

Combining Botulinum Toxin and Phenol to Manage Spasticity in Children

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Objective: To describe the specific techniques and adverse reactions of using concurrent, multiple injections of both botulinum toxin and phenol to manage spasticity in children with cerebral palsy (CP) and other neurologic conditions.

Design: A retrospective case series.

Setting: A tertiary care children's hospital.

Participants: Consecutive patients (N=68) with spasticity related to CP or other neurologic conditions.

Intervention: Ninety injection sessions combining botulinum toxin and phenol to manage spasticity.

Main Outcome Measure: Documentation of adverse reactions.

Results: The mean phenol dosage was 9.5mL at a mean of 0.6mL/kg per injection dose. The mean botulinum toxin type A (Botox) dose injected was 193U (12U/kg), and the mean of botulinum toxin type B (Myobloc) dose injected was 7750U (530U/kg). The mean number of muscles injected was 14. Adverse reactions are described but were infrequent. Dysesthetic hand pain occurred in 2 patients. One patient developed a systemic reaction to Myobloc.

Conclusions: Using botulinum toxin and phenol injections allowed many muscles to be injected to manage spasticity in children with CP and other neurologic conditions. Using this combination allowed an increased number of injections at the maximal recommended dose.

Key Words: Botulinum toxins; Cerebral palsy; Phenol; Rehabilitation.

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CHILDREN WITH CEREBRAL PALSY (CP) often have spasticity that may lead to contractures and limit their functional abilities. Multiple approaches, including botulinum toxin injections and phenol motor point blocks, are used to manage spasticity. Botulinum toxin is frequently used to manage spasticity in children with CP. Multiple studies¹⁻⁶ have shown reduction in tone and some have shown improvements in function after intramuscular injection of botulinum toxin type A (Botox). The most effective and safest dose of botulinum toxin has not yet been determined. The recommended maximum dosage of Botox is 12 units per kilogram.^{7,8} However, centers have reported injecting larger amounts.⁹ A total

maximum body dose of 300 to 400U per visit has also been recommended.^{7,8} A dose of 3 to 6U/kg of Botox is recommended for effective reduction of spasticity in large muscles. Experience with dosing of botulinum toxin type B (Myobloc) is less than that with botulinum toxin type A.

Children with CP and other neurologic conditions frequently have multiple spastic muscles. The current botulinum toxin dosing recommendations limit the number of muscles that can be injected at 1 time. For instance, in a 20-kg child with diplegic CP, the gastrocnemius, hamstring, and adductor muscle groups are frequently spastic. If one were to inject 4U/kg in each of these muscle groups, the amount injected would be 480U or 24U/kg. If the child also had significant spasticity in other muscle groups, such as the hip flexors or upper-extremity muscles, the dosage would be even higher.

Phenol motor point or peripheral nerve blocks have been used historically to manage spasticity in adults and children. Several studies¹⁰⁻¹⁵ (most published in the 1960s and 1970s) document reduction in muscle tone and some improvement in function after phenol blocks. Phenol can be injected into a mixed sensorimotor peripheral nerve, a motor nerve, or a motor point. The advantage of injecting mixed nerves is easier access. However, this type of injection may lead to painful dysesthesias. Dosages injected have been variable. It has been stated that the lethal dosage is greater than about 8g.¹⁴ It has also been recommended that in an adult no more than 1g be injected on a given day.¹⁴ Several studies^{10,12,15} in children have listed amounts injected into individual nerves but have not listed total dosages injected. Morrison et al¹⁶ reported cardiac dysrhythmias in 3 of 16 children receiving phenol motor point blocks (5% in water) during halothane anesthesia. The dosage range was 6.7 to 70mg/kg, with a mean of 32mg/kg. No correlation was found between dosages or blood concentration and incidence of dysrhythmias. They concluded that phenol administered in these dosages over a average duration of 33 minutes in children with CP anesthetized with halothane was not associated with an increased incidence of cardiac dysrhythmias. However, they also stated that the safe dose and duration of administration have not been established.

Injecting phenol is more difficult than injecting botulinum toxin, because phenol requires a nerve or motor point to be specifically localized by electric stimulation with a needle. Children tolerate this poorly, often requiring general anesthesia.

To manage spasticity in children with CP and other neurologic conditions, we frequently use a combination of botulinum toxin and phenol motor nerve injections. Other pediatric rehabilitation centers are using this same process (Mark Gormley, MD, personal communication, 2003; Dennis Matthews, MD, personal communication, 2003). However, literature describing this treatment is limited. A recent abstract¹³ describes a combination of botulinum toxin type A and phenol motor point injections into 120 patients with spastic CP. On average, 9.6 muscles were injected. Spasticity was reduced by an average of 1 on the Modified Ashworth Scale in muscles injected with botulinum toxin type A and 1.5 in muscles injected with phenol. Complications were reported as negligible. Total dos-

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Table 1: Subjects' Diagnoses

Diagnosis	n
Spastic quadriplegic CP	39
Spastic diplegic CP	24
Spastic hemiplegic CP	3
CNS degenerative disease	2

Abbreviation: CNS, central nervous system.

age was not stated, but maximum dosage of phenol did not exceed 1g.

