Focal Management of Spasticity in Cerebral Palsy

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Abstract

Spasticity is the most common presentation of all neurologic alterations in children with CP. When the neurologic system loses motor control function and postural stability or weakens but has organizational ability to functionally respond, it will increase muscle tone to compensate. However, there are cases where this response over reacts and it develops pathologic spasticity which causes impairment. Therefore, when treating children with spasticity, the basic supposition is that muscle tone is good and the amount of muscle tone should be modulated for the individual's maximum benefit. Spasticity may be generalized affecting almost all the muscular system, and generalized increase in tone may be associated with mixed tone conditions where it is combined with movement disorders. The spasticity for these individuals may be very beneficial to modulate the movement disorder. Treatments for generalized spasticity require an approach

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that reduces whole body tone. Children with diplegia often have more localized spasticity problems such as the plantar flexors but may also involve the whole lower extremities. Management options include whole body methods. In children with hemiplegia or unilateral CP, the spasticity tends to be localized to a single side, and the treatment should be more focused on the local problem. There are many treatment options for spasticity including those that affect the whole body to those that have a very localized affect. Some of the treatments also are permanent and cannot be reversed, while others are temporary whose effect disappears when the treatment ends. The remaining discussion in this chapter will focus on the localized effects of spasticity and localized treatments of spasticity.

Keywords

Cerebral palsy · Spasticity · Botulinum toxin · Phenol · Alcohol · Baclofen · Rhizotomy · Neurectomy

Introduction

Spasticity is the most common presentation of all neurologic alterations in children with CP. Increased muscle tone expressed as spasticity must be a very strong chaotic attractor to the organization of residual activity in a child with a central neurologic injury. It is very difficult to understand what the components of the system are that make this spasticity such a strong attractor. Because it has persisted in humans but is seldom seen in animals, this suggests that there is a functional benefit to spasticity. Even though spasticity is a strong chaotic attractor, any judgment about its benefit or harm to an individual cannot easily be made. From modern robotic research, it is known that adding stiffness to joints helps improve fine motor control; and also everyone has experienced a tendency to stiffen when wanting to do very fine delicate movements with their hands. It seems most conceivable that, on the whole, when the neurologic system loses motor control function and postural stability or weakens but has organizational ability to functionally respond, it will increase muscle tone to compensate. However, there are also clear cases where this response over reacts and it develops pathologic spasticity which causes impairment. Therefore, when treating children with spasticity, the basic supposition is that muscle tone is good and the amount of muscle tone should be modulated for the individual's maximum benefit.

Spasticity may be generalized affecting almost all the muscular system, which is the common situation in children with GMFCS IV and V level function. This generalized increase in tone may be associated with mixed tone conditions where it is combined with dystonia and athetoid movement disorders. The spasticity for these individuals may be very beneficial to modulate the movement disorder. Treatments for generalized spasticity require an approach that reduces whole body tone. The whole-body tone management approaches available are oral medications and intrathecal baclofen discussed in separate chapters, "► Medical Management of Movement Disorders in Cerebral Palsy," "► Intrathecal Baclofen Therapy For Cerebral Palsy: Assessment and Medical Management". Children with diplegia (lower extremity bilateral) in the GMFCS I, II, and III often have more localized spasticity problems such as the plantar flexors but may also involve the whole lower extremities. Management options include whole body methods as noted above as well as dorsal rhizotomy, which is a technique of cutting sensory nerves from the lower extremities to reduce spasticity. The indications for this technique which provides permanent decrease in spasticity remain under significant debate. The risks of removing beneficial tone and creating a weak patient who is unable to increase tone when needed in addition to the surgical compilations have to all be considered "► Dorsal Rhizotomy for Spasticity Management in Cerebral Palsy". In children with hemiplegia or unilateral CP, the spasticity tends to be localized to a single side, and the treatment should be more focused on the local problem. There are many treatment options for spasticity including those that affect the whole body to those that have a very localized affect. Some of the treatments also are permanent and cannot be reversed, while others are temporary whose effect disappears

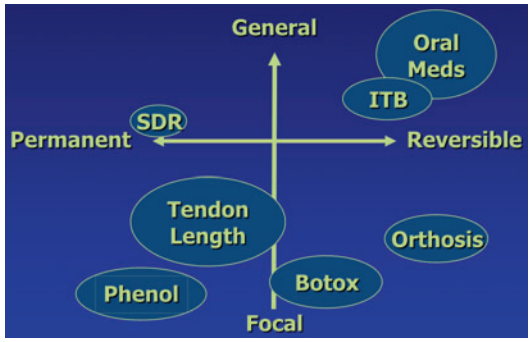

Fig. 1 This chart treatment options from permanent to reversible are on the horizontal axis and from generalized body effects to anatomically localized effects are on the vertical axis. In this concept the oral medications and intrathecal baclofen (ITB) fall into the reversible generalized effects. Rhizotomy (SDR) falls into the permeant with some generalized effects quadrant, although the rhizotomy effects involve primarily the lower extremities only. Orthoses and botulinum toxin are in the focal reversible quadrant, while phenol and tendon surgery fall into the permanent focal quadrant. It is not completely this simple as tendon lengthening of contractures which may also reduce spasticity tends to slowly reoccur, and botulinum toxin has permanent scarring effect on the muscle (This concept was originally presented to me by Kerr Graham)

when the treatment ends. These treatment options can be demonstrated graphically with a four quadrant chart (Fig. 1). The remaining discussion in this chapter will focus on the localized effects of spasticity and localized treatments of spasticity.

Natural History

The long-term and chronic effects of spasticity upon the localized structures are significant. Specifically, the spasticity as has an impact on the neuromotor junction by causing some disorganization, it has a direct effect on muscle growth causing reduced muscle fiber growth and increase tendon length. The chronic effects also include impact bone configuration and bone growth. An overview of these impacts will be discussed. Another important element of spasticity is that it has the natural evolution during growth of the child. Babies at birth are almost never spastic. The spasticity tends to develop from about the first to the third or fourth year of life. It's gradual increase in tone is often one of the major abnormalities parents notice. After peaking at approximately age 3–5 years of age, the spasticity tends to slowly decrease into the adolescent years. This change in spasticity has been the best documented from the Swedish database as reported by Hagglund (Hagglund and Wagner 2008) (Fig. 2).

