Hypertonia Management in Cerebral Palsy: Past ideas and lessons, Current practice and outcomes, Future innovations and possibilities.

AACPDM 72nd Annual Meeting, October 13, 2018
Montreal, Quebec, Canada

Objectives:
1. Summarize the available tools for tone management, their potential limitations and benefits.
2. Examine the current literature regarding the use of tone management modalities.
3. Explore less common uses of surgical techniques for symptom relief in cerebral palsy.
4. Review current efforts with deep brain stimulation therapy in cerebral palsy and learn early patient results.

The History of Hypertonia Management in Cerebral Palsy

The 19th and 20th Century

Sherrington, MD 1898
British Physiologist
Discovered a mechanism of spasticity
Spasticity developed from loss of inhibition from supraspinal structures
Developed neurosurgical techniques (in cats)
“Dorsal rhizotomy reduces spasticity in decerebrate animals”

Surgery on Peripheral Nerves

Lorenz 1887
First peripheral neurectomy (Oburator Nerve)
In combination with orthopedic surgery (adductor myotomy and tenotomy)

Stoffel 1912
Tibial neurectomy (“spastic foot”)
Median neurectomy (“spastic pronation of the forearm and hand”)

The History of Spasticity Management

Foerster 1908
German Neurologist and Neurosurgeon
First dorsal spinal root surgery
“Dorsal Rhizotomy”
- LES – 1915
  - lesional with spastic deficits
  - Take caudal second, from L1 to the L4, opening L4
  - Use electrosurgery to cut a median line
  - Encouraging results
  - LESSON: Tone reduction is great, but sensory deficits marked

LESSON: Dorsal rhizotomy is NOT reliably useful for U.S. spasticity

LESSON: Dorsal rhizotomy is NOT reliably useful for U.S. spasticity
Phenol in spasticity-history

- Earliest use of phenol for spasticity: by intrathecal route — Nathan, 1959 and Kelly, Gautier-Smith, also 1959 simultaneously reported intrathecal injections for relief of spasticity.
- Nerve Blocks with aqueous phenol— Khalili and colleagues in 1960's
- Phenol motor point blocks—Halpern and Meelhuysen in 1965

Oral Medications

- Diazepam 1966
  - Binds near the GABA(A) receptor increasing GABA's affinity for GABA(A) receptors, resulting in more presynaptic inhibition
  - Binds at the reticular formation (consciousness and alertness) and at spinal polysynaptic pathways (stretch reflex)
  - Produces generalized relaxation in spasticity and athetosis
  - Gracies et al. Muscle and Nerve, 1997
  - LESSON: balance the side effects of sedation with tone reduction

Surgery on Spinal Roots

- Munro 1945
  - Ventral root sectioning for severe spasticity
  - T12–S1
  - Caused severe weakness
  - LESSON: “Reserve this for severe refractory tone as seen in anoxic BIV”

- Gross 1956
  - French neurosurgeon
  - Introduced the concept of e-stim
  - Technique:
    - Cut 80% (4/5) L1–S1
  - LESSON: Leaving 20% allowed maintenance of sensory function in 70% of patients
  - Noted incidental improvement in UE tone and better speech and better swallowing function

- Kottke and Heimburger 1970
  - Superior cervical rhizotomy for UE tone
  - C1–C3
  - (not C4–C6 2/2 preserving the diaphragm)
  - (not C5–C6 2/2 preserving UE sensation)
  - LESSON: Only slightly reduces spasticity (70% reducing tonic neck reflexes?)

Dorsal Root Entry Zone surgery

- Sindou 1972
  - Technique:
    - Microsurgical “rhizotomy” in the “dorsal root entry zone” and the “dorsal horn”, aka the “DREZotomY”
  - LESSON: Recommended for use in severe quadriplegia (anoxia) and patients with severe UE tone due to resistant severe facial hypotonia
Oral Medications

The History of Spasticity Management

- **Dantrolene 1973**
  - Potentially effective against spasticity and athetosis
  - Long-acting skeletal muscle relaxant - effect is on the muscle rather than CNS
  - Inhibits the release of Ca++ at the sarcoplasmic reticulum
  - Found to be helpful in approximately 50% of the patients
  - LESSON: significant side effect is weakness
  - Nance and Young, Phys Med Rehabil Clin North Am, 1996

- **Levodopa 1972**
  - Effect is at the basal ganglia
  - LESSON: best used in those with athetoid cerebral palsy
  - Rosenthal et al, Neurology, 1972

Surgery on Spinal Roots

The History of Spasticity Management

- **Fraioli and Guidetti 1977**
  - Technique: “Partial Dorsal Rhizotomy”
  - Cut dorsal ½ of the root just before the dorsal-lateral sulcus
  - LESSON: we can avoid sensory loss by leaving a large part of the nerve root intact.

