The role of Botulinum toxin in the multi-disciplinary treatment of post-stroke spasticity

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### Questions to be discussed

- What is spasticity?
- How frequent is problematic spasticity?
- What treatment modalities are there?
- How to organize our spasticity team?
- How to assess and evaluate patients?
- What is the role of BoNT?

### What is spasticity?
**Definition of spasticity?**

“velocity dependent increase in muscle tone with exaggerated tendon jerks resulting in hyper-excitability of the stretch reflex in association with other features of the Upper Motor Neurone Syndrome.”

J W Lance 1980

“disordered sensori-motor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles”

Pandyan 2005 (Spasm Consortium)

Neurogenic/reflexogenic muscle stiffness vs. Non-neurogenic/tissue muscle stiffness

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**Upper motoneuron syndrome**

- **Positive symptoms**
  - Spasticity (Lance)
  - Increased flexor reflexes
  - Spastic dystonia
  - Spastic co-contraction

- **Spasticity**
  (Spasm consortium)

- **Negative symptoms**
  - Decreased selective muscle control/dexterity
  - Weakness
  - Fatigue

- **Secondary changes in spastic muscles**
  - Stiffness
  - Contractures
  - Fibrosis
  - Atrophy
Complexity of movement pattern

- Spastic hypertonia (Increased muscle tone)
- Increased tendon reflexes
- Increased musculo-cutaneous reflexes
- Spastic dystonia
- Dyskinesia
- Cocontraction
- Pathologic spread of reflexes

How frequent is disabling spasticity?
### Prevalence of spasticity

#### Table 1. Epidemiology of spasticity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
<th>Prevalence spasticity</th>
<th>Prevalence disabling spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>715/100,000 (14)</td>
<td>31% (16-18)</td>
<td>12% (16, 17)</td>
</tr>
<tr>
<td>MS</td>
<td>190/100,000 (10)</td>
<td>66% (22)</td>
<td>26% (22)</td>
</tr>
<tr>
<td>CP</td>
<td>170/100,000 (11)</td>
<td>85% (19, 20)</td>
<td>22% (27)</td>
</tr>
<tr>
<td>SCI</td>
<td>32.3/100,000 (12, 13)</td>
<td>65% (21)</td>
<td>27% (21)</td>
</tr>
<tr>
<td>TBI</td>
<td>150/100,000 (15)</td>
<td>35% (23)</td>
<td>19% (28)</td>
</tr>
</tbody>
</table>

*Abbreviations: MS (multiple sclerosis), CP (cerebral palsy), SCI (spinal cord injury), TBI (traumatic brain injury).*

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### Theoretical epidemiology of Spasticity in Finland

<table>
<thead>
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<th>Prevalence</th>
<th>Prevalence spasticity</th>
<th>Prevalence disabling spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>39325</td>
<td>12190</td>
<td>4719</td>
</tr>
<tr>
<td>MS</td>
<td>10450</td>
<td>6897</td>
<td>2717</td>
</tr>
<tr>
<td>CP</td>
<td>9350</td>
<td>7948</td>
<td>2057</td>
</tr>
<tr>
<td>SCI</td>
<td>1760</td>
<td>1144</td>
<td>475</td>
</tr>
<tr>
<td>TBI</td>
<td>8250</td>
<td>2888</td>
<td>1568</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>69135</strong></td>
<td><strong>31067</strong></td>
<td><strong>11536</strong></td>
</tr>
</tbody>
</table>
Regional differences in treatment with BoNT type A doses/ 100 000 inh.

Quantified as equipotent doses per 100 000 inh. Dysport 500U– Botox 200U – Xeomin 200U

Source IMS 2013, volume

Spasticity portion of total hospital BoNT use
doses per 100 000 inhabitants in Sweden

Quantified as equipotent doses per 100 000 inh. Dysport 500U– Botox 200U – Xeomin 200U

Source IMS 2013, volume
How many patients are having BoNT treatment?
4-24 % (?)

Potential number of patients with disabling Spasticity?
> 10 000 in Finland

What is the reason for this discrepancy?

What can and should be done?
- Implications for health care
- Implications for health economy
- Spasticity treatment as an indicator for post-stroke severity

Where are all the patients with Disabling Spasticity?
How can we find them? ... and can we manage?

What treatment modalities are there?
Treatment options

- Training, frequency and intensity (Body function and activity)
- Botulinum toxin
- Oral medication
- Intrathecal medication (ITB)
- Nerve block
- Casting and orthoses
- Aids, new or adaptation
- Surgery

Treatment algorithm

1. Describe patient problem and analyze its causes
2. Treat aggravating stimuli
3. Formulate treatment goals

- Physical treatment and training
  - Focal spasticity
  - Multifocal spasticity
  - Regional spasticity
  - Generalised spasticity
- Chemonervectomy of muscles with BoNT-A
- Denervation of muscle/nerve with phenol
- Surgical treatment: Hand surgery, Orthopedic surgery, Neurosurgery
- Systemic oral drugs
- Intrathecal baclofen (ITB)
- Kombinationsbehandling
How to organize and train your spasticity team?