Effects of Spasticity on Nerves

Because the lesion in CP is central, all other more distal changes are presumed to be secondary. The best recognized change in spasticity is hyperreflexia, which occurs because of a decreased inhibition from the cortical spinal tracts. As a normal child grows, the rate of muscle contraction and the ability to increase power by cerebral cortex modulation continues to increase until the child is approximately 10 years old (Connolly and Forssberg 1997). Although this change has been well documented by studying the ability of increased rapid alternating movements in children and adults (Lin et al. 1996), it is not clear where these changes occur. In CP, this more immature pattern of slow corticospinal and pyramidal tract potentials persists (Connolly and Forssberg 1997). There is an increased latency and a decreased ability to recruit large numbers of motor fibers at the same time (Dietz and Berger 1995). Some of this activity is modulated through changes in the excitability of the spinal motor neurons, which are also sensitive to joint position or, probably more specifically, muscle length. The strength of the ankle reflex is very sensitive to ankle joint position as measured by the H-reflex, which is initiated through stimulation of a peripheral sensory nerve. This change is much greater than can be explained by mechanical positioning (Connolly and Forssberg 1997). As noted earlier, there has to be some tension in the muscle while the muscle is at rest for it to function properly. Some of this tension seems to disappear when the individual is under neuromotor blockade anesthesia. It has been postulated that active

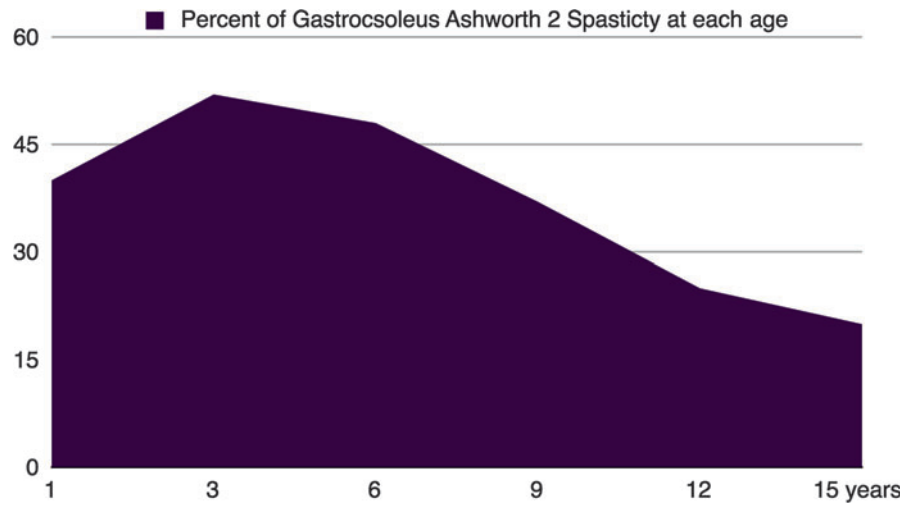

Fig. 2 This chart showing the percent of gastrocsoleus muscles with Ashworth 2 level spasticity from age 1 to 15. This data is abstracted from 266 children who had 3521 recorded examinations (Hagglund and Wagner 2008)

neuronal stimulation is required to maintain this muscle tone (Connolly and Forssberg 1997); however, no direct evidence of this has been found. It is this element of increased neurologic stimulation not generating an active EMG that seems to increase most when tone increases in CP. Because many of these children also demonstrate abnormalities in temperature regulation and blood flow in the extremities, some regulatory abnormality in the sympathetic nervous system may be involved. At this time, however, there is no direct evidence to support this theory. There is evidence that the neuromotor junction becomes more disorganized with chronic spasticity (Robinson et al. 2013), but how this impacts spasticity over time is not clear.

Effects of Spasticity on Muscles and Tendons

Hypertonia and hypotonia have the most dramatic secondary effects on the muscle. The well-observed effects of spasticity on skeletal muscle include decreased longitudinal growth of the muscle fiber length, decreased volume of the muscle, change in motor unit size, and change in the fiber type and neuromotor junction type. In the mouse model, the spasticity causes loss of approximately 50% of the longitudinal growth of the muscle fiber, resulting in contractures (Ziv et al. 1984). Muscles in children with CP are always very thin in addition to being short, which means that these muscles are also weak, as a muscle's strength is related to its cross-sectional area (Fig. 3). Understanding strength has been an extremely confusing topic in spastic muscle evaluation. The mechanical definition of strength is defined by how much load a structure can support. When discussing strength of a limb, such as the strength of plantar flexion at the ankle, the strongest ankle tends to have a severe fixed flexion contracture, but this is not the strength for which most clinicians are looking. Usually, the term strength is used to describe the ability to move a load or to do work, which is called active strength, whereas the contracture is a passive strength. By creating a significant contracture, the spastic muscle has great passive strength but low active strength compared with normal muscles. Active strength is altered more in spastic children because of the difficulty of avoiding co-contraction, as there is less antagonist inhibition in spasticity. Motor units tend to get larger and have slower responses with longer latency periods combined with a large shift to the slow-twitch type 1 fibers (Dietz and Berger 1995; Castle et al. 1979). All these changes mean the muscle responds slower during contraction and,