- **Fasano 1976**
  - Technique: “Functional Dorsal Rhizotomy”
  - Use of bipolar e-stim to select abnormal nerve rootlets

Surgery on Peripheral Nerves

The History of Spasticity Management

- **Gros 1977**
  - French Neurosurgeon
  - Introduced the concept of unipolar e-stim to localize the functions of different fascicles of the nerve for more selective neurotomies

- **Simelz Lyon, France 1980**
  - Used bipolar e-stim and microdissection to further localize the nerve functions and be more selective

- **Garland and colleagues 1980**
  - Orthopedic surgeon
  - Microsurgical partial neurotomies of the median nerve
  - Combined with finger and wrist flexor lengthenings

- **Brunelli and Brunelli 1983**
  - Orthopedic surgeons
  - Microsurgical partial neurotomies of the ulnar nerve

- **Decq 1997**
  - Sectioning of branches of the brachial plexus for shoulder spasticity
Surgery on Spinal Roots

The History of Spasticity Management

- Peacock 1986
  - Intraoperative monitoring during selective posterior rhizotomy technique and patient outcome
  - Technique described as needle electrodes placed in muscle groups of each lower extremity:
    - adductors
    - quadriceps
    - hamstrings
    - tibialis anterior
    - gastrocnemius
  - After August 1986, additional electrodes were placed in the external anal sphincter

Selective Dorsal Rhizotomy: efficacy and safety in an investigator-masked randomized clinical trial

  - N=21 SDR + PT, N=17 PT only
  - SDR: group I = 52 with 26% rootlets cut (range 14-50%)
  - SDR group had a significant reduction in spasticity, while the PT only group did not.
  - Ambulation status at 12 months was equivalent, but at 24 months the SDR group had exceeded the PT only group.
  - LESSON: SDR is excellent at reducing spasticity and improves gait outcomes over time

Surgery on Spinal Roots

The History of Spasticity Management

  - N=11
  - Immediate reduction in spasticity
  - Increased ROM early and nearly normal ROM at 10 years post SDR
  - No effect on cadence, but improved step length to normal range at 3 years post SDR
  - 5/11 had orthopedic surgery
  - LESSON: a control group needs to be studied to evaluate definitively for benefits

Oral Medications

The History of Spasticity Management

- Gabapentin
  - Structurally similar to GABA – does not activate GABA receptors, instead it works by increasing brain levels of GABA
  - Studied in MS, SCI and heme facial spasm – not studied in CP
  - LESSON: consider it for use in cerebral palsy?

Injectable Medications

The History of Spasticity Management

- Botulinum Toxin A
  - First used by ophthalmologists for strabismus and blepharospasm
    - 1983
    - Koman, Mooney, Smith and Goodman → tx’d external ocular varus
    - Wall et al. → tx’d thumb-in-palm deformity
    - 1994
    - Cosgrove, Corradin and Graham → tx’d LE spasticity
    - 1997
    - Cosgrove, Corradin et al. → tx’d hemicerebral CP spasticity

Oral Medications

The History of Spasticity Management

- Alpha-2 adrenergic agonists (Clonidine/Tizanidine)
  - 1993
  - Hyperpolarize motor neurons
  - Decrease the release of excitatory amino acids
  - Effect on interneurons
  - Effect on presynaptic inhibition
  - LESSON: hypotension, depression, dry mouth, nausea/vomiting, reversible liver enzyme elevations (2-5%)
    - Young et al, Neurology, 1997
    - Gracies et al, Muscle Nerve, 1997
    - Alonso, Semin Neurol, 1991

Gait before and 10 years after rhizotomy in children with cerebral palsy spasticity

  - N = 11
  - Immediate reduction in spasticity
  - Improved ROM early and nearly normal ROM at 10 years post SDR
  - LESSON: consider it for use in cerebral palsy?
Injectable Medications
The History of Spasticity Management


- Simpson DM et al.
- Neurology 2008;70:1691–1698

LESSON: Botulinum neurotoxin should be offered as a treatment option for the treatment of spasticity in adults and children.

Intrathecal Baclofen (ITB) Pumps
The History of Spasticity Management

Intrathecal Baclofen for Management of Spastic Cerebral Palsy: Multicenter Trial

- Richard Gilmartin, MD; Derek Bruce, MD; Bruce B. Storrs, MD; Rick Abbott, MD; Linda Krach, MD; John Ward, MD; Karen Bloom, MD; William H. Brooks, MD; Dennis L. Johnson, MD; Joseph R. Madsen, MD; John F. McLaughlin, MD; Joseph Nadell, MD
- N=51, age 4-31 (mean = 10)
- 44 patients proceeded to the long term trial
- followed 4-43 months (mean = 28 months)
- Effective in reducing spasticity of cerebral origin.
- Relatively safe
- 42/51 patients reported adverse events but they were manageable
- Nausea/vomiting
- Drowsiness
- Hypotonia
- Seizures
- Somnolence
- Constipation

Intrathecal Baclofen for Generalized Dystonia in Cerebral Palsy

- “In patients with dystonia, the average daily dose = 575 mcg/day”
- Albright, J Neurosurgery, Jan 1998, Vol 88(p.73-6)

LESSONS: ITB is useful in treating spasticity and dystonia of cerebral origin, but further studies are needed; complications are common but frequently manageable.