In the present study, we describe the management of spasticity in children treated with a combination of botulinum toxin injections and phenol motor nerve blocks. This article describes (1) the specific techniques we used, including individual and total dosages of both botulinum toxin and phenol, (2) the number and location of muscles injected, and (3) adverse reactions encountered.

METHODS

Setting

A retrospective chart review was conducted at a regional tertiary children's hospital, Primary Children's Medical Center, Salt Lake City, UT. The charts were those of children with CP or other neurologic conditions receiving a combination of botulinum toxin type A (Botox) or botulinum toxin type B (Myobloc) and phenol motor nerve blocks for management of spasticity. The review covered the 18-month period between January 2002 and June 2003 and was approved by the institutional review board at the University of Utah.

Participants

Included were 68 consecutive cases of children (47 boys, 21 girls) with spasticity related to CP or other neurologic conditions who received a combination of botulinum toxin and phenol injections. These subjects received a total of 90 injection sessions. Mean age at the time of injection was 6 years (range, 1y 8mo to 18y 9mo). Diagnoses of the subjects are listed in table 1.

Procedure

All injections were performed in the Rapid Treatment Unit under general anesthesia. Patients were premedicated with 0.5mg/kg of midazolam and 15mg/kg of acetaminophen administered 30 to 40 minutes before the procedure. General anesthesia consisted of inhalational anesthesia administered by the anesthesia staff via facemask. Postprocedure pain control consisted of intravenous morphine sulfate as needed or acetaminophen rectal suppository if not given before the procedure.

Botulinum toxin type A (Botox) was diluted in preservative-free, sterile saline to a concentration of 100U/mL. Muscles injected with Botox and botulinum toxin type B (Myobloc) were localized by using stretch and palpation or electric stimulation. The toxin was then infiltrated in the area of maximal muscle mass with a 27-gauge 1¼-in needle, a 27-gauge 37-mm Botox Injection Needle,^a or a 30-gauge 25-mm injectable monopolar electromyography needle electrode.^b

Phenol was diluted with sterile water to a concentration of 6%. The motor nerve's general location was found through surface stimulation with a DigiStim 3 Plus peripheral nerve stimulator.^c Subsequently, specific localization was done by using 1 of the 2 injection electrode needles listed earlier. A 200-ms pulse width square wave ranging in intensity from 1 to

3mA was used during needle localization. The needle was positioned to elicit a maximal contraction, into which 0.25 to 0.5mL of the phenol solution was infiltrated after a negative aspiration. Contractions were observed for about 30 seconds. If the stimulation-induced contraction persisted, an additional 0.25 to 0.5mL of the phenol solution was injected. If the contraction was eliminated, the needle was repositioned slightly and phenol was injected into the area of greatest contraction. This procedure was repeated until no further contractions were noted or a dosage of 3.0mL had been injected. The motor nerves to these muscles were localized by finding contractions in the targeted muscles and avoiding contractions in more distally innervated muscles.

Patients and caregivers were told to avoid vigorous stretching and not to increase the child's routine activity level for 1 to 2 weeks after injections.

The amounts of botulinum toxin and phenol injected were recorded. All participants were seen for follow-up. Adverse reactions were recorded.

RESULTS

Sixty-eight children received 90 botulinum toxin and phenol injection sessions. Most received 1 set of injections but 10 individuals received 2 sessions, 5 subjects received 3 sessions, and 1 child received 4 sessions. The mean phenol dosage injected was 9.5mL (600mg), with a range of 1 to 19mL. A mean of 0.6mL/kg (40mg/kg) was injected, with a range of 0.1 to 1.4mL/kg (6–84mg/kg). The mean amount of Botox injected was 193U with a range of 100 to 400U (n=52). A mean of 12U/kg was injected, with a range of 2.2 to 12.2U/kg. The mean amount of Myobloc injected was 7750U, with a range of 2500 to 15,500U. A mean amount of 530U/kg was injected, with a range of 116 to 1066U/kg. The mean number of muscles injected was 14, with a range of 7 to 21 muscles. The muscles injected with phenol were the adductor longus, gracilis, adductor magnus, semitendinosus and semimembranosus, rectus femoris, and medial gastrocnemius. The muscles most commonly injected with phenol were the adductor and hamstring muscle groups. The 3 most common patterns of muscles injected are shown in table 2.

