Improving Spasticity Management in Stroke Patients

No disclosures...

OBJECTIVES
Will have a better understanding of...
- Spasticity review and measurement/Pearls
- Oral medication
- Chemodenervation agents
- Baclofen pumps/studies
- Alternative medication
- Treatment/Algorithm with review
Spasticity

First described by Lance in 1980

“A motor disorder characterized by velocity dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting in hyper-excitability of the stretch reflex, as one component of upper motor neuron syndrome (UMN)”

Lance J. Spasticity/Symposium synopsis 1980

Spasticity

- Occurs in about 30% of stroke patients
- Onset variables/25% will develop spasticity in first 6 weeks
- Upper extremities mostly involved
  - Elbow = 79%
  - Wrist = 66%
  - Ankle = 66%

PATTERN:
Arm Spasticity – Internal rotation and shoulder adduction with flexion of elbow, wrist, and fingers.
Lower Limb – Adduction, extensors of knee with equinovarus foot
Pathophysiology

- Loss of inhibitory control by descending corticospinal tracts
- Increased dependence on rudimentary brainstem-mediated descending motor tracts
- Increased sensitivity of stretch
  - Activates muscle spindles
- Pathological branching of spinal interneurons
- Hyperexcitability of alpha motor neurons

**Benefits of Spasticity**
- May help some with ambulation secondary to extensor tone
- May help with transfers (stand pivot)
- May assist in maintaining muscle bulk
- May assist in preventing DVT or osteoporosis
- Decrease of pressure ulcer formation
- If increase in spasticity, look for new noxious stimuli

**Complications of Spasticity**
- Interferes with function
- Difficulty in movement
- Abnormal posture
- Can cause discomfort or pain
- Difficulty in sitting and transfers
- Difficulty and hygiene and dressing
- Increased risk of heterotopic ossification (H/O)
- Increased risk of decubitus ulcers
- Contractures
- Joint subluxation/dislocation

**Modified Ashworth Scale (MAS)**

<table>
<thead>
<tr>
<th>Clinical Scale for Spastic Hypertonia</th>
<th>0</th>
<th>1</th>
<th>1+</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>No increase in tone</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Slight increase in muscle tone, manifested by a catch and release or minimal resistance at the end of the ROM when the affected part(s) is moved in flexion and extension</td>
<td></td>
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<tr>
<td>Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM</td>
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</tr>
<tr>
<td>More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved</td>
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</tr>
<tr>
<td>Considerable increase in muscle tone, passive movement difficult</td>
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</tr>
<tr>
<td>Affected part(s) rigid in flexion or extension</td>
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</tbody>
</table>
Modified Ashworth Scale

- Measures resistance to passive stretch
- Commonly used as a primary or secondary outcome measurement in clinical trials
- The most universally recognized metric
- Easy to perform and has a long history of use
- Tardieu Scale
  - Actually measures spasticity

Non-pharmacological Treatment

- Identify and avoid triggers/avoidance of noxious stimuli
- Physical treatments
  - Stretching, splinting/serial casting
- Postural management and standing
  - Systems to maintain alignment when sitting, standing, or lying in bed/skin inspection
- Exercises
  - Strengthening exercises improve motor control and function
- Other modalities:
  - Functional electrical stimulation, thermal, vibration, biofeedback, relaxation techniques

Medication
Oral medication

Baclofen (Lioresal)
- GABA Analog binds to GABA B receptors
- Inhibits Ca++ influx to presynaptic terminals
- P.O. dosage 5-80mg (some reports up to 300mg/day)

Side Effects:
- Somnolence
- Memory impairment
- Seizure risk with rapid withdrawal or hallucinations
- Weakness
- Increased Liver Function Tests
- Impaired Renal Function impairs clearance

Oral medication

Tizanidine (Zanaflex)
- Central Alpha 2 adrenergic agonist – (Clonidine Analog)
- Dose 2-36mg
- Presynaptic inhibition of motor neurons
- Effects 1-2hr after admit

Side Effects:
- Sedation/can be significant
- Monitor liver functions tests
- Avoid use with Cipro/or Fluroquinolones
- Weakness, dry mouth
- Caution with impaired renal function

Pharmacotherapy

Dantrolene
- Acts to inhibit sarcoplasmic reticulum release of Ca++
- Only peripheral acting spasticity medicine
- Acts directly on muscle with minimal central side effects
- 25-400 mg

Side Effects:
- Somnolence
- Hepatotoxicity/Peak at 3-12 month after starting
- Monitor liver function tests closely
Diazepam
- GABA A Hyperpolarization
- 4-60 mg/day
- Post synaptic facilitation of spinal cord GABA
- Consider for night time spasticity

Risks:
- High abuse/addiction potential
- Respiratory & CNS depression (caution especially with pain meds)
- 50% lifetime risk of dementia
- Not ideal choice for elderly

Clonidine oral or transdermal patches
- Alpha 2 antagonist/control
- 0.1-0.4 mg
- Convenient patch form