Synchronized Infusion System

- approved by the FDA in 1992 for spinal origin spasticity
- in 1996 for cerebral origin spasticity

Intrathecal Baclofen in Cerebral Palsy Movement Disorders

- ITB reduces spasticity in patients with cerebral palsy in doses lower than baclofen but with clinically greater effects.
- Other ITB improves gait and upper extremity function.
- The Medtronic Pump is exceedingly reliable.
- Overdose errors are typically caused by programming errors and not pump malfunction.
- ITB reduces generalized dystonia in cerebral palsy, though higher doses are typically needed for the treatment of spasticity.


Infusion of Intrathecal Baclofen for Generalized Dystonia in Cerebral Palsy

- “ITB reduces spasticity in patients with cerebral palsy in doses lower than oral baclofen with considerably greater effects.
- ITB reduces generalized dystonia in cerebral palsy, though higher doses are typically needed for the treatment of spasticity.”


AACPDM Treatment Outcomes Committee Review Panel
Evidence of the effects of intrathecal baclofen for spastic and dystonic cerebral palsy

- Available features were reported and reviewed by the outcomes committee (May 2000)
- Spasticity
- Dystonia
- Limited evidence of efficacy regarding the outcomes reviewed
- Further studies are needed; complications are common but frequently manageable.

LESSONS: ITB is useful in treating spasticity and dystonia of cerebral origin, further studies are needed, complications are common but frequently manageable.

Entering the 21st Century

Reviewing Current Practice Trends in Tone Management

How we treat tone today
Oral medications for Hypertonia: what does the current literature say?

Oral medications for Hypertonia: Current Literature

All recent papers discuss defining goals of care:

- Optimizing comfort / care
- Quality of life
- Freedom from medication side effects
- Avoidance of polypharmacy impact as able in a patient with likely many comorbidities

No new class A or B data are available for oral medications.

What to tell my patient then?

Oral medications: Current Literature

- Levodopa/carbidopa
- Trifluoperazine
- Gabapentin
- Clonidine
- Tetrabenazine
- Baclofen
- Clonazepam
- Acetazolamide
- Zonagen
- Carisoprodol
- Tizanidine
- Dantrolene
Oral medications: Current Literature

But wait!

**Advances in management of movement disorders in children**

There is little evidence from randomised controlled trials on the best therapeutic strategies for the management of movement disorders in children; evidence to determine best practice for the management of abnormalities of tone and movement are particularly lacking.

**Oral medications: Current Literature**

What does the data look like?

**Dystonia: Treatment**

What does the evidence look like?

**Neurotoxins and alcohols**

Current practice trends & The Literature
HYPERTONIA MANAGEMENT IN CEREBRAL PALSY: PAST, PRESENT AND FUTURE

Neurotoxins

- Abobotulinum toxin A (Dysport)
- Incobotulinum toxin A (Xeomin)
- Letibotulinum toxin A (Botulax)
- Rimabotulinum toxin B (Myobloc)
- Daxibotulinum toxin A (phase 1; 6-9 mon duration)
- Type A – E combo

Table 1. Botulinum toxin pharmacol. properties: twitch test [10]

<table>
<thead>
<tr>
<th>Neurotoxin</th>
<th>Mouse</th>
<th>Human</th>
<th>Types</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abobotulinum</td>
<td>0.75</td>
<td>1</td>
<td>Type A–E</td>
<td>6–9 mon</td>
</tr>
<tr>
<td>Incobotulinum</td>
<td>0.05</td>
<td>1</td>
<td>Type B</td>
<td>3–6 mon</td>
</tr>
<tr>
<td>Letibotulinum</td>
<td>0.25</td>
<td>2</td>
<td>Type A</td>
<td>6 mon</td>
</tr>
</tbody>
</table>


- Abobotulinum toxin (Dysport)
- PLL spasticity equinus gait: randomized, double blind, placebo controlled trial
- High dose (15U/kg/leg, max 1,000 U)
- Moderate dose (10U/kg/leg)
- Placebo
- Significant difference in MAS, PGA at 12 wks
- 32% didn't have return of spasticity >28 wks


Chang, et al 2017: letibotulinum vs onabotulinum

- 144 pts w/ CP, equinus gait
- Randomized to leti vs ona
- Physician Rating Scale
  - Botulax: 60% improved
  - Botox: 61% improved
- Modified Tardeau Scale: both improved
- GMFM: both improved
- Adverse events: no difference

Scaglione 2016: Botox, Dysport, Xeomin conversion

- Previously treated patients who improved
- MAS
  - 15U/kg/leg: 83%
  - 10U/kg/leg: 70%
  - Placebo: 56%
- PGA
  - 15U/kg/leg: 91%
  - 10U/kg/leg: 87%
  - Placebo: 63%
Hypertonia management in cerebral palsy: past, present and future