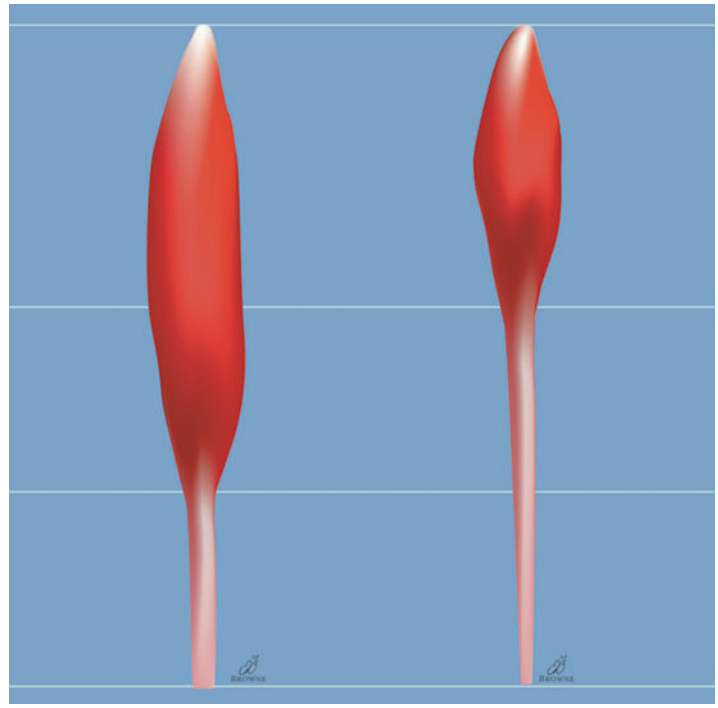

Fig. 3 The effect of spasticity on the growth and development of skeletal muscle results in a muscle that has fewer muscle fibers, shorter fiber length, and a longer tendon. This aberration results in a muscle that is weaker because of decreased cross-sectional area and has less excursion, resulting in decreased joint range of motion because of the shorter fiber lengths

combined with the changes in the nerve, has a longer latency period. Children with spasticity were recently found to be resistant to succinylcholine, and on further investigation, it was found that the neuromotor junction contains immature subunits. The effects of spasticity on skeletal muscle are pervasive and often experienced by neuro-orthopedists; however, a physiologic explanation of how increased tone causes all these changes is still unknown (Robinson et al. 2013) "▶ Neuromotor Junction Changes in Cerebral Palsy".

There is a grave need for basic research and understanding of muscle response to spasticity. There has been much more interest in understanding the muscle changes due to spasticity in the last 10–15 years. Most recent detailed findings are reported in an associated chapters, "▶ Muscle Changes at the Cellular-Fiber Level in Cerebral Palsy," "▶ Gross Anatomic Muscle Changes in CP". In the context of dynamic control theory, these changes seem to be revolving around a strong, stable attractor whose basic factor seems to be a simplifying control for a damaged motor control system, which is slowing the response time, stiffening the system, and providing passive strength in the face of absent active strength. This stable chaotic attractor seems to be organizing around the functional benefit of the organism, which can now support weight in stance and is able to move in space, although at a slower rate than normal. Although there are no good detailed explanations at this time from the maturation perspective of exactly what determines these changes, they all make sense in the dynamic control model. The major problem of this chaotic attractor is that it seems too stable and there is an overreaction in many children, with the changes in themselves becoming functionally limiting and causing problems "▶ Neurologic Control of the Musculoskeletal System: Implications for Cerebral Palsy Management".

Effects of Spasticity on Bones

Changes in the bones caused by spasticity are modulated by muscular changes. The most common effects are dislocated hips; scoliosis; foot deformities, such as planovalgus feet or equinovarus feet; bunions; knee contractures; and elbow, shoulder, and wrist joint contractures.

Torsional malalignments of the femur and tibia are common as well. A major part of this text discusses the management of these deformities. These secondary deformities, such as dislocated hips, have been very well defined and have clear mechanical etiologies (Miller et al. 1999). These deformities all have clear and strong pulls to develop toward easily understood chaotic attractors. In the hip, on one side the muscle will become contracted causing adduction, and on the other side, it will become contracted in abduction. Therefore, both hyperadduction and hyperabduction are stable attractors. With a decreased level of fine motor control and spasticity, the neutral position of the hip is not a stable region. This concept also applies to other affected joints.

Functional Effects of Spasticity on Sitting, Gait, and Activities of Daily Living

There are many functional effects of spasticity, some of which help children and some of which cause major problems. For children who are ambulatory, the spasticity causes typical spastic gait patterns. These gait patterns are discussed in other chapter "▶ Cerebral Palsy Gait Pathology".

Children who are able to do minimal weight bearing for transfers or household ambulation are often greatly aided in these activities by the spasticity, which provides the strength and stability for weight bearing. These same children may have problems relaxing in seating positions and therefore are difficult to seat. They may also have so much spasticity that activities of daily living, such as dressing and toileting, are difficult. Each child requires a careful assessment of the specific problems and benefits caused by the spasticity. There is a tendency for family members and some clinicians to equate the spasticity to CP. It is often difficult for them to see the benefits provided by the spasticity.

Treatments

When planning for treatment of the spasticity, the benefits and problems should be carefully considered. Everyone must realize that no matter how successful the treatment of the spasticity is, the child will still have CP. It should always be kept in mind that the goal in treating spasticity is to never remove all muscle tone. It is much better to conceptualize spasticity treatment similar to treating hypertension. Clearly, the treatment of hypertension would not be successful if all the blood pressure were removed. There is considerable similarity between no blood pressure and no muscle tone. The ideal treatment of spasticity would be a situation where the tone is decreased only at the time and in the anatomic area when and where it causes problems. The spasticity would then be preserved in all situations in which it is helping the child. It is also important to remember that some of the secondary effects in the muscle noted above may also have direct effects from the primary lesion. For example, the strength of a muscle contraction is mediated by the cerebral cortex impulse. Therefore, in a child with CP, this ability to modulate strength may be a primary deficiency due to the brain lesion. After the child has been evaluated with an assessment of the specific benefits and problems of spasticity, available treatment options should be considered.

The treatment of muscle tone may be applied at different locations in the neuromuscular system. Treatment options start in the central nervous system with the use of medications, electrical stimulation, or surgical ablation. In the peripheral nervous system to the level of the muscle, medication and ablation are the main choices. At the muscle level, medication, electrical stimulation, or surgical lengthening are the treatment options. Treatment options to be further discussed in this chapter will be limited to focal or localized treatments.