Risk:
- Decreased blood pressure
- Withdrawal or rebound after long-term usage, dry mouth

Less common spasticity medications
- Chlorpromazine (Thorazine)
- Glycine
- Threonine
- Cannabinoids
- Opiates
Chemoneurolysis

Phenol
- 2-7%
  - Lower concentration demyelination with decreased axonolysis
  - > 5% chemical denervation > 6 month duration

Ethyl Alcohol
- 45-100% concentration
- Less used
- Less toxic

Complications: dysesthesia/pain/systemic reaction with phenol

Chemodenervation

<table>
<thead>
<tr>
<th>Serotype</th>
<th>Established Name</th>
<th>Trade Name</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Abobotulinumtoxin A</td>
<td>Dysport</td>
<td>Ipsen</td>
</tr>
<tr>
<td>A</td>
<td>Onabotulinumtoxin A</td>
<td>Botox</td>
<td>Allergan</td>
</tr>
<tr>
<td>A</td>
<td>Icobotulinumtoxin A</td>
<td>Xeomin</td>
<td>Merz</td>
</tr>
<tr>
<td>B</td>
<td>Rimabotulinumtoxin B</td>
<td>Myobloc</td>
<td>Scottie</td>
</tr>
</tbody>
</table>

Botox - Mechanism of Action Video

https://www.youtube.com/watch?v=dkpohXE06pg
Chemodenervation - Costs

Botox 100 units: $601 per vial

Xeomin 100 units: $482 per vial

Dysport 300 units: $491 per vial

Myobloc 5,000 units: $531 per vial

* Per Cox Pharmacy Ambulatory Inventory Specialist as of 11-2-17

Chemodenervation – Type A Differences

<table>
<thead>
<tr>
<th>Stabilization</th>
<th>Botox 100 Unit vial</th>
<th>Dysport 300 Unit vial</th>
<th>Xeomin 100 Unit vial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excipients</td>
<td>Human Serum Albumin 0.5 mg/vial</td>
<td>Human Serum Albumin 0.125 mg/vial</td>
<td>Human Serum Albumin 1 mg/vial</td>
</tr>
<tr>
<td></td>
<td>NaCl 0.9 mg/vial</td>
<td>Lactose 2.5 mg/vial</td>
<td>Sucrose 4.7 mg/vial</td>
</tr>
<tr>
<td>Shelf Life</td>
<td>36 months (100 U vial)</td>
<td>24 months (300 U vial)</td>
<td>36 months (100 U vial)</td>
</tr>
<tr>
<td>Storage Temperature</td>
<td>2-8 C (36-46 F)</td>
<td>2-8 C (36-46 F)</td>
<td>-20-25 C (-4-77 F)</td>
</tr>
<tr>
<td>Post Reconstitution</td>
<td>24 hrs 2-8 C (36-46 F)</td>
<td>4 hrs 2-8 C (36-46 F)</td>
<td>24 hrs 2-8 C (36-46 F)</td>
</tr>
</tbody>
</table>

Summary of Chemodenervation

Botulinum-toxins

- Best for focal spasticity (recommend EMG guidance)
- Combined with other treatment options
  - Oral antispasticity meds
  - PT/stretching/splinting, etc.
  - Adjunct to baclofen pumps
  - Not so painful
- Phenol – low cost, long term efficacy
- Risks:
  - Dysesthesias, painful, systemic reaction and collateral non-selective tissue destruction
Intrathecal Baclofen

- Directly delivers baclofen to Intrathecal space
- Less sedating than oral meds
- Programmable
- Can use with Chemodenervation, therapy, and oral meds

ITB Pump

SISTERS Study

(RANDOMIZED STUDY [SISTERS])
NOV, 2009-SEPT, 2016

National Library of Medicine
Multicenter/International randomized, controlled, open-label, parallel-group study

Compare the effects of Intrathecal Baclofen (ITB) vs Best Medical Treatment (BMT)

Both had physiotherapy

What is it?
- Post stroke > 6 months
- At least 2 extremity involvement
- Severe spasticity (Modified Ashworth Scale (MAS) >/= 3) in at least 2 muscle groups
- Run phase 2 -25 days
- 6 month active trial
- PT follow protocol entire study
- MAS baseline/3months & 6 months with FIM scores

What is it?

