Antimuscarinics for Overactive Bladder

Overactive bladder (OAB)

- Storage dysfunction, due to MS-related neurogenic detrusor overactivity (NDO)
- Symptoms – urinary urgency and frequency, nocturia, and/or incontinence

Antimuscarinics

- Block activity of detrusor and suburothelium
- Few trials in patients with MS
  - Oxybutynin, solifenacin – small trials in MS population
  - Propiverine, tolterodine, trospium chloride – studied in patients with NDO
- Non-selective – block all muscarinic receptor subtypes, throughout body
  - Low tolerability; common side effects include dry mouth, blurred vision, and constipation
  - May also cause urinary voiding difficulty
  - May have adverse drug interactions with other MS symptomatic treatments

Tornic J et al. *Curr Neurol Neurosci Rep*. 2018;18:54.

Mirabegron for Overactive Bladder

Mirabegron

- β_3-adrenoreceptor agonist
- Detrusor relaxant
- FDA-approved for OAB with NDO
- In placebo-controlled trials in general population (total N > 60,000), significant improvement in
  - Frequency, severity of urgency
  - No. of incontinence episodes
  - Dry rate
  - Quality of life
- Comparable efficacy to anticholinergics in general population
  - Confirmed in 2 trials in MS
- Favorable safety profile – nasopharyngitis only AE statistically more frequent relative to placebo
- Limited research into efficacy and safety in MS

AE, adverse event; NDO, neurogenic detrusor overactivity; OAB, overactive bladder.

Krhut J et al. *Res Rep Urol*. 2022;14:167-175.

Botulinum Toxin for Overactive Bladder

Botulinum Toxin for Refractory OAB[1]

- Intradetrusor injection
- FDA-approved for OAB due to NDO, 200U[2]
- In placebo-controlled trials in MS, improved:
  - Frequency of urgency
  - % with incontinence episodes
  - Dry rate
  - Involuntary detrusor contractions
  - Urinary retention
- Common adverse events in MS population
  - Urinary tract infection
  - Post-void residual
- Because of high risk of developing voiding dysfunction, consider limiting to population capable of self-catheterization

NDO, neurogenic detrusor overactivity; OAB, overactive bladder.

1. Kaviani et al. *Urol Clin North Am.* 2017;44:463-474; 2. Botox (onabotulinumtoxinA). Prescribing information. Allergan USA, Inc. 2022.

Neuromodulation for Overactive Bladder

Sacral Neuromodulation

- **Implanted** device that stimulates pelvic nerves
- Established therapy in general population for **medically-refractory** overactive bladder
- Small trials and observational studies in the MS population found improvements in urinary symptoms, catheterization frequency, and quality of life
- Adverse events: stimulation-related pain and hardware malfunctions

Percutaneous Tibial Nerve Stimulation

- Stimulation of posterior tibial nerve
- Mechanism of action unclear; possibly by depolarizing afferent fibers that inhibit bladder motor neurons in spinal cord
- In MS: improvement in urinary dynamics, urinary frequency, and post-void residual
- Only small trials and case-studies in MS population
- Implantable, battery-free devices being developed

Rahnama'i MS et al. *Mult Scler*. 2020;26:1274-1280.

Illustrations: Averbeck et al *Int Braz J Urol*. 2020;46:891-901 (CC) [Sacral]; Rahnama'i MS et al. *Mult Scler*. 2020;26:1274-1280. (http://CC/BY-NC/4.0/) [Tibial].

Treatments for Voiding Dysfunction

Causes of incomplete bladder emptying include:

- Detrusor external sphincter dyssynergia
- Detrusor underactivity (less common)
- Iatrogenic causes, including treatment for overactive bladder

Clean Intermittent Catheterization – First-Line Treatment

- Reduced risk of urinary tract infection compared with indwelling catheters
- Associated with decreased risk of urinary tract complications and increased quality of life
- May not be an option for many patients due to MS-related physical limitations

Alpha-1 Adrenergic Blockers

- Inhibit innervation of bladder neck and sphincter
- Only pharmacologic option for voiding dysfunction – first-line therapy for men with benign prostatic hypertrophy
- Very little research in the MS population
- Potential treatment option for men with MS, especially with comorbid prostate enlargement

Tornic J et al. *Curr Neurol Neurosci Rep*. 2018;18:54; Moussa M et al. *Intractable Rare Dis Res*. 2021;10:62-74.

Surgical Options for Lower Urinary Tract Disorders

Surgery – if refractory to or ineligible for all other options

- Overactive bladder
  - Augmentation cystoplasty (increasing bladder size)
    - Preserve renal function or restore continence
  - Suprapubic indwelling catheter
  - Non-continent urinary diversion
- Voiding dysfunction
  - External sphincterotomy

Moussa M et al. *Intractable Rare Dis Res*. 2021;10:62-74.