Peripheral Nervous System

Another way to decrease spasticity is by intervention at the level of the peripheral nerves. The only options involve lesioning of the nerve, either chemically or by physical transection. This lesioning mainly involves addressing the motor nerves instead of the sensory nerves, which are addressed by a rhizotomy. Chemical lesioning is often at least partially reversible. The chemical agents range from short-acting to long-acting local anesthetics, alcohol, and phenol. The use of local anesthetics to block nerve transmission was usually advocated as a way of doing diagnostic tests to see if a child would benefit from a surgical lengthening procedure (Carpenter 1983). This concept makes little sense today because the blockade of nerves does not affect the contracture, which usually is the major problem to be surgically addressed. With today's modern diagnostic gait laboratories, this type of diagnostic evaluation has little use. In the 1970s, the use of alcohol was also advocated as a diagnostic and therapeutic way to reduce spasticity. Alcohol injections generally provide a decrease in tone for 1–3 months (Carpenter and Seitz 1980). Phenol is an even more caustic agent and will destroy the nerve, so the spasticity will stay reduced for 18–24 months; however, it is a very painful injection usually done under general anesthesia. Both alcohol and phenol were very popular in the 1970s and into the early 1980s. Because of the toxic nature of these drugs and because the injections were painful, general anesthesia was required. With the availability of botulinum, there is only a rare role for their use to manage spasticity today. The use of the alcohol or phenol for chemo denervation has very low data support in the published literature combined with the risks of scarring fibrosis have little indication excepted for very limited indications such as anterior branch obturator nerve denervation (Quality Standards Subcommittee of the American Academy of et al. 2010; Park et al. 2014; Tilton 2003).

Direct surgical ablation of the motor nerve also has a long history as a means of reducing spasticity. Sectioning of the obturator nerve to decrease adductor spasticity at the hip is the most common indication (Matsuo et al. 1986; Sharma et al. 1989). In general, this procedure should be done only in nonambulatory children, and then only the anterior branch of the obturator nerve should be sectioned. Anterior branch obturator neurectomy is typically done in adolescents with severe adductor spasticity or in younger children with severe hip dysplasia in whom an attempt is being made to reduce the hip and allow the dysplasia to recover without doing hip reconstruction. Occasionally there may be a child in whom neurectomy is a reasonable option in the upper extremity (Msaddi et al. 1997), where the flexor muscles can be denervated by dissecting out the motor branches of the ulnar nerve. Also, there are reports of doing gastrocnemius neurectomy or neurotomies to control ankle equinus (Doute et al. 1997; Deltombe et al. 2001); however, this is not a good idea from a mechanical perspective, as the muscle would lose strength. Overall, for the control of spasticity, peripheral neurectomy has a minimal role in the management of spasticity in the child with CP.

Localized management of severe spasticity and movement disorder in the upper extremity can be especially difficult. This is the situation where the combination of denervation utilizing neurotomy and chemodenervation is often most applicable. There is a significant problem with pain from the impact on sensory nerves with these techniques to the point where the goal of making the limb flail may be achieved but the chronic pan becomes a major problem. Exploring all options such as intrathecal baclofen and, when movement disorder is a component, deep brain stimulation before moving to aggressive denervation is preferred. Experience with one patient shows this problem as he ended, finally as a young adult having his arm amputated at the shoulder to be relieved of the pain (Case 1).

Neuromotor Junction and the Muscle

Botulinum Toxin (Botox)

Botulinum toxin (Botox) is a neurotoxin that is extracted from *Clostridium botulinum,* an anaerobic bacteria that typically causes food poisoning.

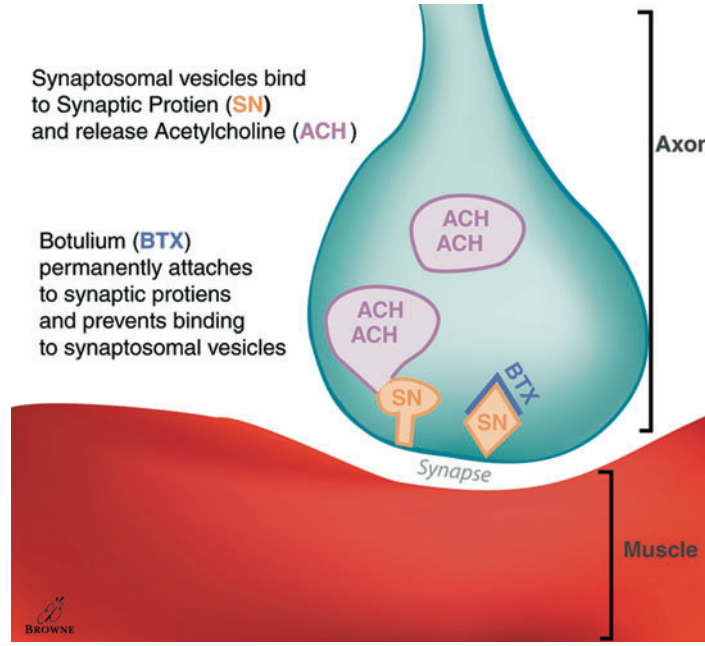

Fig. 4 Botulinum toxin affects the neuromotor junction by irreversibly binding to the synaptic receptors to which the synaptosomal vesicles bind. This prevents the synaptosomal vesicles from releasing the acetylcholine into the neuromotor junction; therefore, activation of this neuromotor junction is no longer possible

Botulinum toxin was initially used to treat strabismus in 1973 (Jankovic and Brin 1997). It was approved for use to treat blepharospasm in 1987 and, since that time, has been approved to treat cervical and oral dystonia in adults. Almost every medical problem seems to have developed a reason to use botulinum toxin. The uses of this drug include spasticity, dystonia, cystitis, essential hyperhidrosis, facial wrinkles, facial asymmetry, debarking dogs, bruxism, stuttering, headaches, back spasms, bladder spasms, achalasia, anal spasms, constipation, vaginismus, tongue protrusion, and nystagmus. There are very few drugs on the market today with such widespread use. Botox is serotype A and is currently the most available therapeutic toxin of the seven available serotypes, although botulinum serotype B is sold as MYOBLOC. The differing therapeutic effects of the different serotypes are not clearly defined. In my experience, patients who develop resistance to serotype A will often respond to several injections of type B toxin. The botulinum toxin binds irreversibly to the neuromotor junction, preventing the junction from functioning. This creates a permanent blockade, and the current theory holds that the peripheral nerve sprouts new distal fibers and forms a new neuromotor junction. This process requires approximately 3–4 months. After new neuromotor junctions are formed, normal motor function returns (Fig. 4). This widely held view is not well documented scientifically (Bonner et al. 1994; Ma et al. 2005). The toxin is a large protein molecule approximately 150 kilodaltons (kDa) in size (Brin 1997). Botulinum toxin is frozen to preserve the drug and its function and requires reconstitution with saline at the time it is thawed. Because it is a large molecule, the solution should not be vigorously shaken or injected rapidly through a small-bore needle or the turbulence created could potentially denature some of the protein. When Botulinum toxin is injected into the muscle, it causes a decreasing gradient of denervation approximately 3 cm in radius from the injection site (Borodic et al. 1994). Therefore, botulinum toxin injected into the muscle will cause temporary denervation followed by reinnervation, which takes approximately 3–4 months. Significant weakness occurs with a decrease in spasticity. The effect of this decrease in active spasticity is clear; however, this drug has no effect on the fixed contracture that may also be present.

