THE IMPACT OF BOTULINUM TOXIN ON PEOPLE WITH UMN SYNDROMES

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ASSISTIVE TECHNOLOGY CLINIC
OBJECTIVES

- Review the definition of “spasticity”
- Examine assessment tools used to set Rx goals
- Consider the medical treatment options available
- In particular Botulinum Toxin A (BoNT)
- Discuss some examples of UE and LE adjunctive therapies post BoNT
- Appraise the evidence in the literature with regards to BoNT and adjunctive therapies
- Questions
SPASTICITY - DEFINITION

• The generally accepted definition and the one you will most see in the literature is by Lance (1980) who defined spasticity as:

• “A motor disorder characterized by a velocity dependent increase in tonic stretch reflexes with exaggerated tendon jerks, resulting from hyperexcitabilty of the stretch reflexes, as one component of the upper motor neuron syndrome”

SPASTICITY

• The term “spasticity” is used broadly to refer to many kinds of skeletal muscle over activity.
SPASTICITY CLASSIFICATIONS

• In children it is a common symptom of cerebral palsy.

• In adults – common in Stroke, MS, TBI, SCI, and anoxic-ischemic encephalopathy

• In Parkinsons and other movement disorders - dystonia

• In dementia patients it is known as paratonia
UPPER MOTOR NEURON

- In all these conditions, damage occurs to the upper motor neuron pathways (UMN)

- Originate in the motor cortex, brainstem and carry on through the spinal cord.
EFFECTS OF DAMAGE TO UMN

**IMMEDIATE EFFECTS**
- The immediate effects of an UMN injury are
  - weakness, paralysis
  - loss of coordination
  - Loss superficial abdominal reflexes
  - These are called the negative effects.


**DELAYED EFFECTS**
- Exaggerated stretch reflexes
- Flexor and extensor spasms,
- Deep tendon hyper reflexia
- Clonus
- Disinhibition of nocioceptive (protective) reflexes
- Disinhibition of primitive reflexes
- Loss of reciprocal inhibition
- Spastic co-contraction
- and other associated reactions.
- These are called positive effects
Damage to Higher Centers = UMN

Immediate Consequences (Negative Signs)
- Paralysis
- Immobilization in Shortened Position

Immediate Consequences (Positive Signs)
- Rearrangement of Spinal Activity
- Altered Supraspinal Patterns of Activity

Immediate Consequences (Mixed Negative and Positive)
- Various Types of Muscle Overactivity
  - Spasticity (↑ phasic & tonic stretch reflexes, clonus), flexor and extensor spasms
  - Co-contraction, associated reactions, spastic dystonia

Delayed Consequences (Positive Signs)
- Contracture
SPASTICITY - DEFINITION

• Sheean (2006) suggests that this delay (the positive effect) arises through neuronal plasticity,

• Structural or functional rearrangement of the CNS occurs over time, which cause motor and sensory changes.

• Once developed, it usually doesn’t change.

SPASTICITY - DEFINITION

- So generally speaking, spasticity refers to a form of hypertonia

- Likely due to the delayed or positive effects of an injury to the upper motor neuron pathways

SPASTICITY - DEFINITION

• Burridge et al. (2005) define spasticity as: “disordered sensory motor control resulting from an UMN lesion, presenting as intermittent or sustained involuntary activation of muscles”

PATTERNS OF SPASTICITY

• **FOCAL**
  Localize to an isolated area of the body. A hand or wrist or an ankle or foot.

• **GENERAL**
  Affects more than one body part. Overall muscle tightness and lack of coordination.

• **REGIONAL**
  Affects a large area of the body. For example, the waist and down as seen in late stage MS, SCI or CP.
COMPLICATIONS OF SPASTICITY

• Spasticity as a secondary complication of an UMN syndrome can become more of a limiting factor than the actual disease itself.

• It affects bed mobility, positioning, seating, skin integrity transfers, bowel and bladder function, hygiene, gait, hand and arm function, splinting, etc.

• So how do we identify, assess and begin to treat it?
IDENTIFYING THE ISSUES

- Identifying the problems usually depends on your practice environment:

  - **IN/OUT PT REHAB:**
    - Usually the **THERAPISTS** working with the patient identify the problem
    - Begin to notice the delayed effects
    - Limb use Assessment: MMT, PROM, start to see flexor/extensor synergies
    - Affects Gait and Balance and Upper Limb use
    - Transfers: Level of assistance varies
    - ADL’s
    - Pain increases
IDENTIFYING THE ISSUES

- LTC /COMMUNITY
- Usually the NURSES OR CAREGIVERS that identify the problems
- Having difficulty bathing and dressing the patient
- Bed mobility is reduced
- Skin integrity is affected – pressure sores
- Transfers are being affected, level of assistance increases
- Seating and Mobility: Sliding out of their wheelchairs
REFERRAL FOR SPASTICITY MANAGEMENT

• Once identified – What do you do?