Sisters

Functional Improvement Score (FIM Score)
- ITB – increased 2.68
- CMM decrease 2.58
- P value 0.054
### Adverse Events

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Implanted N = 25</th>
<th>BMT/Non-Implanted N = 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>14 (56%)</td>
<td>6 (17.1%)</td>
</tr>
<tr>
<td>Device</td>
<td>9 (36%)</td>
<td>NA</td>
</tr>
<tr>
<td>Procedure</td>
<td>6 (24%)</td>
<td>1 (2.9%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Serious events</th>
<th>Implanted N = 25</th>
<th>BMT/Non-Implanted N = 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>6 (24%)</td>
<td>1 (2.9%)</td>
</tr>
<tr>
<td>Device</td>
<td>4 (16%)</td>
<td>NA</td>
</tr>
<tr>
<td>Procedure</td>
<td>1 (4%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

### Most common adverse events

<table>
<thead>
<tr>
<th>Adverse events (most common)</th>
<th>Implanted N</th>
<th>BMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscular weakness</td>
<td>4 (16%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Hypotonia</td>
<td>3 (12%)</td>
<td>0</td>
</tr>
<tr>
<td>Urinary Retention</td>
<td>3 (12%)</td>
<td>0</td>
</tr>
<tr>
<td>Somnolence</td>
<td>0%</td>
<td>3 (8.6%)</td>
</tr>
<tr>
<td>Fall</td>
<td>3 (12%)</td>
<td>0</td>
</tr>
</tbody>
</table>

### Sisters Results

- 1st study with stroke patients on ITB vs Conservative Medical Management (CMM)
- Significant improvement in UE spasticity with ITB
- Adverse side effects > with ITB vs BMT or CMM
- Improvement in generalized spasticity with ITB
- Function improvement gains with ITB
- Somnolence reported in CMM/BMT group only
Drawbacks

- Increased weakness with ITB vs CMM
- Increased falls
- Urinary retention
  - **With above still had better increase in FIM scores**
  - **Study did not add Chemodenervation**
  - **Uncertain long term affects**

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Lastly...

Don’t forget our surgical options

- **Orthopedic**
  - Lengthening
  - Tendon transfers
  - Releases
  - TAL
  - SPLATT (Split Anterior Tibial Tendon Transfer)

- **Neurosurgery**
  - Selective dorsal rhizotomy
  - Cerebellar deep brain stimulators
  - ITB pumps

The Stroke Rehabilitation Team

- Occupational Therapist
- Physical Therapist
- Speech Therapist
- PT aide
- PT assistant
- OT aide
- OT assistant
- Respiratory Therapist
- Nursing
- Support partner
- Stroke Survivor
- Neurologist
- Primary care physician

Spasticity Pearls

1. Don’t just look at Modified Ashworth Score

2. How is spasticity affecting their lives (what is their goal for treatment)

3. Observe:
   Walking, transfers, wheelchair propulsion, positioning

Pearls cont...

4. Lidocaine block Trial – Reversible

5. Botulinum Neurotoxin A - pharmacological treatment of first focal spasticity

6. Medical Management should always be supplemented by therapeutic management for optimal improvement
Pain Management & Spasticity

1. 65% of patients with spasticity report pain
2. Does treatment of spasticity decrease pain
3. Botulinum Toxin A decrease pain in hemiplegic stroke patient with shoulder pain & spasticity
   A) Injections shoulder muscle groups (Internal rotator/adductors/pec major & teres major)
   **No difference between placebo and injections for pain

Analgesia

Analgesia for Botulinum Toxins Injection

- Procedures:
  - Brachial plexus blocks
  - Bier block
  - Sedation
  - ICE/Vapocoolant spray
  - EMLA (lidocaine/prilocaine topical)* reported best
Alternative Spasticity Treatments

1. Review of Medicinal Marijuana for spasticity management
2. Synthetic Cannabinoids
   A) Marinol – Oral THC
   B) Cesamet – Synthetic Oral THC Analogue
3. Phytocannabinoids
   A) Sativex (Canada/UK) – Herbal cannabis extract

Active Ingredients

Anandimide
- Endocannabinoid – pain, depression, appetite, memory, fertility

Delta-9-tetrahydrocannabinol (THC)
- Most psychoactive – "feeling high"
- High concentrations in sativa species, moderate in indica species

Cannabidiol (CBD)
- Less psychoactive – "feeling relaxed"
- Higher concentrations in indica species vs. sativa species
Safety Issues
- Doubles chance of driving accidents
- Dependence and withdrawal can occur
- Strongly associated with other illicit drugs
- Negatively impacts IQ with adolescents
- Effects on Respiratory Health (most also smoke tobacco)
- Increased risk cardiovascular side effect and increased stroke risk

Clinical Trial
- Mostly open label trials
  - Tolerable and safety/few major adverse effects
  - Positive self reporting effects of spasticity intensity
- Less clear evidence of objective decrease in spasticity
  - No change in Ashworth scores
- Very little drop out in studies

Spasticity Tx Conclusions
- Multidisciplinary/multi modal approach
- Know when to treat and when not to treat
  - What to treat
- It is never too late to treat spasticity
- Chemodenervation has shown to be safe and > tolerability
- Review patient goal in order to individualize patient treatment
- Continue to monitor on continual basis to maintain or sustain functional gains
“Would ‘good enough’ be good enough for you?”

QUOTE FROM AAPM&R CONFERENCE 2017

References


*Carlock MD, Ben. Spasticity of Spinal Origin. AAPMR Conf 2017*

*Cherry Jun MD. Spasticity. 3/5/17 Univ Washington program*