The role of botulinum toxin for children with CP is continuing to evolve; however, its main use is to control spasticity. Others have promoted botulinum toxin as a pain control drug to use

postoperatively to decrease postoperative muscle spasms (Barwood et al. 2000), a concept that does make some sense. We have found this especially helpful after rectus femoris and hamstring surgery. The major use of botulinum toxin to treat children with CP is to decrease localized spasticity in a situation where some functional gain is expected. The typical situation is a 3- to 4-year-old child with a very spastic gastrocnemius who has problems wearing an orthosis. The botulinum toxin injection allows much more comfortable brace wear. Botulinum toxin can be used in the cervical paraspinal muscles for severe hyperextension, opisthotonic posturing, upper extremity contractures with severe spasticity, or in hamstrings or adductors with significant spasticity. Botulinum toxin injection to the adductors is not recommended as a treatment of spastic hips, except in a closely controlled clinical research trial, because there is a well-documented treatment that yields excellent results and deviation from these guidelines may increase the risk that more children will need hip reconstructions. A well-controlled study showed no benefit to the prevention of hip displacement (Willoughby et al. 2012); however several other less well-controlled studies suggest a potential to delay subluxation (Yang et al. 2008; Fehlings 2005). A dose of 5–10 units per kilogram of weight is typically used and can be divided between two or three sites. Some studies report using up to 20 units/kg (Kawamura et al. 2007) or 30 units/kg (Delgado et al. 2017). The dose should be diluted with 1–2 ml saline per 100 units of Botulinum toxin and injected with a small (25- to 27-gauge) needle into the neuromotor junction-rich zone of the target muscle. This zone is generally at the junction of the proximal and middle one-third of the muscle. The injections are usually done in a fan-shaped fashion to help diffusion, and only local topical anesthetic is used, such as Emla cream (Fig. 5). Care should be taken not to inject the drug intravascularly; however, this has never been reported as a significant problem. Parents should expect the maximum effect to become present in 48–72 h. It is possible to reinject other muscles in 4 weeks, by which time all the drug will be tissue fixed or degraded.

Botulinum toxin is a short-acting drug by the nature of the way the neuromotor junction recovers. This character of the drug is good if the result of an injection is not considered beneficial; however, it is usually a drawback because the injection does provide a positive effect, which is subsequently lost. Repeat injections after 3–6 months are possible, but an immunity or decreased response to the toxin develops in many children. In our experience, most children have about 50% less benefit with each subsequent injection, and all children whom we have treated with more than four or five injections have developed complete non-responsiveness. This lack of response is very frustrating for the child and family because the drug initially provided a very positive beneficial effect (see Case 1).

The well-documented effect of botulinum toxin is to decrease spasticity and strength in the injected muscle, with the tone and strength recovering in the subsequent 3–6 months. This has been the outcome of many well-controlled studies and multiple systematic reviews (Fonseca et al. 2017; Quality Standards Subcommittee of the American Academy of et al. 2010; Hoare et al. 2010). The documentation of the functional long-term benefits is very limited (Ryll et al. 2011; Baird and Vargus-Adams 2010). The limited functional benefit beyond short-term spasticity reduction in upper extremity use is also widely reported (Wasiak et al. 2004; Rawicki et al. 2010). Some families report a longer beneficial side effect; however, most studies looking at objective findings see little change after the initial positive effect. There may be longer-lasting functional gains in some children, which may suggest that there is a reorganization that occurs such that the patient may settle around a slightly different chaotic attractor. It should also be noted that almost all the studies are evaluating children and few studies have good case control or follow children for more than 6 months. Therefore, it is very hard to sort out botulinum effect from normal growth and neurologic development. The temporary change related to botulinum injection may also allow physical therapy to have a positive effect on the individual's motor control system to shift the dynamic function. Also, many

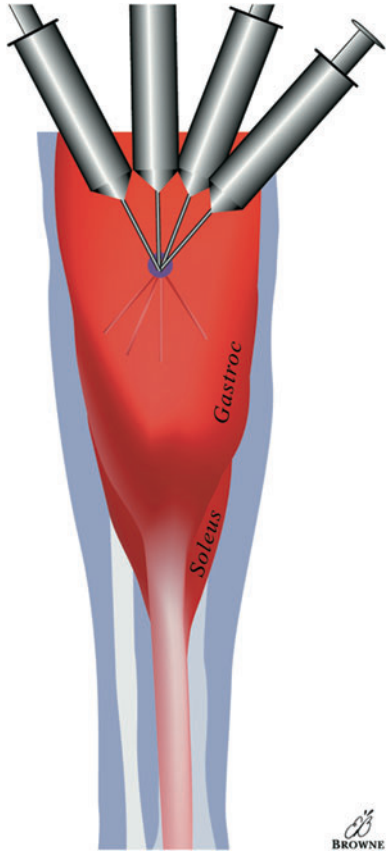

Fig. 5 Botulinum toxin is diluted with 1–2 ml saline and injected into the neuromotor junction-rich zone of the muscle to be blocked. This neuromotor-rich zone is usually in the proximal one-third and two-thirds junction area. The botulinum is injected in a fan-shaped pattern with an understanding that it diffuses over approximately 3 cm from the injection site. For the gastrocnemius, separate medial and lateral injections may be made

clinicians believe that botulinum toxin should be used in conjunction with other modalities, such as therapy, bracing, or casting (Molenaers et al. 2010; Love et al. 2010). Because of its temporary nature, this concept has good merit as a way of trying to gain more long-term functional improvement. Combining modalities makes it even harder to determine the impact of a specific treatment and how it impacts normal neurologic development. Also if considerable effort with multiple modalities only pushes a child slightly away from a very stable chaotic attractor, the long-term prognosis is poor because the child will settle back to where she was when the efforts started. It is unclear at this time how often botulinum toxin can benefit a child by truly moving the dynamic motor control to a substantially new attractor area. There are many mentions in the literature that the use of botulinum toxin with other therapies may delay or reduce the need for orthopedic surgery; however, to date there is no scientific evidence to support this claim. Another major problem with botulinum toxin is that it is extremely expensive. As more companies develop other serotypes, perhaps competition will cause the price to drop.