**TrapoX botulinum toxin**
- Modify heavy chain of C terminus of A with B heavy chain
- Increases distal axon binding by 350%
- More endocytosis of light chain
- Increases duration of effect to 6-9 months
- Allows for less protein less frequently
- Higher risk of distal weakness if spreads

**Delgado, et al unpublished**
- 84 patients w/ CP
- E-stim followed by U/S
- E-stim in muscle:
  - 99% accuracy LE
  - 78% accuracy forearm muscles
- Didn't do it the other way around

**Grigoriu, et al 2015: Comparing E-stim vs Ultrasound**
- E-stim vs U/S: no significant difference
- EMG less accurate
- All better than manual palpation
- EMG great for active muscles
- All complimentary
- Can use palpation or motion to help with localization

**Picelli, et al 2013: compared palpation, e-stim, U/S**
- Randomized controlled trial
- Forearm muscles injected with Btx
- MAS, Tardieu scale
- U/S > palpation
- E-stim > palpation
- U/S = E-stim

**Hastings-Ison, et al 2015: Btx frequency**
- Randomized controlled trial
- Btx for spastic equinus
- Onabotulinum (Botox) into gastroc
  - Every 12 month group
  - Every 4 month group
- 6U/kg/leg
- No difference in ROM

**Dursun, et al 2017: Btx & PT vs Btx, PT, & casting**
- Randomized controlled trial
- Spastic equinus in CP
- Btx & PT vs Btx, PT, and 3 wks SLC
- Both had significant improvements in PROM, MAS, Tardieu, OGS, PGA
- Casting group > non-casting group
Combination EMG & E-stim

Phenol

Phenol in spasticity: history

- Earliest use of phenol for spasticity - by intrathecal route
  - Nathan, 1959 and Kelly, Gautier-Smith, also 1959 simultaneously reported intrathecal injections for relief of spasticity.
- Nerve Blocks with aqueous phenol - Khalili and colleagues in 1960's
- Phenol motor point blocks - Halpern and Meelhuysen in 1965

Wong, et al 2004
Phenol vs BTX in Ambulatory CP

- Phenol or BTX used in Amb. CP
- Gait analysis before and after treatment
- Increase in velocity and cadence, BTX > Phenol
Ofluoglu, et al, 2003
Retrospective review of phenol to obturator

- Phenol decreases tone
- Increases base of support (less scissoring) while walking

Karri, Mas, Francisco, Li, 2017:
Retrospective review of phenol

- 185 adults (n=293)
- CVA 42%, TBI 29%, SCI 24%
- 78% on oral spasticity Rx
- E-stim & U/S 69%, U/S 27%
- 3.5ml mean per nerve, 11ml mean total
- Obturator 36%, sciatic 27%
- 55% had post-injection assessment
- 85% subjective improvement
- Pain 4%, swelling 3%, dysesthesia 0.7%

Summary of Phenol Block

- Administration: Injected into motor points of involved muscle
- Duration of effectiveness: 4-12 months
- Advantages
  - Use is widely approved
  - Lasts longer than botulinum toxin
  - Cumulative effect often occur

Summary of Phenol Block (cont’d)

- Can be used with botulinum toxin to allow more injection sites and larger doses per site
- A good phenol block can reduce tone better than botulinum toxin, but technically more difficult
- Most often use phenol for easy to find nerves, i.e. obturator and musculocutaneous; then use botulinum toxin elsewhere
- Effective for plantarflexion and shoulder adduction

Summary of Phenol Block (cont’d)

- Drawbacks
  - Can be painful
  - May require general anesthesia during administration
  - Takes more skill to administer

Summary of Phenol Block (cont’d)

- Complications
  - Transient dysesthesias and numbness
  - Hematomas possible, negating effects of treatment
  - With large intravascular injection, systemic effects such as muscle tremors and convulsions, also depressed cardiac activity, blood pressure and respiration possible
  - Fibrosis or stiffness of muscle: “freezer burn”
**Phenol Dosing**
- 30 mg/kg – Matthew, et al.
- 7% = 70 mg/ml
- 5% = 50 mg/ml
- 0.5 ml/kg considered safe

**Common Injection Sites**
- Most common/easiest to inject
  - obturator nerves (to hip adductors)
  - musculocutaneous nerve (to biceps)
- Moderately difficult to inject
  - nerves to gastrocnemius, pectoralis, latissimus dorsi
- Most difficult to inject
  - nerves to hamstring, forearm muscles

**Hip Adductors**
- Anterior approach
  - Lat. to add. longus tendon near inguinal crease
  - Superficial and branch of obturator
  - Deeper – post. branch of obturator

- Medial approach
  - Posterior medial to add. tensors tendon
  - Post. branch 45° angle posterior
  - Ant. branch towards ASIS

