Management of the Spastic Child
Division of Child Neurology, Developmental Pediatrics and Genetics

Spasticity Management

- What is the need
- What the concerns
- What are the possible solutions
- What are the best options

Spasticity Management

Definitions:

The Taskforce on Childhood Motor Disorders defines spasticity as "hypertonia in which one or both of the following signs are present:
- resistance to externally imposed movement increases with increasing speed of stretch and varies with the direction of joint movement
- resistance to externally imposed movement rises rapidly above a threshold speed of joint angle"

From AAN/CNS Practice Parameter

Spasticity Management

Definitions: Mayo Clinic (from their website)

- Cerebral palsy is a disorder of movement, muscle tone or posture that is caused by injury or abnormal development in the immature brain, most often before birth.
- Signs and symptoms appear during infancy or preschool years. In general, cerebral palsy causes impaired movement associated with exaggerated reflexes or rigidity of the limbs and trunk, abnormal posture, involuntary movements, unsteadiness of walking, or some combination of these. The effect of cerebral palsy on functional abilities varies greatly.
- People with cerebral palsy often have other conditions related to developmental brain abnormalities, such as intellectual disabilities, vision and hearing problems, or seizures. A broad spectrum of treatments may help minimize the effect of cerebral palsy and improve a person's functional abilities.

Spasticity Management

Definitions: Wikipedia (from their website)

- Cerebral palsy is an umbrella term encompassing a group of non-progressive, non-contagious motor conditions that cause physical disability in human development, chiefly in the various areas of body movement.
- Cerebral palsy is caused by damage to the motor control centers of the developing brain and can occur during pregnancy, during childbirth or after birth....

Intrauterine Periventricular Leukomalacia
Spasticity Management

Definitions:

- CP prevalence was recently reported to be 3.6 cases per 1000 in 8-year-old children, with very little variation among Western nations.
- CP is the most common cause of spasticity in children, and the majority of children with CP are affected by spasticity.

From AAN/CNS Practice Parameter

Management Issues:

- Alleviation of spasticity may not always be desirable; some patients may experience a decline in function with spasticity reduction.
- Over the last 20 years, several pharmacological antispasticity treatments (benzodiazepines, dantrolene, baclofen, and tizanidine; neuromuscular blocking agents such as botulinum toxins A and B [BoNT-A and BoNT-B, respectively]; chemical denervation using phenol and alcohol; intrathecal baclofen [ITB]) have been adapted for use in patients with CP.

Oral medications and ITB are used when a generalized antispasticity effect is desired. Chemical denervation agents are used to treat localized (one extremity) or segmental (lower body, hemibody) spasticity.
Gaps in Care

- There is a paucity of research on treatment of spasticity in CP.
- Physicians often focus on treating impairment (spasticity) but not activity/participation.
- There is strong evidence for efficacy of BoNT-A use in spasticity but no evidence for efficacy of other medication use in spasticity.

Clinical Questions

1. What is the efficacy and safety of BoNT-A, BoNT-B, phenol, or alcohol injection for treating spasticity in children with CP?
2. What is the efficacy and safety of diazepam for treating spasticity in children with CP?
3. What is the efficacy and safety of dantrolene for treating spasticity in children with CP?
4. What is the efficacy and safety of oral baclofen for treating spasticity in children with CP?
5. What is the efficacy and safety of tizanidine for treating spasticity in children with CP?
6. What is the efficacy and safety of ITB for treating spasticity in children with CP?

Literature Review

- 978 abstracts
- 218 articles

Inclusion criteria:
- Studies of CP, static encephalopathy, spasticity, hemiplegia, tetraplegia, quadriplegia, diplegia
- Studies of oral antispasticity medications; intrathecal baclofen; BoNT, phenol, and alcohol injections
- Limited to human subjects
- All foreign languages with English abstracts

Exclusion criteria:
- Articles not peer-reviewed
- Articles on patients over 19 years of age with CP
- Articles with fewer than nine patients studied

Analysis of Evidence

Question 1: What is the efficacy and safety of BoNT-A, BoNT-B, phenol, or alcohol injection for treating spasticity in children with CP?

Conclusion

Conclusion:
- For children with CP, BoNT-A is established as an effective treatment to reduce spasticity in the upper and lower extremities (Class I and II evidence), but there is conflicting evidence regarding functional improvement. The available evidence suggests that BoNT-A is generally safe in children with CP. However, severe generalized weakness may occur.
**Recommendations**

**Recommendations:**
- For localized/segmental spasticity in the upper and lower extremities of children with CP that warrants treatment, BoNT-A should be offered as an effective and generally safe treatment (Level A).
- There is insufficient evidence to support or refute the use of BoNT-A to improve motor function in this population (Level U).
- There is insufficient evidence to support or refute the use of BoNT-B, phenol, and alcohol injections as a treatment for spasticity in children with spastic CP (Level U).

**Clinical Context**

- At the time of this writing, the US Food and Drug Administration (FDA) has not approved BoNT-A for the treatment of spasticity in children. BoNT-A is approved for the treatment of spasticity in children and adults in Canada and several other countries. Different formulations are not bioequivalent and may have different therapeutic efficacy and safety profiles.

- The AAN recently published an evidence-based review on the safety and efficacy of BoNT for the treatment of adult and childhood spasticity.

**Clinical Context, cont.**

- A Level A recommendation was given for the use of BoNT-A as a treatment of spasticity in the lower extremities (equinus and hip adductor spasticity) and a Level B recommendation was given for the treatment of spasticity in the upper extremities of children with CP.
- It is common practice to use BoNT-A in combination with serial casting, orthoses, and physical therapy and occupational therapy. Typically, there is a 3- to 4-month clinical response requiring repeated injections. Some experts recommend using the smallest dose of BoNT-A and avoiding injecting more frequently than every 3 months to minimize the risk of antibody resistance.

**Clinical Context, cont.**

- On the basis of postmarketing reports from its Adverse Event Reporting System, the FDA released on February 8, 2008, an "early communication" describing a “relative handful of systemic reactions” after BoNT injection (A or B) for limb spasticity associated with CP. At the time of this writing, the FDA has not completed the review of reported serious adverse events (Aes) related to BoNT, and has made the following recommendations:
  - Understand that potency determinations expressed in “Units” or “U” differ among the BoNT products; clinical doses expressed in units are not comparable from one botulinum product to the next.
  - Be alert to the potential for systemic effects following administration of BoNT such as dysphagia, dysphonia, weakness, dyspnea, or respiratory distress.
  - Understand that these effects have been reported as early as 1 day and as late as several weeks after treatment.
  - Provide patients and caregivers with the information they need to be able to identify the signs and symptoms of systemic effects after receiving an injection of BoNT.
  - Tell patients they should receive immediate medical attention if they have worsening or unexpected difficulty swallowing or talking, trouble breathing, or muscle weakness.

**Analysis of Evidence**

**Question 2:** What is the efficacy and safety of diazepam for treating spasticity in children with CP?
Conclusion

Conclusion:
- Diazepam is probably effective for the short-term treatment of spasticity in children with CP (one Class I study and one Class II study). None of the studies formally addressed whether diazepam improved motor function. Ataxia and drowsiness were identified in the side-effect profile of most studies.

Recommendations

Recommendations:
- Diazepam should be considered as a short-term antispasticity treatment in children with CP (Level B).
- There is insufficient evidence to support or refute the use of diazepam to improve motor function in this population (Level U).

Clinical Context

- The incidence of AEs associated with diazepam, such as drowsiness, sedation, hypersalivation, and weakness, are important limiting factors for long-term use.
- Experts caution that the prolonged use of this medication can produce physical dependence and recommend against abrupt discontinuation.  

Analysis of Evidence

Question 3: What is the efficacy and safety of dantrolene for treating spasticity in children with CP?

Conclusion/Recommendation

Conclusion:
- There is conflicting evidence regarding the effectiveness of dantrolene in reducing spasticity in children with CP. Dantrolene frequently causes side effects in children with spastic CP, such as weakness, drowsiness, and irritability.

Recommendation:
- There is insufficient evidence to support or refute the use of dantrolene for the treatment of spasticity in children with CP (Level U).

Analysis of Evidence

Question 4: What is the efficacy and safety of oral baclofen for treating spasticity in children with CP?
Conclusion/Recommendation

**Conclusion:**
– There is conflicting Class II evidence regarding the effectiveness of oral baclofen in reducing spasticity and improving function in children with CP. Systemic toxicity was found in some patients.

**Recommendation:**
– There is insufficient evidence to support or refute the use of oral baclofen for the treatment of spasticity or to improve motor function in children with CP (Level U).

Clinical Context

– Baclofen is widely used in clinical practice to treat spasticity in children with CP. Experts recommend starting baclofen at the lowest possible dose ($5-10$ mg/day divided into three doses a day)\(^5\) to minimize AEs like drowsiness and sedation.

– The dose is gradually tapered until discontinuing because abrupt discontinuation may cause withdrawal symptoms, including increased spasticity, hallucinations, confusion, hyperthermia, and seizures.\(^{11}\)

Analysis of Evidence

**Question 5: What is the efficacy and safety of tizanidine for treating spasticity in children with CP?**

**Note:** One small Class II placebo-controlled parallel study treated 10 children with a mean age of 4.1 years (range 2–15) with tizanidine $0.05$ mg/kg/day and 30 children with placebo for 6 months.

**Conclusion/Recommendations**

**Conclusion:**
– Tizanidine is possibly effective to treat spasticity in children with CP. No toxicity was found in this small study.

**Recommendations:**
– Tizanidine may be considered for the treatment of spasticity in children with CP (Level C).

– There is insufficient evidence to support or refute the use of tizanidine to improve motor function in this population (Level U).

Clinical Context

– Tizanidine’s antispasticity effect has been demonstrated in adults with multiple sclerosis and spinal cord injury.\(^{20}\) Little information is available to assist practitioners with the effective use of this drug to treat spasticity in children.

– Because tizanidine is extensively metabolized by the liver, hepatic impairment may have a significant effect on its pharmacokinetics.

– AEs related to tizanidine use in adults include hypotension, sedation, asthenia, dry mouth, dizziness, hallucinations, and hepatotoxicity. Their incidence in pediatric patients has not been studied.

Analysis of Evidence

**Question 6: What is the efficacy and safety of ITB for treating spasticity in children with CP?**
**Conclusion/Recommendation**

**Conclusion:**
- Data are inadequate concerning the use of continuous ITB as an antispasticity treatment in children with CP. CSF leaks, seromas, catheter-related complications, and wound infection occur frequently, and other, milder complications occur less frequently.

**Recommendation:**
- There is insufficient evidence to support or refute the use of continuous ITB for the treatment of spasticity in children with CP (Level U).

**Clinical Context**

- In 1996, ITB received FDA approval to treat spasticity of cerebral origin. A major factor in the lack of Class I and II evidence may be the difficulty of performing a randomized control trial or crossover trial in subjects with ITB pumps.
- Catheter-related complications, pump pocket collections, and wound infections remain a concern, and ongoing efforts aim to reduce their incidence.
- One retrospective study of the safety of ITB in children (N=200) found that 11% had CSF leakage, 7% had catheter-related problems, and 5.5% developed infections.21

**Future Research**

- The AS has been used by most spasticity studies. It measures muscle resistance to passive movement but fails to describe the velocity of the stretching movement and therefore is inadequate to measure spasticity and distinguish it from other types of hypertonia (e.g., dystonia).
- Standardized and validated spasticity scales and clinically relevant measures sensitive enough to detect change should be used to qualify and quantify spasticity according to its current definition (e.g., Tardieu Spasticity Scale).

**Future Research, cont.**

- None of the oral medications used to treat spasticity in children has been adequately tested for safety and efficacy. There are minimal or no data regarding the pharmacokinetics or appropriate dosing parameters to treat children. These critical questions deserve serious research efforts.
- The effects of both spasticity and the treatment of spasticity on activity and participation as defined by the International Classification of Function, Disability and Health of the World Health Organization need to be studied in children with CP.22

**Future Research, cont.**

- Although there is sufficient evidence to recommend BoNT-A as an effective antispasticity treatment in children with CP, its beneficial effects on function, ease of caregiving, activity, and participation need to be established. More data about safety and long-term effects are also needed.
- The efficacy and safety of BoNT-B, phenol, and alcohol chemodenervation as treatments for spasticity in children with CP need to be determined.
- The efficacy and safety of oral baclofen and the long-term continuous intrathecal pump administration of this medication need to be determined in children with CP.

**Future Research, cont.**

- The few available treatments to reduce generalized spasticity are associated with a high incidence of AEs and complications.
- There is an urgent need to find safer and more effective treatments to help children affected by generalized spasticity due to CP. A first step could be to investigate medications that have shown antispasticity effect in adult patients (e.g., gabapentin).23
References


References, cont.


So, how do I translate this into a plan of action?
Hypothesis:
A cascade of actions exists that are beneficial, but increasingly costly and invasive.

1) Physical Therapy
While this is not the least costly, it is the least invasive. It is ordered before children reach Child Neurology attention, it is often performed in the home. It has demonstrated benefit.

2/24/2012

Hypothesis:
A cascade of actions exists that are beneficial, but increasingly costly and invasive.

2) Oral Medications – either Baclofen or Benzodiazepines
While this is the least costly, it is more invasive. It is ordered for children by a physician usually after the child has already begun Physical Therapy. Although the medicines are safe and effective, primary care providers rarely initiate therapy, although it is safe to do so.

Dose – Clonazepam 0.02 mg/kg/day in divided doses
Baclofen – begin at 0.5 mg/kg/day increase q7 days to 1.5 mg/kg/day
Both of these drugs need to be compounded

2/24/2012

Hypothesis:
A cascade of actions exists that are beneficial, but increasingly costly and invasive.

These are:

3) Botulinum Toxin Injections
This therapy begins the upward spiral of costs. Economic analysis has not been done to reconcile costs to benefits. It is clearly effective, is usually performed by Child Neurology. Other providers may provide injections. Knowledge of the anatomy is a limiting factor for many physicians. Patient selection is key. You must understand the patient’s disease before injecting. There is nothing which can reverse the effect after 24 hours, the effect lasts three months.

2/24/2012

Hypothesis:
A cascade of actions exists that are beneficial, but increasingly costly and invasive.

2/24/2012

Modified Ashworth Scale

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<th>RS</th>
<th>Muscle under stretch</th>
<th>Score</th>
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<tr>
<td>0</td>
<td>No increase in muscle tone</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Slight increase in muscle tone</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>No increase in resistance through range of movement</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Slight increase in resistance through range of movement</td>
<td></td>
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<tr>
<td>4</td>
<td>Resists stretch in passive movement difficult</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Resists stretch with muscle tightening or clonus</td>
<td></td>
</tr>
</tbody>
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The modified Ashworth scale

2/24/2012
3) Botulinum Toxin Injections

Safety Concerns:
- **a)** Dosing – manufacturer’s recommendation 10-12 units/kg, significant support for higher doses up to 20 units/kg
- **b)** LD50 in rhesus monkeys has been measured at 37 - 40 units/kg
- **c)** Should not administer more than every 3 months

^ Mayer, Simpson Spasticity 2002
*Brin, Comella, and Jankovic in Dystonia 2008

**Hypothesis:**
A cascade of actions exists that are beneficial, but increasingly costly and invasive.

These are:
4) Intrathecal Baclofen

This is much more invasive, and has complications including CSF leakage. There is a risk of death should the pump be allowed to completely empty.

5) Dorsal Rhizotomy

Should be used in diplegic children
Summary

I believe there is a cascade that should be considered. Patients should be selected thoughtfully. But there is much that can be done to improve the lives of children with Spasticity.

1) Physical Therapy
2) Oral Medications – either Baclofen or Benzodiazepines
3) Botulinum Toxin Injections
4) Intrathecal Baclofen
5) Dorsal Rhizotomy