Adverse reactions included dyesthetic pain in the upper extremity in 2 children, one diffusely in the hand and the other

Table 2: The 3 Most Common Injection Patterns

	Phenol Injections	Botulinum Toxin Injections
Pattern 1	Adductor longus	Medial gastrocnemius
	Gracilis	Lateral gastrocnemius
	Adductor magnus	
	Semitendinosus	
	Semimembranosus	
Pattern 2	Adductor longus	Lateral gastrocnemius
	Gracilis	Upper-extremity muscles
	Adductor magnus	
	Semitendinosus	
	Semimembranosus	
Pattern 3	Adductor longus	Lateral gastrocnemius
	Gracilis	Upper-extremity muscles
	Adductor magnus	
	Semitendinosus	
	Semimembranosus	
	Medial gastrocnemius	
	Biceps brachii	

in the anterior forearm and the palm after phenol injection into the biceps brachii muscle. Pain in both was well controlled with gabapentin and resolved within 6 weeks. Another child had pain with stretching of the adductor muscles for about 3 weeks after phenol injections. Another had pain in the posterior aspect of the thigh for about 2 weeks after phenol injections into the hamstring muscle group. One child had episodes of vomiting and a seizure a week after botulinum toxin and phenol injections. The child had not had seizures before this. No other seizures were noted, and no specific etiology was determined. Eight days after phenol and Myobloc injections, 1 child developed a systemic reaction to Myobloc with constipation, difficulty chewing, and generalized weakness. This reaction gradually resolved over the following 6 weeks. This child had received a total dosage of 12,000U of Myobloc (980U/kg).

We did not count as adverse reactions those participants who had difficulty walking for several days after the injections.

DISCUSSION

Using botulinum toxin and phenol injections concurrently permits more spastic muscles to be treated during a single anesthesia. The average number of muscles injected by using this technique in this group of children was 14. Injecting this many muscle groups by using either botulinum toxin or phenol alone would require higher than the recommended dosages of either medication and could lead to increased likelihood of adverse reactions.

We chose to inject larger, proximal muscles with phenol and smaller, distal, and deeper muscles with botulinum toxin. Because less botulinum toxin is used for smaller muscles, the cost is lower. It is easier to localize a deeper, smaller muscle for botulinum toxin injection than to localize its motor nerve for phenol injection. Phenol was used in muscle groups in which nerve localization minimizes diffusion onto a mixed or sensory nerve. Botulinum toxin was used in muscles with an increased probability of diffusion onto a sensory nerve.

With the techniques described and the amounts injected, complications were infrequent. We chose to inject motor nerves rather than peripheral sensory motor nerves with phenol to avoid dysesthesia. Two children had neuropathic pain in their hands for several weeks after injection. The pain in both these children was well controlled with gabapentin. Another child had pain with stretching in the groin for several weeks after injections, and 1 child had pain in the posterior aspect of the leg for about 2 weeks after injections. One child had a systemic reaction to Myobloc.

We changed our technique for injection of the biceps brachii muscle after the 2 children developed hand pain. We moved the injection site distally and laterally in the muscle. After this change, we had no further reports of pain after the injection. Before this study, 2 children were observed (JLG) with dysesthetic type pain in the leg and foot after medial hamstring injections. After these episodes, the injection site was also moved distally and medially in the hamstring muscle group to avoid diffusion onto the sciatic nerve. Parents and caregivers were encouraged to have their child avoid vigorous stretching and vigorous mobility for 1 week after the procedure. This instruction was also given by Glenn.¹¹

Reported complications were similar to other studies.^{10,12,15} Easton et al¹⁰ injected spastic muscles with 5% phenol in 42 children who had various neurologic conditions. These were intramuscular injections. One child had pain after vigorous stretching in the gastrocnemius soleus muscle group. No other toxic reactions were described. The amount of phenol injected was 0.1mL per stimulated site, with up to 10 to 20 injections in

the hamstring and adductor muscle groups and 25 to 40 in the gastroc-soleus muscle groups. No total dosage was given.

Spira¹² injected 61 children with spastic CP with a 5% phenol solution. The tibial and obturator nerves were most commonly injected. The dosage was 2 to 5mL per nerve. The total dosage per kilogram was not given. Complications included decreased ability to walk for several days in some patients. Seven patients had pain and paresthesias. Six of them had injections into the tibial nerve, and 1 had injection into the brachial plexus.

Yadav et al¹⁵ performed peripheral nerve blocks using a 6% phenol solution in 116 children with spastic CP. Most of the injections were given into the obturator or posterior tibial nerves; 1 to 3mL was injected into each nerve. Five patients developed paresthesia after posterior tibial nerve block. No patients with obturator nerve blocks developed paresthesia. Three patients had pain lasting a few days to a month at the site of the injection or in the distribution of the nerve. One patient had complete loss of sensation and 2 had weakness that improved quickly.