**Hip Adductor**
- Groove btw gracilis and add. magnus
- Branch of obturator runs along ant. portion of muscle

**Phenol to obturator**
(try to get to <1 mA)
HYPERTONIA MANAGEMENT IN CEREBRAL PALSY: PAST, PRESENT AND FUTURE

Patient Selection
- Patients refractory to more conservative treatment
- Multifocal spasticity not addressed by botulinum toxin alone
- Patients resistant to botulinum toxin

Gastrocnemius
- Distal to popliteal crease
- Lateral and medial to midline
- Avoid posterior tibialis nerve
- Several motor points

Biceps
- Medial border
- 1/3 from axillary
- Avoid median nerve and brachial artery

Current Practice trends in Selective Dorsal Rhizotomy
- Surgical technique
- Rootlet selection
- Short term outcomes data
- Long term outcomes data
- Additional research findings

Neurosurgery
Current practice trends & The Literature

SDR Technique
- Cauda Equina
  - Larger opening
  - Anatomical localization
  - Most used
  - Long term outcomes data
  - Less bone removal
  - Less blood loss
  - Less painful
- Conus
  - Smaller opening
  - Venous drainage add risk
  - Less bone removal
  - More blood loss
  - More painful
- Keyhole interlaminar dorsal rhizotomy
  - No bone removal
  - Microsurgery
  - Localization less precise
  - Predetermined percentage of rootlets based on clinical findings

AACPDM ANNUAL MEETING, CINCINNATI, OHIO, USA
Many surgeons have many opinions on which technique is best.

- Some surgeons do one technique always
- Some surgeons choose their technique based on goals of the procedure, age of the patient, risks or patient/family preference
- No studies have been done comparing the outcomes of patients stratified by surgical technique

SDR Rootlet Selection

- Done differently at different institutions and by different surgeons
- Some add L1 and/or S2

Non-selective:Rootlet is identified and a given percentage is cut
- Gross—Selective: Rootlet is identified, divided into three parts, and each is stimulated at high level; the most pathologic appearing are cut; 33-67% are cut.
- Micro—Selective: Rootlet is identified, divided into multiple rootlets (10-20+), and each is stimulated at the lowest possible level and evaluated for abnormality; 20-40% are typically cut.

No correlation has been identified between highly spastic muscle groups/levels and number of rootlets cut following monitoring.

Questions remain as to whether or not “selective” vs. “random” root selection is superior.

Summary of short term outcomes

Many researchers have published on their short term outcomes with Selective Dorsal Rhizotomy.

Selective Dorsal Rhizotomy: meta-analysis of three randomized controlled trials

- Three short term outcome studies analyzed together
- Thirty patients, 15 SDR and 15 controls
- At 4, 9, or 11 months, or 12 and 24 months.
- 9 of 25 SDR patients did not complete.
- Conclusion: confirms clinically important long term benefits. There is no statistically significant advantage in the SDR group – improvements are of clinical but not statistical significance.

Current Practice trends in Selective Dorsal Rhizotomy

- Many researchers have published on their short term outcomes with Selective Dorsal Rhizotomy.

Summary of short term outcomes: assessment of selective dorsal rhizotomy

HYPERTONIA MANAGEMENT IN CEREBRAL PALSY: PAST, PRESENT AND FUTURE

AACPDM ANNUAL MEETING, CINCINNATI, OHIO, USA

15

Study Design

- Retrospective Analysis
- Subjects
  - Gait analysis 6-18 months prior to SDR
  - Gait analysis 8-36 months subsequent to SDR
  - SDR performed 1994-2003
    - Gillette Children’s Specialty Healthcare, or Shriner’s Hospital for Children—Twin Cities Unit

Outcome Measures

- Gillette Gait Index
  - Overall measure of gait pathology
- Gillette Functional Assessment Questionnaire
  - 10 level walking scale
- Oxygen Cost
  - Net nondimensional cost
- Ashworth Score
  - Sum of specific muscles

Outcome Categories

- Neutral
  - Pre: within typical range, Post: outside typical range
- Improved
  - Pre: outside typical range, Post: outside typical range, but closer to typical
- Corrected
  - Pre: outside typical range, Post: within typical range
- Maintained
  - Pre: within typical range, Post: within typical range
- Unchanged
  - Pre: outside typical range, Post: further outside typical range
- Worsened
  - Pre: within typical range, Post: outside typical range

Function: Gillette FAQ

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number</th>
<th>Age</th>
<th>Follow</th>
<th>Exp. Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>55</td>
<td>76</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>81</td>
<td>69</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>136</td>
<td>72</td>
<td>21</td>
<td>11</td>
</tr>
</tbody>
</table>

Age and Follow - 4y Time in Years

Mean pre = 7.3
Mean post = 8.2
Increase of 0.9 levels

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number</th>
<th>Age</th>
<th>Follow</th>
<th>Exp. Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>55</td>
<td>76</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>81</td>
<td>69</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>136</td>
<td>72</td>
<td>21</td>
<td>11</td>
</tr>
</tbody>
</table>