The Spasticity Team

- Treat the right patients
- With the right combination of treatments
- As efficient as possible
  - Patient outcome
  - Cost efficacy
- Not what treatment, but rather what combination of treatments
Role of the Health care system

- Identify health problems
- Refer patients at the right time
- Supporting with adequate treatment
  i.e. physio- or occupational therapy

A system is greater than just the sum of individual parts...

....and therefore has the possibility to go further than the individual parts alone
The patient needs to be part of the team

Patient view

Professional view

Communication

Treatment plan

Evaluation

Patients view

- Who am I?
- What is important for me?
- What is my ideas of a good life?
- What has been my happy moments and disappointments?
- What do I want to achieve?

Spasticity is not the issue, it is the sum of limitations and possibilities what I can do and achieve
Professional view

- Pathophysiology (spasticity vs contracture)
  - Difference in pattern with different etiology
  - UMNS
- Treatment effects (and side effects of the treatment)
  - Differences with different treatments, systemic, focal, etc.
  - Differences in expected effect depending on etiology
  - Differences in side-effects depending on age, etiology, and gender
- Evaluating signs and symptoms
  - How big of a problem is the spasticity compared to other problems

Communication (skills of the physician/therapist)

- Very difficult!
- The only sure thing is…….
  - We will misunderstand the patient in some aspects
  - The patient will misunderstand us in some aspects
- How to handle this?
  - We have to develop and increase our communication skills
  - Confirming type of communication – we confirm the information given….
    - "I understand that you said…………is that what you meant?"
  - Using structured PROM’s (Patient Related Outcome Measures)
  - Reach consensus on Goals (documented and signed (?))
Treatment plan - repetition 😊

- Structured and coordinated
- Based on the agreed treatment (rehabilitation) goals
  - Preferably use standardized instrument like GAS / PROMs
- Realistic expectations (physician has to agree the goals)
- Structured and documented treatment plan has to answer:
  - What...
    - when.....
    - where to perform activities

Evaluation according to PROM´s and goals

Patient-Centric Approach to Spasticity Management

In the past we looked at patient as an object to be treated. Now we are going towards having the patient as a team-member, sharing her knowledge of herself, being a subject in the treatment process.
How to assess and evaluate patients?

ICF – body function, activity and participation

Patient evaluation
- Goal setting
- Treatment planning
- Treatment
- Reevaluation
- Modification of treatment

Health condition disorder or disease

Body functions & structure
- Activity
- Participation

Environmental factors
- Personal factors

http://www.who.int/classifications/icf/en/
Process of Patient Management

- Step 1: Define the problems of the patient
- Step 2: Patients resources and restraints
  - Cognitive function, emotions, sensory and motor function, ROM etc
- Step 3: Is there spasticity?
- Step 4: What treatment options do we have?
- Step 5: What can we achieve with our treatment?
- Step 6: Set the treatment goal together with the patient/caregiver!
- Step 7: Plan evaluation of treatment

Indications for Treatment

- Improved function (Transfer, Dexterity)
- Decrease symptoms (Relieve pain, decrease spasms)
- Ease use of orthoses
- Posture / bodily apprehension
- Decrease burden of care
  - Hygiene, bowel and bladder management, positioning, dressing
- Optimize / adjuvant for other treatments
- Hinder or delay need of surgery
### Examples of Outcome Measurement

<table>
<thead>
<tr>
<th>Bodily function</th>
<th>Activity/Participation</th>
<th>HrQoL/Health economy</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS</td>
<td>VAS</td>
<td>QoL instruments</td>
</tr>
<tr>
<td>Ashworth / REPAS</td>
<td>GAS</td>
<td>Global life satisfaction</td>
</tr>
<tr>
<td>Modified Tardieu</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PENN spasm score</td>
<td>COPM</td>
<td>Cost-effectiveness</td>
</tr>
<tr>
<td>Range of motion (ROM)</td>
<td>Gait analysis</td>
<td>Burden of care</td>
</tr>
<tr>
<td>Strength</td>
<td>Speed / endurance in</td>
<td></td>
</tr>
<tr>
<td></td>
<td>gait or wheelchair</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(10m FGT/CGT)</td>
<td></td>
</tr>
<tr>
<td>Neuroflexor</td>
<td>PEG test</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Box and block test</td>
<td></td>
</tr>
<tr>
<td>EMG</td>
<td>ARAT</td>
<td></td>
</tr>
<tr>
<td>Pendulum test</td>
<td>WMFT</td>
<td></td>
</tr>
</tbody>
</table>