• Referral to a specialist (Physiatrist or Neurologist) or spasticity clinic is warranted

• Key to successful spasticity management is working collaboratively with the patient, caregivers and the team

• Communication from patient and care-givers extremely important for identifying realistic goals of Rx.

• Without this goal directed therapy – impossible to treat
SPASTICITY CLINIC GOALS

Tools:
- GAS - Goal Attainment Scale
- COPM - Canadian Occupational Performance Measure

  Allows patient to be fully involved in management plan

Typical goals include:
1. Improve function / mobility / dexterity
2. Facilitate other therapies
3. Ease discomfort due to muscle shortening and postural changes
4. Improve body image
5. Improve ADLs, hygiene
6. Decrease caregiver burden
7. Improve positioning in wheelchair
8. Improve skin integrity (ie pressure sore management, decrease shearing, etc.)
9. Delay or prevent surgery
SPECIFIC SPASTICITY ASSESSMENT TOOLS

- Modified Ashworth Scale (MAS),
  - This is the most commonly used assessment of spasticity
  - Considered the “gold standard” used in all the evidence based studies

- Tardieu Scale
  - Takes into account resistance to passive movement at both slow and fast speed (hence the velocity dependence that Lance mentions).

- REPAS — Resistance to Passive Movement Scale

- Biotone™ (new tool – not yet available)
MODIFIED ASHWORTH SCALE


- Measures resistance during soft tissue passive stretching. Developed in 1964

- Considered the gold standard, cited in all the literature

- An ordinal scale; ranging from 0 (no increase tone) to 4 (affected part rigid in flexion or extension).

- Changed (in 1987) to the Modified Ashworth Scale (MAS) to include the additional grade termed 1+
  (Bohannon & Smith, 1987)
TARDIEU SCALE

- Scale takes into account resistance to passive movement at both slow and fast speed (hence the velocity dependence that Lance mentions).
- The Tardieu describes two joint angles R1 and R2;
  - R1 is the angle of muscle reaction, defined as the angle in which a catch or clonus is found during a quick stretch (V3).
  - R2 is the full PROM is taken at a very slow speed (V1).
- R1 is then subtracted from R2 and this represents the dynamic tone component of the muscle. (Boyd 1999)
- Important because it can differentiate between non-neural factors (contracture) and neural factors (spasticity)
REPAS is a 26-item test used to assess resistance to passive movement in all four limbs of the body.

- 16 movements of upper limbs,
- 10 movements of lower limbs.

- Each item is rated by using the Ashworth Scale.

- The sum of the values represent the REPAS score which may range from zero (no resistance for any item) to 104 (limbs rigid for all items).

- It provides a global evaluation of spasticity status.
IBME BioTone™ System

Chris McGibbon, PhD and Andrew Sexton, PEng, Institute of Biomedical Engineering at the University of New Brunswick

Spasticity

*Instrumented stretch-reflex test*

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**Elbow Spasticity Report**

Patient ID: NS007 - Flexor
Sex: Male
Age: 59 years
Height: 170 cm
Weight: 84.8 Kg

Diagnosis: ABI(CVA)
MAS score - Clinician (c): 1+
    BioTone (b): 1+
BT-SRFX score: 4.8

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Fibre optic Goniometer - Chris McGibbon, PhD and Andrew Sexton, PEng, IBME, UNB-Fredericton.
TREATMENT OPTIONS

- Oral antispasticity medications:
  - Baclofen, Diazepam, Tizanidine,
  - Dantrolene

- Intrathecal Baclofen pumps

- Neurosurgical Rx:
  - Dorsal root rhizotomies –effective only at level of rhizotomy
  - Neurectomy –motor nerves only, rarely done

- Chemodenervation
  - Phenol injections
  - Botulinum Toxin-A

- Injections of BoNT have revolutionized the treatment of spasticity because it has few adverse effects and been shown countless times in the literature to significantly reduce muscle hypertonicity

SEROTYPES

- There are 7 serotypes (A-G) of botulinum toxin
- For focal spasticity available in 2 serotypes: Type-A and Type B (not used in Canada)

Type A comes in three formulations:

1. **Botox ® Allergan Inc.** was the only formulation used in Canada (until 2009) and is approved for many more uses than the others and is often used for “off label” type purposes

2. **Xeomin ® Merz Pharmaceuticals** arrived in 2009 - limited to UE limb spasticity, cervical dystonia, and blepherospasm

3. **Dysport ® Ipsen Pharmaceuticals** – arrived in Canada 2013 - cosmetic use only – but now actively getting into the therapeutic field of usage.
MECHANISM OF ACTION

- Prevents the release of acetylcholine from nerve terminals thereby averting muscle contraction and triggering slackening of the spastic muscle. Effects last for 3-4 months.
**BoNT MECHANISM OF ACTION**

- **BLOCKING**
  - Once inside cell, botulinum toxin type A blocks release of acetylcholine transmitter via chemical denervation of the neuromuscular junction.

- **RESPROUTING**
  - After a while - chemical denervation of neuromuscular junction stimulates nerve sprouting.

- **RE-ESTABLISHING**
  - Within 3-6 months a single nerve sprout establishes new neuromuscular junction. Muscle tone is restored and spasms return, making it necessary to repeat injections.
APPROVED USES IN CANADA

• Botulin Toxin Type A approved uses in Canada include:
  • Focal Spasticity
  • Dynamic equinus foot in CP
  • Cervical Dystonia
  • Hyperhidrosis of Axilla
  • Strabismus
  • Blepherspasm
  • Hemifacial Spasm
  • Cosmetic (wrinkles—specifically for glabellar lines)

• Therapists are often requesting “off label” uses
  • Particularly when requesting treatment for LE spasticity or regional spasticity
  • These interventions require units that are hundreds of times greater than the approved doses
  • Funding – needs to be pre-approved through ODB, Trillium, Insurance etc
  • Much depends on the skill of the physician and the method of injection used.
METHODS OF INJECTION

• Physician must select a method for ensuring precise needle localization

• Manual needle placement

• When injecting muscles that are difficult to palpate, guidance using an electromyography (EMG) device

• Or ultrasound-guided technique allows accurate guidance for the injection of BoNT

Final patient selection for BoNT injection is determined by:

- Establishing the appropriate treatment goals
- Ensuring that the posture is not a fixed contracture via assessment
- (usually established via x-ray or EMG)
- Determining that the spasticity is amenable to intervention
- Identifying the target muscles responsible for the problem
- Finally: Calculating the optimal dose of BoTN – here’s where you really need to work closely with the physician or spasticity management team
- Need the right amount of mix between reduced spasticity and BoTN induced weakness.
- Then you begin your adjunctive therapies.
ADJUNCTIVE THERAPIES

• COMMON ADJUNCTIVE THERAPY:

• STRETCHING, SPLINTING, CASTING, TAPING

• CONVENTIONAL PHYSIOTHERAPY

• SEATING / WHEELCHAIR POSITIONING

• FUNCTIONAL ELECTRICAL STIMULATION (FES)
ADJUNCTIVE THERAPIES

- NOT SO COMMON:
  - CONSTRAINT INDUCED MOVEMENT THERAPY
  - EXTRACORPOREAL SHOCK WAVE THERAPY
  - ROBOTICS/EXOSKELETONS
EVIDENCE FOR ADJUNCTIVE THERAPIES


- Looked at 268 randomized controlled trials assessing adjunct therapies post botulinum toxin injection for treatment of spasticity

- 8 adjunct therapies were identified:
  - Stretching
  - Casting and splinting
  - Taping
  - Conventional physiotherapy
  - Functional Electrical Stimulation
  - Modified CIMT
  - Robotics _ Motorized arm ergometer
  - Extracorpeal shock wave therapy

- Extracted data and assessed for risk of bias using Physiotherapy Evidence Database (PEDro) scale graded according to Sackett’s levels of evidence of the 268 studies screened only 17 met selection criteria
EXAMPLE 1
UE SPASTICITY

• Internally rotated, adducted shoulder
  – Pectoralis major
  – Latissimus dorsi
  – Teres major
  – Subscapularis
• Excessive flexor tone at elbow
  – Brachioradialis
  – Biceps brachii
  – Brachialis
• Pronated forearm with spastic wrist and finger flexors
  – Pronator teres
  – Pronator quadratus
  – Flexor digitorum profundus
  – Flexor digitorum superficialis
  – Flexor carpi radialis
  – Flexor carpi ulnaris

• Goal:
• Functional use of affected limb post stroke

L MCA STROKE
STRETCHING / SPLINTING

- Treatment;
- BoNT injection via EMG guidance
- Stretching
- Splinting
- Conventional PT/OT:
- Repetitive task oriented training for the affected limb
EXAMPLE 2
LE SPASTICITY