Age and Follow - 4y Time in Years

Mean pre = 7.3
Mean post = 8.2
Increase of 0.9 levels
HYPERTONIA MANAGEMENT IN CEREBRAL PALSY: PAST, PRESENT AND FUTURE

10/12/2018

AACPDM ANNUAL MEETING, CINCINNATI, OHIO, USA

Summary of long term outcomes

Current Practice trends in Selective Dorsal Rhizotomy

Function: Gillette FAQ

Walking more than 15-50 feet outside the home but usually uses wheelchair or stroller for community distances or in congested areas

Walking outside for community distances, but only on level surfaces (cannot perform curbs, uneven terrain, or stairs without assistance of another person)

Walking outside the home for community distances, easily gets around on level ground, curbs, and uneven terrain, but has difficulty or requires minimal assistance or supervision with running, climbing and stairs

Walking outside the home for community distances, is able to get around on curbs and uneven terrain in addition to level surfaces, but usually requires minimal assistance or supervision for safety

Many researchers have published on their long term outcomes with Selective Dorsal Rhizotomy

• 2011
  • F/U > 5 years, Pediatric patients, lumbar level SDR, cerebral palsy
  • 21 articles
• 1998-2010 (966 children)
  • Only 3 studies showed level III evidence (45 children)
  • Therefore, low strength and quality of evidence given low numbers.

LESSONS:
• positive long term effects on body structure and body function ICF domains.
• Long term effects on activities and participation domains and risk of spinal deformities remain uncertain.

Interestingly, of the 3 level III studies examined, 1 showed improvement in gait and one did not. The main difference between the studies: the two studies that found improvement in gait were on GMFCS level I-III patients and the study which showed no long term gait gains had an average GMFCS level of III.

Level of activity and participation in adults with spastic diplegic cerebral palsy 17-26 years post selective dorsal rhizotomy.

• Long-term functional benefits of selective dorsal rhizotomy for spastic cerebral palsy
  • Dudley et al., Neurosurg Ped 2013; vol 12; pp. 142-50
  • Conclusion: “Benefits of SDR are durable through adolescence and into early adulthood” and include:
    • Improved muscle tone
    • Gross motor function
    • Performance of ADLs
    • Decreased need for adjacent orthopedic procedures or Botox injections
    • Most likely to display these long-term benefits are those in GMFCS Groups I, II, and III, with:
      • Spastic diplegia
      • Less hip adductor spasticity
      • Preoperative GMFM score greater than 60

Summary of long term outcomes

Current Practice trends in Selective Dorsal Rhizotomy

Long-term functional benefits of selective dorsal rhizotomy for spastic cerebral palsy

Summary of long term outcomes

Current Practice trends in Selective Dorsal Rhizotomy

Summary of long term outcomes

Current Practice trends in Selective Dorsal Rhizotomy

Summary of long term outcomes

Current Practice trends in Selective Dorsal Rhizotomy

Summary of long term outcomes

Current Practice trends in Selective Dorsal Rhizotomy

Summary of long term outcomes

Current Practice trends in Selective Dorsal Rhizotomy

Summary of long term outcomes

Current Practice trends in Selective Dorsal Rhizotomy
Current Practice trends in Selective Dorsal Rhizotomy

Summary of long term outcomes:

Long-term effect of selective dorsal rhizotomy on gross motor function in ambulant children with spastic bilateral cerebral palsy, compared with reference centiles.

- For 5 and 10 years post SDR
- Conclusion: none of the patients deteriorated in motor function 10 years post SDR.

A prospective cohort study investigating gross motor function, pain, and health-related quality of life 17 years after selective dorsal rhizotomy in cerebral palsy

- Tedroff 2014
- Dev Med Child Neurol, 57: pp. 484-90
- Conclusion: Patient gross motor function was found to peak 3 years post SDR and declined by the 17 year follow-up GMFM score

Comprehensive Long-Term Outcomes Following Selective Dorsal Rhizotomy

Tom F. Novacheck, MD, Meghan E. Munger, MPH, Nanette Aldahondo, MD, Linda Krafl, MD, Michael H. Schwartz, PhD

1 Gillette Children’s Specialty Healthcare, St. Paul, MN, USA
2 Courage Kenny Rehabilitation Institute, Minneapolis, MN, USA

Goals

- Evaluate comprehensive outcomes 10-17 years after SDR
- Spasticity
- Gait
- Function
- Pain
- Quality of Life
- Subsequent Treatment

ICF DOMAINS

• Activity
• Participation
• Body Function and Structure

Hypothesis

SDR will lead to better outcomes and fewer subsequent treatments compared to a control group

Inclusion Criteria

SDR group
- Spastic diplegic CP
- SDR between 1995 and 2005
- Pre-SDR three-dimensional (3-D) computerized gait analysis
- Follow-up ≥ 8 years
- 16-25 years old at follow-up
HYPERTONIA MANAGEMENT IN CEREBRAL PALSY: PAST, PRESENT AND FUTURE

Strongly: Retrospection Identified Control Group

- propensity Model (Random Forest Algorithm):
  - age
  - gait
  - stature
  - function
  - CP subtype
  - treatment history
  - plantarflexor spasticity

Strength: Retrospectively Identified Control Group

95% accurate

- Sensitivity: 80%
- Specificity: 98%
- Pos. Pred. Value: 89%
- Neg. Pred. Value: 97%

Survey Measures

- Surveys at follow-up
  - DNR Satisfied with Life Scale
  - WHO's Quality of Life-BREF
  - Frequency of Participation Questionnaire
  - Functional Assessment Questionnaire
  - Functional Mobility Scale

Survey Measures

In brief...

- No difference in pain
  - Both groups had “low pain interference”
- No difference in QOL
  - Both group reported high QOL
- No difference in Gillette FAQ
- No difference in energy expenditure in gait
- Spasticity better in SDR group
- Fewer procedures in the SDR group (ortho and injections)
- Improvement in GMFCS Level in the SDR group
- Better GDI in the Control group

Current Practice Trends in Selective Dorsal Rhizotomy

- Gait:
  - “Changes in gait which occur before and during the adolescent growth spurt in children treated by selective dorsal rhizotomy.”

Current Practice Trends in Selective Dorsal Rhizotomy

- Weight Gain
  - Ambulatory children with cerebral palsy do not exhibit unhealthy weight gain following selective dorsal rhizotomy
  - Gutknecht et al., Dev Med Child Neurol, 2015, 57: 1070 – 5

Summary of additional findings

In Hemiplegic CP

- “Selective dorsal rhizotomy in children with spastic hemiparesis”
- Reduced spasticity in all patients, improved gait 1 – 10

Weight Gain

- All children fare well GMI levels showed improved functional performance and independence in daily activities up to 10 years postoperatively
- No evidence of unhealthy changes in BMI post SDR

Summary of additional findings

In brief...

- In Hemiplegic CP
  - “Selective dorsal rhizotomy in children with spastic hemiparesis”
- Reduced spasticity in all patients, improved gait 1 – 10

- Functional performance in self care and mobility after selective dorsal rhizotomy: a 10 year practice-based follow up study
  - Josenby et al, Dev Med Child Neurol, 2015, 57; 286 - 293
- All children from all GMFCS levels showed improved functional performance and independence in daily activities up to 10 years postoperatively

- Weight Gain
  - Ambulatory children with cerebral palsy do not exhibit unhealthy weight gain following selective dorsal rhizotomy
  - Gutknecht et al., Dev Med Child Neurol, 2015, 57: 1070 – 5
- No evidence of unhealthy changes in BMI post SDR

- No difference in pain
  - Both group had “low pain interference”
- No difference in QOL
  - Both group reported high QOL
- No difference in Gillette FAQ
- No difference in energy expenditure in gait
- Spasticity better in SDR group
- Fewer procedures in the SDR group (ortho and injections)
- Improvement in GMFCS Level in the SDR group
- Better GDI in the Control group

Summary of additional findings

In Hemiplegic CP

- “Selective dorsal rhizotomy in children with spastic hemiparesis”
- Reduced spasticity in all patients, improved gait 1 – 10

Weight Gain

- All children fare well GMI levels showed improved functional performance and independence in daily activities up to 10 years postoperatively
- No evidence of unhealthy changes in BMI post SDR

AACPDM ANNUAL MEETING, CINCINNATI, OHIO, USA
Current Practice trends in Intrathecal Baclofen Pumps

The effect of continuous intrathecal baclofen on sitting in children with severe cerebral palsy

Gray et al, 2014

Results:
- No significant difference was found in sitting before ITB treatment compared to sitting following insertion of ITB pump.
- No specific age group or classification of motor impairment demonstrated significant deterioration in sitting following ITB treatment.

Conclusion: Sitting does not improve or deteriorate in children following treatment with ITB, independent of age or severity of motor impairment.

Current Practice trends in Intrathecal Baclofen Pumps

ITB additional research

Long-term follow-up on continuous intrathecal Baclofen therapy in non-ambulant children with intractable spastic Cerebral Palsy

Van et al, 2013

European J Neurol, Vol 10, pp. 302-306

Results: decreased pain, improved ease of care, improved mental health

Current Practice trends in Intrathecal Baclofen Pumps

Controlled study of the effects of continuous intrathecal baclofen infusion in non-ambulant children with cerebral palsy

Morton et al, 2011

Dev Med Child Neurol, 53:736-741

Followed the patients over 18 months
- Caregiver Questionnaire was the main measure of quality of life: showed marked improvements in their overall score involving comfort, positioning, transfers, personal care

Current Practice trends in Intrathecal Baclofen Pumps

“IntraVENTricular baclofen as an alternative to intrathecal baclofen for intractable spasticity or dystonia: outcomes and technical considerations”

Turner et al, 2015

European J Neurol, Vol 13, pp. 929-935

N = 20
- Old age
- Offered to patients who failed ITB therapy
- This article describes the lower complication rate with ITB
- It does not describe any tone outcomes
- *essentially abandoned at this time*
Deep Brain Stimulation

Current trends &
The Literature

DBS: Quick Review

- In the US in 2003, the Medtronic Activa DBS device was granted limited FDA approval for primary and segmental dystonia in patients 7 years and older under a Humanitarian Device Exemption.

- The exemption allows targeting of the globus pallidus pars interna (GPI) nucleus or the subthalamic nucleus (STN).

DBS: Current Literature

- Dystonia primary or secondary or something new?
- Jinnah 2014, A new classification!


DBS: Current Literature

- Reviewing a few select studies oldest to newest

- Vidailhet 2005, prospective multicenter trial in patients with primary generalized dystonia who received double blind video assessment 3 months after surgery:
  - 29% improvement in the BFMDRS-m scale with DBS on compared to off.
  - After 12 months these patients with DBS turned on showed a 51% reduction in BFMDRS-m and 44% improvement in disability score.
DBS: Current Literature

- Kupsch 2006, DBS for primary generalized or segmental dystonia with double blind, multi-center, randomized trial controlled with sham stimulation for 3 months.
  - DBS improved scores BFM0RS-m and disability scores by 39.8% and 38% compared to baseline.
  - Sham group showed only 4.9% and 11% improvement in commensurate scores.

DBS: Current Literature

- Mills 2014, secondary (structural) dystonia and DBS review of available literature:

<table>
<thead>
<tr>
<th>Study/Dystonia Type</th>
<th>N</th>
<th>Scale/Score</th>
<th>Baseline Score</th>
<th>Follow-up Score</th>
<th>Percent Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitek et al. 2006</td>
<td>26</td>
<td>BFMDRS-m</td>
<td>40</td>
<td>26</td>
<td>57.5%</td>
</tr>
<tr>
<td>Mark et al. 2013</td>
<td>7</td>
<td>BFMDRS-m</td>
<td>55</td>
<td>30</td>
<td>31.5</td>
</tr>
<tr>
<td>Dyck et al. 2013</td>
<td>6</td>
<td>BFMDRS-m</td>
<td>55</td>
<td>30</td>
<td>45.5</td>
</tr>
<tr>
<td>Gilden et al. 2013</td>
<td>1</td>
<td>BFMDRS-m</td>
<td>55</td>
<td>30</td>
<td>45.5</td>
</tr>
<tr>
<td>CP</td>
<td>68</td>
<td>BFMDRS-m</td>
<td>64.9±18.54</td>
<td>49.9±18.3</td>
<td>23.9%</td>
</tr>
</tbody>
</table>

DBS: Current Literature

- Debate: Schjerling 2013, randomized double-blind crossover trial comparing subthalamic and pallidal deep brain stimulation for idiopathic (sporadic) / tardive dystonia

DBS: Current Literature

- Much controversy still surrounds:
  - Patient selection
  - Implantation method
  - Multiple target stimulation (STN + GPi?)
  - The future of shaping stimulation fields
  - Electrophysiological biomarkers that might provide real time feedback to assist with chrono-stimulation

Palliative Rhizotomy

Current Trends & The Literature
OF Future Directions and possibilities
HYPERTONIA MANAGEMENT IN CEREBRAL PALSY: PAST, PRESENT AND FUTURE

**Albright, Tyler-Kabara, 2007: Palliative Rhizotomy**
- 6 pts with spastic and dystonic CP, GMFCS IV-V
- Not candidates for ITB
- Long-term improvement in dystonia and spasticity
- No adverse effects

**Ghany, et al, 2016: Ventral and Dorsal Rhizotomy for CP**
- 50 pts. with CP
- Mixed dystonia and spasticity
- L1-S5 laminotomy and roots
- 50-80% of dorsal rootlets selectively cut
- 4-6 ventral rootlets dissected per root
- 50-80% of ventral rootlets dissected
- At 12 mon MAS mean dropped from 4 to 2
- BAD scale significantly dropped 5 to 12

**Palliative Rhizotomy**
- Ventral and dorsal rhizotomy
- Conus or cauda equina level
- Non-selective
- Aggressive percentage of rootlets cut
  - 50-75% at each level
  - L1-S2 typical
- Can decrease standing, weakens

**Palliative Rhizotomy**
- For GMFCS IV-V
- Usually severe dystonia +/- spasticity
- Usually permanent tone reduction
- Can see some return of dystonia after 1-2 years
- Can do cervical roots too
- Gillette has 30 patients and a very large majority has a significant improvement

**Albright, Tyler-Kabara, 2007: Palliative Rhizotomy**
- 6 pts with spastic and dystonic CP, GMFCS IV-V
- Not candidates for ITB
- Long-term improvement in dystonia and spasticity
- No adverse effects