitation...