BOTOX

Information compiled and presented
By Cerebral Palsy Association of BC

(604) 515-9455 or 1-800-663-0004

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Minutes of BOTOX Seminar: by Dr Richard Beauchamp (March 16, 2000)

CEREBRAL PALSY AND BOTOX

Cerebral palsy covers a broad range of abnormal motor or movement disorders. What does it encompass?

(a) Spasticity

This is the most common and is mainly caused by an increase in the Stretch Reflex or Spastic Reflex. In other words, when a muscle is pulled it reacts by suddenly pulling backwards.

(b) Athetosis

This describes abnormal muscle movements and this 'uncontrollable' movement could be in either the arms or the legs. In athetosis, there is some spasticity and this can be removed surgically but the presence of an athetoid component (The component that makes movement uncontrollable) makes surgery unpredictable because it would result in athetosis worsening. What actually happens is that when spasticity is removed, an athetoid component - which can be worse than the spastic component - is uncovered.

(C) Dystonia

This is a term for abnormal muscle tone; the tone fluctuates from being very tight to being floppy or loose. This is a common term mostly given to adults with Cerebral Palsy.

(d) Ataxia

This is just another term for abnormal balance

One other way of treating Cerebral Palsy other than with BOTOX is by electromyography. This entails putting electrodes on the muscles to enable children to walk back and forth in order to determine which muscles are abnormally firing. Those that are can then be singled out and relaxed.

History of BOTOX: Botulinam Toxin Type A

The BOTOX toxin was extracted from the bacteria that are responsible for food poisoning (Bocholina) during the late 60's to the early 70's.

Initially, the toxin was used for eye muscle problems, e.g. in cases where one eye muscle is weaker and the other stronger ('squint'), the toxin is injected into the stronger eye muscle - relaxing it - and thus resulting in permanent correction of the problem.

The toxin only commenced being used for the treatment of cerebral palsy in the latter part of the 70's; and even then, it wasn't until '1995 that it was officially approved for use for persons under '12 in Canada. In this respect, Canada is ahead of the U.S.A. in that the latter has not yet officially approved the use of BOTOX in under 12's.

There are seven (7) neurotoxins of which the most commonly used is BOTOX A. It was the first to be discovered and is used clinically.

Cerebral Palsy affects mainly the muscles, in particular where the nerves - or neuros - come into the muscle of the limb and where they (nerves and muscles) attach. This place where they attach is known as the neuro-muscular junction. As the nerves transmit impulses across the neoro-muscular junction, the muscles contract and this causes involuntary spastic movements. Administration of BOTOX by injection stops this and stabilizes movement.

Who benefits from BOTOX?

Not everyone needs to have his or her spasticity removed. Some patients need to have some degree of spasticity in order to walk, stand, etc. In other words, some patients rely on their spasticity for their strength and removing it would weaken them.

Children born with Cerebral Palsy should have BOTOX injections as early as possible before their muscles contract and stay permanently shortened. As they grow older and their muscles are constantly in spasms, the children's muscles get shorter as the bones grow longer and deformities occur. At this stage, it is too late to relax the muscles by BOTOX injections but there is the option of surgery. All in all, younger patients are more amenable to BOTOX than older ones hence the need to administer the toxin at an early age.

Cost

BOTOX comes in vials of 100 International Units and is freeze-dried and reconstituted (mixed). The average price of each vial is $340 Canadian. Normally, 10 I.U.'S per kilogram body weight are injected. So, a child weighing 10 kilograms will have 100 units (i.e. one vial) as their maximum dose.*

BOTOX by itself without anything else is not appropriate for management of children with cerebral palsy; it is just a stage in the overall management program.

* BOTOX is NOT covered by insurance. However, one of our members found out that her Insurance Company has insurance cover for BOTOX. For more details, please contact your Insurance Company.

The ABCs of BOTOX

This article on Botulinum toxin A was prepared by Dr. Deirdre E. McLean, Pediatric Physiatrist at the Queen Elizabeth II Health Sciences Centre in Halifax. It was first published in the September 1998 *edition of the newsletter of the Cerebral Palsy Association in Alberta.*

What is Botulinum toxin A?

This is a question physicians and therapists who treat children with CP are being asked more and more often. In North America, Botulinum toxin A has been used to treat limb spasticity associated with CP and other disorders since the early 199Os. It is injected directly into the spastic muscles that need to be treated. Botulinum toxin A is a strong neuromuscular blocking agent that acts by partially weakening over-active, spastic muscles. The weakening is not permanent and usually wears off with 3 to 4 months.

How does Botulinum toxin A work in children with cerebral palsy?

The goals of Botulinum toxin A treatment will vary for each individual child, but in general, it is used to improve overall function by decreasing limb spasticity. Treatment with Botulinum toxin A can "unmask" muscle control in affected limbs by reducing unwanted muscle tone. By temporarily weakening muscles, Botulinum toxin A allows affected muscles to be more easily stretched. Joint range of motion is therefore allowed to improve and the likelihood that fixed deformities such as contractures will develop is decreased. Both upper and lower limbs can be treated with Botulinum toxin A. In upper extremities expected outcomes following Botulinum toxin A treatment include improved grasp and decreased pain. In legs that are treated, decreased toe-walking, better brace fit and more comfortable sitting are among the benefits that have been reported following Botulinum toxin A treatment.