Other complications of phenol injections include loss of useful motor function, peripheral edema, local infection, or deep vein thrombosis.¹⁷ In systemic doses of 8.5g or more, phenol may cause convulsions, central nervous system depression, and cardiovascular collapse.¹¹ Our average dosage was 0.6g, with a maximum of 1.1g.

Complications from botulinum toxin injections were also rare. One child who received Myobloc developed symptoms consistent with a systemic reaction. This child received a dosage of 12,000U (980U/kg). We believe that this was an overdose and lowered our maximum dosage after this. Other potential adverse effects of botulinum toxin type A in children include excessive weakness, pain at the injection site, fever, urinary incontinence, and dysphagia.^{7,8} Botulinum toxin type B has been less thoroughly evaluated.

CONCLUSIONS

Injection of both botulinum toxin and phenol lowers tone in the short run. Further studies are needed to determine optimal dosages and injection sites. Glenn¹¹ points out that a poor correlation exists in the literature between quantity of phenol and effectiveness. The literature on botulinum toxin also varies with regard to optimal dosage. Evaluating long-term cost effectiveness and long-term complications, especially after repeated injections, are also necessary.

References

1. Chutorian AM, Root L. Management of spasticity in children with botulinum-A toxin. *Int Pediatrics* 1994;9:35-43.
2. Cosgrove AP, Corry IS, Graham HK. Botulinum toxin in the management of the lower limb in cerebral palsy. *Dev Med Child Neurol* 1994;36:386-96.
3. Friedman A, Diamond M, Johnston MV, Daffner C. Effects of botulinum toxin on upper limb spasticity in children with cerebral palsy. *Am J Phys Med Rehabil* 2000;79:53-9.
4. Koman LA, Mooney JF 3rd, Smith BP, Walker F, Leon JM. Botulinum toxin type A neuromuscular blockade in the treatment of lower extremity spasticity in cerebral palsy: a randomized, double-blind, placebo-controlled trial. *BOTOX Study Group. J Pediatr Orthop* 2000;20:108-15.
5. Reddihough DS, King JA, Coleman GJ, Fosant A, McCoy AT. Functional outcome of botulinum toxin A injections to the lower limbs in cerebral palsy. *Dev Med Child Neurol* 2002;44:820-7.
6. Sutherland DH, Kaufman KR, Wyatt MP, Chambers HG. Injection of botulinum A toxin into the gastrocnemius muscle of patients with cerebral palsy: a 3-dimensional motion analysis study. *Gait Posture* 1996;4:269-79.

7. Graham HK, Aoki KR, Autti-Ramo I, et al. Recommendations for the use of botulinum toxin type A in the management of cerebral palsy. *Gait Posture* 2000;11:67-79.
8. Russman BS, Tilton A, Gormley ME. Cerebral palsy: a rational approach to a treatment protocol, and the role of botulinum toxin in treatment. *Muscle Nerve Suppl* 1997;6:S181-93.
9. Gormley ME, Gaebler-Spira D, Delgado M. Use of botulinum toxin type A in pediatric patients with cerebral palsy: a three-center retrospective chart review. *J Child Neurol* 2001;16:113-8.
10. Easton J, Ozel T, Halpern D. Intramuscular neurolysis for spasticity in children. *Arch Phys Med Rehabil* 1979;60:155-8.
11. Glenn MB. Nerve blocks. In: Glenn MB, Whyte J, editors. *The practical management of spasticity in children and adults*. Philadelphia: Lea & Febiger; 1990. p 27-58.
12. Spira R. Management of spasticity in cerebral palsied children by peripheral nerve block with phenol. *Dev Med Child Neurol* 1971;13:164-73.
13. Swaminathan K, Kim H, Beck T, Glanzmann A. Efficacy of motor point injections using botulinum toxin type A and phenol in children with spastic cerebral palsy: a retrospective study of 120 patients [abstract]. *Arch Phys Med Rehabil* 2001;82:1295.
14. Wood KM. The use of phenol as a neurolytic agent: a review. *Pain* 1978;5:205-29.
15. Yadav SL, Singh U, Dureja GP, Singh KK, Chaturvedi S. Phenol block in the management of spastic cerebral palsy. *Indian J Pediatr* 1994;61:249-55.
16. Morrison JE, Matthews D, Washington R, Fennessy PV, Harrison M. Phenol motor point blocks in children: plasma concentrations and cardiac dysrhythmias. *Anesthesiology* 1991;75:359-62.
17. Macek C. Venous thrombosis results from some phenol injections [news]. *JAMA* 1983;249:1807.

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