### 10 meter Comfortable Gait Test

![Image of a person walking on a corridor](image-url)
Goals….goals….goals….goals

SMART
Specific
Measurable
Achievable and realistic
Resource sensitive
Timed

Different versions of Goal Attainment Scaling

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+2</td>
<td>Much more than expected: improvements clearly exceed the defined therapeutic goal</td>
</tr>
<tr>
<td>+1</td>
<td>Somewhat more than expected: improvement slightly exceeds the defined therapeutic goal</td>
</tr>
<tr>
<td>0</td>
<td>Expected goal: attains the defined therapeutic goal</td>
</tr>
<tr>
<td>−1</td>
<td>Less than expected: slight improvement, but below the defined therapeutic goal</td>
</tr>
<tr>
<td>−2</td>
<td>Equal to start: the patient's initial condition; no change</td>
</tr>
<tr>
<td>−3</td>
<td>Worse than at start</td>
</tr>
</tbody>
</table>

Turner-Stokes. Clin rehabil 2010
Ertzgaard et al J Rehabil Med 2011
Turner-Stokes J Rehabil Med 2011
What is the role of BoNT?

Neurotransmitter Exocytosis: Intracellular Inhibition with BoNT

- Botulinum Toxin Endocytosed
- Light Chain Cleaves Specific SNARE Proteins
  - Types B, D, F, G
  - Types A, C, E
  - Type C
- SNARE Complex Does Not Form
  - Membranes Do Not Fuse
- Botulinum Toxin
  - SV2-receptor
- Neurotransmitter Not Released

Reproduced with permission from Aman SS, et al. ANNA. 2001; 205:1861
**Indications**

- Spasticity (specific) approved indication
- Dystonia approved indication
- Hyperactive detrusor approved indication
- Hyperhidrosis approved indication
- Chronic migraine approved indication
- Tremor not approved
- Achalasia not approved
- Stuttering not approved
- Pain not approved
- Vaginism not approved
- Etc

"Pubmed today" publications:
- Botulinum toxin (BoNT) 17046
- Spasticity 13029
- BoNT AND spasticity 1356
- BoNT AND spasticity AND stroke 374
Evidence for BoNT-A

1. It is the most widely studied pharmacological intervention for focal post-stroke spasticity
2. A vast number of placebo controlled studies have shown good effect on spasticity (body function)
3. Several studies have shown effect on activity, e.g. Goal attainment scaling, gait etc.
4. Some evidence for cost efficacy
5. Several international guidelines for post-stroke spasticity recommend BoNT as first line of treatment for focal spasticity

Timeframe for effect

Effect starts = 12 hours
Clinical effect = 24-72 hours
Maximal effect 4-6 weeks (follow-up)
Average effect duration is 2-4 months (striated muscles)
How often to treat?

- Rule of thumb – not more often than every 12th week.
  - Risk for antibodies
- Be weighed against clinical indication
  - Risk for irreversible complications if treatment is not given
  - Being able to better use of other treatment resources

What muscles to treat?

- A multidisciplinary decision depending on treatment goals!
- Otherwise……more art than science??
Tecniques for muscle identification

- Anatomic localization
- EMG
- Nerve/muscle stimulation
- Ultrasound

Nordic tradition?

- Surface localization
- EMG for identification and depth
- Being sure on location?
- Yes
  - Inject
- No
  - Muscle stimulation
EMG and stimulation

Surrounding Structures

M. flexor pol. Ing

Department of Paediatric and Adult Movement Disorders and Neuropsychiatry - Institute of Neurogenetics - University of Lübeck
Side effects with BoNT

- To much weakness in treated muscles
- Spread to surrounding muscles
- Local pain and haematoma
- Flu-like symptoms
- Botulism
- Loss of effect (immunity? Change in muscles?...)

Our model – one possibility

- First visit after referral
  - physician, physiotherapist, occupational therapist
  - Evaluation and planning including treatment goal
- Second visit
  - Baseline evaluation, e.g. 10 meter gait etc
  - Treatment
  - Initiation of post injection treatment
- 6 week post-injection follow-up
  - Physio- occupational therapist evaluation
- 3-4 months
  - Second treatment
- One year follow-up
  - Evaluation according to baseline. Decision on continued treatment
BoNT and

- BoNT-A treatment should not be THE treatment, but combined with other treatment modalities.
- High intensity training/High volume = patient must be instructed to perform exercises themselves or with help.
- Systematic use of Guided self-rehabilitation

- Treat earlier and more coordinated