Spasticity in MS

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Disclosures

- I have received personal compensation for speaking from Sanofi-Genzyme and Teva Pharmaceuticals.
- I will be discussing off label and non FDA approved treatment.
Objectives

- Describe the epidemiology of spasticity in MS
- Choose the appropriate therapies for the management of spasticity in MS:
  - Pharmacologic
  - Non-pharmacologic
Overview

- Increased resistance of muscle(s) to an imposed stretch. Presents as intermittent or sustained involuntary muscle activation.

- Due to damage to the upper motor neurons of the cortical spinal tract.

- Affects the majority of persons with MS.

- One of the most disabling symptoms.

- Negative impact upon health and ability to work.
## Prevalence

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Subjects</th>
<th>Spasticity Diagnosis</th>
<th>Country</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodin, 1999</td>
<td>168</td>
<td>PSR</td>
<td>USA</td>
<td>70%</td>
</tr>
<tr>
<td>Rizzo et al, 2004</td>
<td>20,380</td>
<td>PSR</td>
<td>USA</td>
<td>85%</td>
</tr>
<tr>
<td>Milinis et al, 2015</td>
<td>701</td>
<td>PSR</td>
<td>UK</td>
<td>85%</td>
</tr>
</tbody>
</table>
Epidemiologic Trends

- Patients with more severe spasticity tend to be:
  - Older
  - Male
  - Disabled or unemployed
  - Longer duration of disease
  - More relapses

- Direct relationship to QOL
  - Fatigue
  - Depression
  - Anxiety
  - Pain
  - Bladder problems
Management of Spasticity

- Multi-disciplinary team management
- Patient, caregiver, nursing staff, therapist, orthotist, nurse practitioner, physician assistant, pharmacist, physician

Full assessment

- Address triggers that may have worsened spasticity
- Multi-modal therapeutic approach
Assessment

- Neurological Exam

- Scales:
  - Ashworth
  - Modified Ashworth
  - Penn Spasm Frequency Scale and Spasm Frequency Scale
  - Multiple Sclerosis Spasticity Scale (PSR)
  - NRS
  - Others
Pharmacologic Management

Oral Agents
Oral Medications

- (3) Approved for spasticity
- Baclofen, tizanidine, (dantrolene)
- Other oral agents:
  - Benzodiazepines: diazepam and clonazepam*
  - Gabapentin*
  - Carisoprodol**
  - Cannabis-based drugs***
    - * off label; ** disorder of MSK system; ***legal and other restrictions
General Principles

- Stepwise monotherapy approach typically preferred to combination drug use
- Gradually titrate to minimize side effects
- Gradual taper to avoid withdrawal
- Monitor LFTs
- Monitor for muscle weakness, sedation, respiratory depression
Baclofen

- GABA - the main inhibitory neurotransmitter in the mammalian central nervous system
- GABA analogue and GABA-B receptor agonist. Inhibits monosynaptic and polysynaptic reflexes at the spinal level.
- More effective when started at earlier stages
- Start at a low dose: 5 mg TID and increase gradually (by 5-15 mg/d Q 3days) until optimal effect is achieved (usually between 40-80 mg daily). More frequent dosing up to 5x/d may be helpful.
- Side effects: drowsiness, dizziness, weakness
Tizanidinide

- Centrally acting alpha-2 receptor agonist. Modulates release of glycine (inhibitory) and excitatory NT.
- To reduce spasticity without causing muscle weakness
- Start 2 mg at night, then titrate slowly to 36 mg/d divided up to 2-3 x/d
- Side effects: sedation, dizziness, lack of energy, dry mouth, elevated transaminases, orthostatic hypotension
Benzodiazepines

- Diazepam and clonazepam commonly used
- Diazepam: GABA A agonist. Increases presynaptic inhibition of polysynaptic and monosynaptic reflexes
  - 2-10 mg given in 2-4 x/d up to max of 30 mg/d
- Clonazepam: despite few supportive data used for phasic spasticity
- FDA black box warning. Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death.
- Rebound or withdrawal symptoms may occur following abrupt discontinuation or large decreases in dose. Use caution when reducing dose or withdrawing therapy; decrease slowly and monitor for withdrawal symptoms
Cannabinoids

- THC and cannabidiol (CBD) are the main cannabinoids in Cannabis sativa. CB1/CB2 receptor agonists in CNS

- CAMS study - investigated PO cannabis extract (THC + CBD) vs THC vs placebo in 630 patients with MS with spasticity (2005)

- Data from the 80% of patients in the 12 months follow up study showed evidence of a small treatment effect for THC on muscle spasticity as measured by change in Ashworth score from baseline to 12 months

- There were no major safety concerns. Overall, patients felt that these drugs were helpful in treating their disease
Cannabinoids

- Nabiximols (Sativex) approved in many European countries and Canada
- Oral spray of THC and CBD
- The efficacy of Sativex as add-on therapy in patients with MS who have moderate to severe spasticity has been demonstrated in several clinical trials, although <50% of patients are responders.
- Generally well tolerated without serious adverse events
Non-pharmacologic

- Rehab interventions
  - ROM and Stretching
  - Structured exercises
  - Positioning
  - Strengthening
- Home based programs
- Hippotherapy
- Repetitive magnetic stimulation (iTBS/rTMS)
Summary

- Spasticity has a high prevalence
- Broad and adverse impact
- Set goals of treatment
- Multimodal approach to ameliorate
- Importance of maximizing mobility and providing adequate treatment
Thank you for your attention
Key References


- Zajicek, JP et al. Cannabinoids in MS (CAMS) study: safety and efficacy data for 12 months follow up