Complications of Botulinum Toxin

After the initial wide spread use of botulinum toxin in children with CP, there was a general sense that there was almost no risk involved; however, there were sporadic personal comments of deaths occurring. This first received wide spread concern in 2009 with the publication by the US FDA with a block box warning including death as a risk (Kuehn 2009). At this time, they noted reports of four deaths to be temporally related to botulinum injection. At this time, it is not clear which children are at greatest risk for death; however, it is a general consensus among CP specialists that whole-body, spastic quadriplegic children receiving high doses of botulinum toxin are at greatest risk although this is not confirmed. From personal report, I am aware of at least six to ten other deaths related to botulinum injection that are unreported, although I have not had a personal patient die. There is only one reported study in the literature which reports a death due to botulinum in a study treating scoliosis in spastic quadriplegia (Wong et al. 2015). It is our recommendation to limit the dosage to a maximum of 10–12 unit/kg total body dose and to be especially careful with children with severe spastic quadriplegia.

There are multiple other complications that have been reported, the list note in the black box warning related to cerebral palsy include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties; life-threatening swallowing and breathing difficulties can occur. When asked, weakness is relatively a common complaint. I have had two patients with single gastroc injections of

botulinum develop incontinence for 3 months. It is unclear why there are so many complications listed by the FDA and almost no study reporting the outcome of botulinum treatment reports complications. I suspect treating clinicians are often willing to find another excuse to assign to the complaints and are not willing to acknowledge the problems.

In addition to global complications, there has been increased concern with local complications, specifically that the muscle does not recover normally and there are long-lasting negative effects. Studies in rabbits show that the muscle does not recover in 6 months (Fortuna et al. 2015) and the non-injected distant muscle also have long-lasting effect of reduced strength (Fortuna et al. 2013). With repeated injections the muscle damage and recovery deficit seem to get worse (Hart et al. 2017; Rogozhin et al. 2008). A study of two normal humans found reduced gastroc muscle volume by MRI assessment and neurogenic atrophy of muscle fibers 1 year after injection (Schroeder et al. 2009). This limited scientific data supports my personal experience that there is lasting effect with weakness and increased muscle stiffness which gets worse with repeated frequent injections. One to three injection cycles in a young child likely do not have a significant long-term impact; however, there are physicians who inject patients every 4–6 months without regard for any functional benefit, presumably under the assumption that they are preventing the rise of spasticity. There is no published evidence that repeat injections are of benefit especially in the face of there being no functional impact. Based on the limited available data, this only further damages the muscle.

In summary, botulinum toxin to manage spasticity in children with CP is clearly documented to decrease local spasticity for 4–6 months after the initial injection. Current documentation of benefit of repeated injections is not available. There is no evidence available to support long-term functional benefit from botulinum injections. These benefits have to always be balanced against the known and possible complications. Considering this marginal risk/benefit ratio, it is an extremely popular treatment with a large literature base. A current search of "botulinum" and "cerebral palsy" yielded 907 abstracts in Pubmed.

Alcohol and Phenol

Injections into the neuromotor junction region with alcohol and phenol were also popular for a time, especially in the 1970s. Alcohol and phenol have the same problems when they are injected into the neuromotor junction as when they are used for neurolysis. In addition, if large volumes of the drugs are injected into muscles, intramuscular fibrosis can develop (Calderon-Gonzalez and Calderon-Sepulveda 2002). The use of alcohol and phenol for neuromotor junction injections is rarely indicated for the treatment of spasticity in children today. The combination use of phenol and botulinum toxin has been reported and is used in a few centers, which would seem to cause the most complications. The results are not very convincing considering the risks (Gooch and Patton 2004; Kolaski et al. 2008; Ploypetch et al. 2015). The use of phenol on the anterior branch of the obturator nerve which has no sensory elements is safe, well tolerated, and equal likely to nerve crush or neurectomy (Khot et al. 2008; Kwon and Kim 2009). The use of phenol nerve blocks with or without botulinum toxin do not have enough scientific data to suggest that they are effective (Quality Standards Subcommittee of the American Academy of et al. 2010) and the complication profile of phenol is significantly higher especially with dysesthesia to make botulinum a much better choice (Wong et al. 2004). Although mentioned by a number of authors as possibility, intramuscular injection of phenol has no reported benefit and only severe fibrosis as a side effect. There is currently no role for intramuscular phenol injection.

The use of intramuscular alcohol has been reported to be short-acting paralytic with no long-lasting effect (Carpenter and Seitz 1980). The use of alcohol for nerve block has a more

variable period of effectiveness compared to alcohol (Ghai et al. 2012). Since there is very little published data on the use of alcohol either for intramuscular injection or as a neurolytic agent and I have no personal experience, there seems to be no role for its use currently.

Direct Surgical Treatment of the Musculotendinous Unit

A very common and old treatment of spastic muscles is lengthening of the tendon, thereby releasing the contracture. In reality, the contracture is due to a muscle that has not grown sufficiently to its anatomically required length. The classic wisdom often repeated is that muscle tendon lengthening does not directly treat spasticity but only addresses the secondary effects of decreased muscle growth. This understanding of the effects of muscle tendon lengthening is only partly true because the hyperreflexic component of spasticity depends on the specific length and tension where the muscle is being stimulated (Connolly and Forssberg 1997). Thus, the muscle is much more sensitive to initiate a hyperreflexic contraction when the most sensitive region of the length-tension curve is under tension. For an example, with the gastrocnemius having its most sensitive length-tension curve set at 20° plantar flexion, hyperreflexia demonstrated clinically as clonus will be easily initiated in 20° of plantar flexion. By lengthening the tendon and allowing this most sensitive aspect of the muscle length to rest at 10° of dorsiflexion, there will be significant decrease in the spasticity or the ability to initiate clonus when the ankle is at 20° of plantar flexion. By this method, lengthening the tendon has direct functional effects on the spasticity by moving the sensitive region to an area where it is less likely to be initiated during an activity such as gait. Also, lengthening the muscle will give it the ability to generate active plantar flexion moment at the place in the joint range where it is needed, instead of in significant plantar flexion in which children get little additional mechanical advantage from the contraction. This complex effect of muscle length is discussed further in the section on gait "► Cerebral Palsy Gait Pathology". Adjusting muscle length through the use of tendon lengthening is one of the primary options for treating the major secondary muscular effects of spasticity and also has some direct impact on the spastic response of the local muscles.

Orthotics

There has been much discussion in different venues of tone-reducing orthotics, specifically the use of various orthotic designs, such as elevated toe plates, peroneal arch, calcaneal bar, and ankle articulations. All reported studies that objectively evaluated these claims have not found any benefit beyond the mechanical constraint these orthoses provide (Ricks and Eilert 1993; Crenshaw et al. 2000). Based on these published data, there is no direct evidence of an impact on tone by the use of orthotics. There may be some benefit to decreasing sensory input and thereby decreasing muscle tone in some children. Also, based on subjective experience reported by many clinicians, there are a significant number of children, especially those with quadriplegic pattern involvement, whose motor control system shifts to a different chaotic attractor. For example, by keeping the ankle at neutral in an ankle-foot orthosis (AFO), a child has less extensor posturing and sits better and has better arm control. This change in motor control is hard to directly relate to a reduction in spasticity; however, this change does occur. The orthotics have the opposite effect in some children. Often, these children are driven to push into more plantar flexion and hyperextension. These children get a sensory stimulus from the orthotic that drives them toward more of the extensor posturing attractor.

Special tone-reducing casts with molded-in pressure point areas in the soles and extended toe plates have been advocated as a technique for reducing spasticity (Ricks and Eilert 1993; Bertoti 1986). Only small case studies have been reported that suggest a benefit with this technique. However, it seems that the positive effects of wearing casts are directly related to the length of time they are worn (Otis et al. 1985). It is well known that cast wear causes muscle atrophy and weakness, which is the likely effect seen and

labeled as decreased spasticity in these children. In our experience, the benefit of casting usually is approximately two times the length of the cast wear time; therefore, if a child is in casts for 4 weeks, the benefits will last 4–8 weeks. Parents tire quickly of placing the child in casts and then having the effects quickly lost. Casting is very disruptive to the child's lifestyle because they cannot bathe, dressing is difficult, and the application of the cast is very time consuming. For these reasons, we do not find the use of tone-reducing casts of much benefit in children with spastic CP. The ankle orthotics, when they are fitting well, provide similar gains as the use of tone-reducing casts. There are many benefits of these orthotics over casts, including that the orthotic can be removed for bathing, the ankle range of motion can be maintained, and there is less muscle atrophy.

The use of serial casting continues to make good therapeutic sense in very spastic children in the acute recovery phase from closed head injury or any other circumstance where the spasticity is resolving. The use of casts in these children can provide a bridging effect until the spasticity resolves, and they are easier to maintain in orthotics. The primary mechanism for decreasing spasticity by immobilization is probably due to immobilization atrophy of the muscles and perhaps some stretching of connective tissue. There are no convincing data available that suggest that it is possible, through immobilization techniques, to make spastic muscles grow longer. Another reasonable use of serial casting is in cases of severe fixed knee flexion contracture where the goal is to do a knee extension osteotomy. If there is a 60-degree fixed knee flexion contracture and this can be reduced to 30–40°, the extension osteotomy will be much easier and require less rotation of the distal femur. This may provide some stretch to the muscles and the neurovascular structures as well.

Therapy

The use of physical therapy techniques, such as active and passive range of motion, is a well-accepted treatment modality in children with spasticity. There is no objective evidence that a specific therapy can impact the degree of spasticity permanently, although there are activities, such as horseback riding, which patients, parents, and therapists almost uniformly report to decrease spasticity temporarily. This same effect has been reported to us by individuals while riding in boats or doing other rhythmic activities. The effects on spasticity by these activities are hard to explain, but we believe they occur and probably are mediated through complex cerebral cortex sensory perception and motor control program generator interactions. From dynamic motor theory, this may also result from pushing the individual toward a different chaotic attractor that is not very stable, and as soon as the perturbation has subsided, the stronger attractor comes back into force and the individual's motor control system settles back to where it was before the activity. This explanation best describes what patients report; however, it is not very helpful in conceptually understanding what is happening from an anatomic perspective.

Passive stretching is a widely accepted modality for maintaining range of motion; however, objective documentation of the exact benefit is lacking. We have seen many children in patterning therapy programs where they were receiving passive range-of-motion exercises 18–20 h a day. These children do have less spasticity and better range of motion compared with similar children who get very little passive range-of-motion stretching. However, it is unclear how much passive range of motion is required to get a significant benefit, because it is neither practical nor healthy for children's overall development to be doing 18–20 h per day of passive stretching.

The use of vibrators, usually at 100–120 hz, also has been shown to decrease muscle tone, and they are often used by individuals who feel stiff. Some patients with CP report that the use of a vibrator makes their muscles feel less tight. This feeling is a temporary phenomenon and may be related to similar benefits that others report from deep muscle massage.

A Global Approach to Managing Spasticity

There are many options available to treat spasticity. In developing an algorithm, clinicians first have to remember and educate families that spasticity is not CP, and by removing spasticity, the CP will not be cured. Also, the spasticity is an exaggeration of a normal phenomenon, muscle tone, which is an extremely important aspect in normal motor function. Therefore, the goal is never to remove all muscle tone but to adjust the tone so it provides maximum functional benefit to the individual.

The first function of an evaluation for spasticity treatment is to tally the negative and positive aspects of the spasticity. Based on the specific problems the spasticity is causing, the clinician can choose from the available treatment options. First, the clinician needs to determine whether these problems are due to a global increase in spasticity or to increased spasticity in a local region, such as one joint or one limb. For example, the increased tone in the gastrocnemius of a hemiplegic child has very different implications compared with a child who has severe total body involvement and has problems being seated in a wheelchair.

For local problems that involve two to four specific muscles, the focus should initially be on local treatment. Examples of such localized spasticity are spastic wrist flexors and elbow flexors, equinus foot position, and spastic hamstring muscles causing knee flexion contractures. After identifying the problem as local, the clinician has to decide if it is supple spasticity only with full underlying joint range of motion, mainly a fixed muscle contracture due to a short muscle, or a combination of both supple spasticity and fixed contracture. If the problem is dynamic spasticity with no underlying contracture, then the primary treatment options are botulinum toxin injection and an orthotic. If the problem is a fixed contracture, the only option is surgical lengthening of the tendon. If the problem is mixed spasticity and fixed contracture, the options can be combined by starting with a trial of botulinum toxin and orthotics. To gain an adequate result when the botulinum toxin fails, a muscle lengthening should subsequently be done. By far the most common situation is children who fall into the mixed group with dynamic spasticity and contracture; however, there are also children who clearly fall into one or the other groups.

Children whose functional problems related to spasticity involve more than four muscle groups should be considered as the globally involved group. These children should be divided based on whether the problems are mainly caused by sleeping difficulties at night or daytime functional problems. The group of children with primarily nighttime sleeping problems is small, and it is never very clear whether these sleep problems are related to spasticity or whether they are a primary sleep disorder. This group, whose primary problem is nighttime sleeping, should be treated with a trial of oral antispasticity drugs, which occasionally work. Usually, diazepam is our first treatment preference, and we have several patients in our practice for whom this works well. Intrathecal baclofen also improves sleep and can be used if the oral trial fails. For children with daytime functional problems caused by global spasticity, the specific functional problems need to be identified. These functional problems may include difficulty with dressing, seating, and toileting or gait problems. This group should be further divided into those children with multiple functional problems and those with a single problem.

For children with multiple functional problems due to global spasticity, there usually are significantly more problems than functional benefits of the global spasticity. However, it is always important to consider what the functional benefits of the spasticity are for the individual child. If these benefits can be preserved or are much less beneficial than the problems being caused by the spasticity, the main treatment option is the intrathecal baclofen pump.

For children with single functional problems, such as gait or problems with seating, attention should be focused on specific local treatments. For example, for children who have seating problems, a careful assessment of the seating system can often correct the problem by adjusting and

providing a well-fitting seating system. For children whose primary problem is gait, a very careful assessment, usually requiring a full instrumented gait analysis, should be completed to fully understand the interactions of the spasticity, contractions, and skeletal malalignments, which all may be components of their gait impairment. For most children who are independent ambulators and have global increase in spasticity, the primary treatment is correcting the specific individual components of the disability, such as correcting bony malalignments, lengthening contracted muscles, and transferring muscles that are functioning in the wrong phase of gait. The use of intrathecal baclofen may be an option, although the specific indications for its use in this population are still not well developed. For children who are ambulatory with diplegia, dorsal rhizotomy or intrathecal baclofen can be considered between the ages of 3 and 8 years in those individuals with no bony deformities or muscle contractures and only dynamic spasticity.

Children with global spasticity who are having significant upper extremity problems should usually be considered for surgical reconstruction. For children with global spasticity who have specific problems related to functional tasks of daily living, such as self-dressing or toileting, the first treatment should be an intensive evaluation by an experienced physical or occupational therapist. In summary, by combining all the options and careful assessment, children with CP can usually be treated in a way that makes the spasticity become a benefit and not a major component of their impairment.

Cases

Case 1 Joe

At age 4 years, Joe developed a mild bleed from a brain arteriovenous malformation. This condition was surgically treated, and following the procedure. he was left with mild left hemiplegia. This appeared to be a typical spastic hemiplegia until he entered puberty at age 14 years. A significant dystonic movement disorder developed in his left upper extremity, in which the elbow would flex along with strong wrist and finger flexion. An attempted treatment with trihexyphenidyl was unsuccessful. The biceps, forearm flexors, and finger flexors were then injected with botulinum toxin, which provided excellent relief, allowing the limb to remain in good position. Repeat injections were performed every 4–6 months over the next 2 years with gradually diminishing effect. At this time, the dystonia was so severe that finger flexion was causing skin breakdown in the palm, which was very painful. Motor point injection alcohol of the biceps and finger flexors provided only 3 months of relief. The same motor nerves, as well as the motor branches of the radial nerve, were then injected with phenol. This injection caused a severe neuritic pain syndrome for 6 weeks because the phenol also affected the sensory nerves. This injection provided almost 12 months of improvement in the dystonic movement. However, elements of the dystonia returned. The shoulder tended to go into extension and abduction, which was very annoying, because as he walked in school the arm would suddenly fly into extension and abduction, hitting walls or other people (Fig. C1.1). This was extremely annoying and frustrating to him. Because of the severe pain from the previous phenol injection, he refused it and other phenol injections, actually requesting amputation of the limb. It was recommended that Joe go for an evaluation for possible central lesioning to decease the dystonia; however, he refused this because he blamed his first brain surgery for all his current problems. With few other options left, he had a surgical denervation of the upper extremity, cutting the suprascapular nerve, motor branches to the

(continued)

Fig. C1.1

triceps, and deltoid muscles. At the forearm, the motor branches to the finger and wrist flexors and extensors were cut. Because it was difficult to cut all motor nerves without cutting sensory nerves, some isolated motor function remained and got stronger over the next year following the denervation. At this time, the tendons on several finger flexors, the wrist extensor, and the biceps were released. He continued to have pain from the denervation and still some muscle movement and in his mid-20s had a shoulder disarticulation which has brought him relief.

Cross-References

- Cerebral Palsy Gait Pathology
- Dorsal Rhizotomy for Spasticity Management in Cerebral Palsy
- Gross Anatomic Muscle changes in CP
- Intrathecal Baclofen Therapy for Cerebral Palsy: Assessment and Medical management
- Medical Management of Movement disorders in Cerebral Palsy
- Muscle Changes at the Cellular-fiber Level in Cerebral Palsy
- Neurologic Control of the Musculoskeletal System: Implications for Cerebral Palsy Management
- Neuro-Motor Junction Changes in Cerebral Palsy

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