- Plantar flexed, inverted foot (equinovarus)
  - Soleus
  - Gastrocnemius
  - Tibialis anterior
  - Tibialis posterior
  - Extensor hallucis longus

Goal:
To stand and walk

Treatment:
BoNT, Casting, Taping
Conventional PT
CASTING/TAPING
EVIDENCE TO SUPPORT CASTING VS TAPING VS STRETCHING


• Carda et al (2011) studied the effects of casting vs. taping vs. stretching for one week following BoNT injection of the spastic equinovarus foot. After one week of the allocated intervention – all groups received 30 minutes of gait training and 20 minutes of stretching daily for one week with a PT.

• Casting was better than taping or stretching for improving MAS score, ankle passive ROM. 6 minute walking test and speed on the 10 meter walking tests.
• There was no difference between groups in the strength of the ankle dorsiflexors.
• The stretching group showed the least marked modifications in all parameters

• BUT HEY DON’T COUNT STRETCHING OUT YET!

• Carda S., Invernizzi M, Baricich A and Cisari C. Casting, taping or stretching after botulinum toxin type A for spastic equinus foot: a single blind randomized trial on adult stroke patients. Clin Rehabil 2011; 25 (12) : 1119-1127
EXAMPLE 3
PARATONIA

• Static deformity, Thumb in palm, paronychial infection (paratonia)

• Muscles Affected
  – Flexor digitorum profundus
  – Flexor digitorum superficialis
  – Flexor carpi radialis
  – Flexor carpi ulnaris

• Goals:
  • reduce deformity, clear infection, improve care

• Treatment:
  • BoNT injection of finger flexors
  • stretching and splinting
  • Outcomes: MAS, PROM, CB Scale
  • New position maintained by stretching and splinting

Pre-injection

Post injection
EXAMPLE 4
LE REGIONAL SPASTICITY

- Static deformity, Severe Adductor spasm
- Unable to complete perineal care

- Adductor spasticity
  - Adductor magnus
  - Adductor longus
  - Adductor brevis
  - Gracilis

- Other contributors
  - Pectineus
  - Iliopsoas (hip flexor spasticity often presents in conjunction with adductor spasticity)
  - Rectus Femoris


Late stage MS
STRETCHING LE

**Goal:**
- Enable the caregiver to wash and dress pt.
- To decrease caregiver burden

**Treatment:**
- BoNT with stretching

**Rx Outcomes:**
- MAS, QoL, CB scales, etc.
- Functional gain despite dependency

- Although stretching as an intervention had the least improvement in outcomes when compared with other therapies merits further research as an adjunct.
CONVENTIONAL PT
EVIDENCE


- Michael Ka-Wing See,1 Benedict Beng-Teck Taw,1 Edward Man-Tai Chan,2 Linda Yuk-Ying Chan,3 Shuk-Man Lo,4 Terrence Wing-Cheung Kwong,5Gilberto Ka-Kit Leung1 and Wai-Man Lui1Botulinum toxin injection and rehabilitation for neurosurgical patients with spasticity Surgical Practice (2016) 20, 66–72 doi:10.1111/1744-1633.12169

• Giovanelli et al. examined the effects of conventional PT post BoNT injection compared with BoNT alone in individuals with secondary progressive MS with focal spasticity of the upper or lower limbs.

• Found that MAS and Visual Analogue Scale (self report of satisfaction) were better in the group who received PT post injection vs just injection alone.

• Study was limited in the subjective nature of the outcomes and that they lacked a sham intervention in the control group.

• There is much variability in the BoNT injection techniques used such as total dose, method of localization, and dilution.

• Giovanelli M., Boriello G., Castri P, Properini L. and Pozzilli C. Early physiotherapy after injection of botulinum toxin increases the beneficial effects on spasticity in patients with Multiple Sclerosis. Clin Rehabil 2007; 21(4) 331-337.
POSITION IN WHEELCHAIR

- No support through right thigh
- Perched on right ischial tuberosity (developed a pressure sore on right IT)

- Muscles Affected:
  - Iliopsoas
  - Hamstrings

- Goals:
  - Decrease pressure
  - Increase sitting tolerance
  - Allow for use of standing wheelchair
There are no studies to date that have looked at the use of BoNT with seating and mobility systems.

Despite the lack of evidence, BoNT has transformed the way I as an OT practice in this arena of treatment.
SEATING AND POSITIONING

Late Stage CP
Therapists are requesting “off label” uses:
- Requesting treatment for LE and UE spasticity
- Using doses require units that are hundreds of times greater than the approved doses
'Absence of evidence does not mean evidence of absence'
**EVIDENCE TO SUPPORT FUNCTIONAL ELECTRICAL STIMULATION**

Mills, Patricia B., Finalyson, Heather, Sudol, Malgorzata, O'Connor, Russell

- **Functional electrical stimulation** (FES) applies small electrical pulses to paralyzed muscles to restore or improve their function.
- Electrical stimulation is the most frequently studied adjunct therapy to BoNT

- Hesse et al found the addition of electrical stimulation to BoNT decreased MAS score more than with BoNT alone in lower limb spasticity. Hesse S, Reiter F, Konrad M, and Jahnke MT Botulinum Toxin A and short term electrical stimulation in treatment of lower limb spasticity in hemiparetic patients Neurosci Lett 1995; 201(1) 37-40


- With respect to electrical stimulation – each study used different dosing and stimulation parameters (low frequency 4Hz – high frequency 25 Hz) timing, duration, frequency, intensity etc.
EVIDENCE TO SUPPORT CIMT


• Sun et al (2010) did a high quality study of the effects of CIMT vs. Conventional therapy post BoNT injection on chronic stroke patients with upper limb spasticity.

• There was a significant improvement in the MAS and use of their elbows and fingers for the intervention group compared to the control group.

• Very labour intensive treatment – hours of treatment and requires the patient to sign a contract stating that they will do the therapy at home and fill out their Motor Activity Logs

EVIDENCE TO SUPPORT SHOCK WAVE THERAPY

- **Extracorporeal shockwave therapy (ESWT)** is a treatment using focussed energy generated externally to the body and transmitted from a pad through the skin.

- The waves are abrupt, high amplitude pulses of mechanical energy, similar to soundwaves, generated by an electromagnetic coil or a spark in water.

- Santamato et al did a high quality RCT where they examined the effects of FES compared with shock wave therapy post BoNT injections for spastic finger flexors.

- Both interventions were started immediately post injection.

- Results showed that shock wave therapy had significant benefits compared with FES in all outcome measures.

ROBOTICS (UE)


  Showed no differences in outcomes between those that used the arm ergometry and those that had conventional OT and that in fact some showed worsening of their spasticity after use of the arm ergometer.


  They observed that the combination of short robotic treatment with BoNT for post stroke spasticity is effective in reduction of spasticity and improvement of severe motor impairment.
ROBOTICS (LE)

KSRD™ – B’Temia Inc

RE WALK™-Re Walk Robotics Inc.

EKSOSTM Ekso Bionics Inc.
DISCUSSION

• We know that the literature indicates that BoNT can decrease muscle tone.
• But when we combine adjunctive therapies with BoNT there seems to be a lot of inconsistency in the literature. Why the inconsistency?

• Part of the problem is that there is much variability in the BoNT injection techniques used such as total dose, method of localization, and dilution – so we are not really comparing apples to apples.

• Similarly with respect to electrical stimulation, shock wave therapy and robotics each study used different dosing and stimulation parameters timing, duration, frequency,
• (low frequency 4Hz – high frequency 25 Hz) intensity etc. Same with the CIMT studies.

• Given the resource demands of some of these therapies, further research is needed to determine whether the gains outweigh the costs of these interventions.
DISCUSSION

- Although stretching as an intervention had the least improvement in outcomes when compared with other therapies, this does not mean that this intervention does not improve outcomes.

- Stretching is minimally invasive and low resource intervention that is commonly prescribed so it merits further research as an adjunct therapy.

- Same applies to seating and positioning. Although there is no hard evidence supporting the use of BoNT for seating and positioning, we have many observational and case studies that show improvements.

- Mills points out that the outcome measures generally used in the literature relate to body structure and function from the ICF domains rather than activity and participation which are domains that should be evaluated in rehabilitation interventions.
FINAL TAKE AWAYS

• With regards to your patients:

• It is important to recognize spasticity and get it treated

• Find a physician or spasticity clinic in your vicinity that you can work with to get your patients what they need

• Make sure that you include the patients and caregivers in your goal directed therapy
FINAL TAKE AWAYS

• With regards to evidence based practice:

• It is important for clinicians to be knowledgeable regarding the current levels of evidence relevant to their practice even if independent replication of evidence is lacking.

• Further research on how these rehab methods are best delivered with respect to the domains of activity and participation need to be done

• As new rehabilitation methods are emerging consideration should be given to botulinum toxin-A as an adjunct to physical and occupational therapy treatment
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