Will all children with CP benefit from treatment with Botulinum toxin A?

Children between 2 and (3 years of age with "dynamic spasticity" are the best candidates for treatment with Botulinum toxin A. These children are those who demonstrate increased tone when they attempt to move. Children with contractures that remain unchanged despite limb position will not benefit from Botulinum toxin A treatment. Children who are taking medications such as blood thinners or certain types of antibiotics need to let the doctor know in advance. Children who have other neurologic conditions besides CP will need to be considered on a case basis. Girls who may be pregnant should not be treated with Botulinum toxin A.

What does the treatment procedure involve?

Botulinum toxin A must be injected into the affected muscle in order to work. Muscles to be injected are treated first with a topical anesthetic cream (EMLA), which freezes the skin and decreased the discomfort from the needle. One to four injections may be required for each muscle depending on the size of the child. Some smaller muscles, especially those in the arm, may require the doctor to use an EMG machine to correctly locate the muscle to be treated. After the treatment, there are no restrictions on the child's activities. Depending on the goals of the treatment, casts or splints may be necessary after Botulinum toxin A treatment.

Are there any side effects to Botulinum toxin A?

Side effects to Botulinum toxin A treatments are usually minor and temporary. Serious side effects to the treatment are rare. Possible side effects include flu-like symptoms, bruising or infection at the injection site, skin rash or problems with bladder control. Sometimes a generalized body weakness in muscles besides those that are injected, may occur. If breathing muscles or swallowing muscles become weak, the child should be taken to the nearest hospital for observation. Fortunately this development is not very common. There is also a possible risk of antibodies forming to the toxin if several injections are given within a short period of time. Therefore, it is recommended that Botulinum toxin A treatments not be given more often than once every three months.

Summary:

Botulinum toxin A is a potentially useful treatment for spasticity in children with CP. To determine if children might benefit from this treatment, they will require an assessment by a physician experienced in the use of Botulinum toxin A in cerebral palsy. It must be remembered that the effects of Botulinum toxin A are only temporary, and re-injections every three to six months may be necessary to maintain the desired clinical effects. Each child's case is different. For some children, a more definitive procedure such as heel cord lengthening or selective dorsal rhizotomy might be a better treatment plan.

In Manitoba, Botox is a prescription pharmaceutical and therefore it is available like any other prescription drug. Not all children who have CP will benefit from treatment with Botox. If parents or caregivers wish to have more information regarding the potential use of Botulinum toxin A in their child, they should contact their physician.

The C.P.
Community Centre
of Care.

A Special Place of knowledge, Skill and Support

Welcome to the Centre of Excellence
for the treatment of Juvenile Cerebral Palsy.
The Centre of Excellence concept is
built on three pillars: patient-centred care,
specialized knowledge and family support.
The physicians at this Centre possess
specialized knowledge knowledge and skill in the
use of BOTOX® for treating spasticity in
Cerebral Palsy. This pamphlet has been a
designed to answer some of your questions
about the Centre and about BOTOX®
The healthcare professionals at the
Centre of Excellence will be happy to
answer any further questions you may have.

Specialized Knowledge

The physicians and other health professionals at the Centre of Excellence have specialized training and skills in the use of BOTOX® for the treatment of dynamic equinus foot deformity due to spasticity in Cerebral Palsy. They have the knowledge and experience to answer any questions children/youth or parents may have.

The physicians at the Centre of Excellence share their skills with other doctors by offering this Centre of Excellence as a training centre for BOTOX® injectors. Research is ongoing at the Centre and the results of treatment are evaluated to ensure that the most updated in formation and learning are used in improving treatment.

BOTOX® treatment in Cerebral Palsy may not be available everywhere but the Centre of Excellence programs ensure that children/youth can receive the best care possible at many different locations across Canada.

Patient-focused Care

The central focus of the Centre of Excellence program is the child/youth with Cerebral Palsy.

This program is designed to create an environment for the child to feel safe and to provide the child/youth with some control over what happens.

The healthcare professionals at the Centre of Excellence will explain all procedures and offer the child/youth, and the parent, choices wherever possible.

Every effort will be made to keep the child/youth comfortable and make the experience at the Centre of Excellence as pleasant as possible.

Support for the Whole Family

At the Centre of Excellence, patients find more than highly specialized care and attentive professionals. They wilt also find programs to provide support and information for the whole family. Because at the Centre of Excellence we know that Cerebral Palsy affects everyone close to it and that the family is an integral part of patient care.

Some programs at the Centre of Excellence include:

- Support Groups
- Information Video
- Information on Cerebral Palsy

Treating Cerebral Palsy with BOTOX®

This booklet has been developed to provide information about BOTOX® and its use in the treatment of dynamic equinus foot deformity due to spasticity in pediatric Cerebral Palsy patients, two years of age or older. Many of the most common questions are answered here. Read this booklet and ask your healthcare Professional if you have any other questions or if there is anything you are not clear on. The Centre of Excellence staff are here to help.

What is BOTOX®?

BOTOX® (Botulinum Toxin Type A) purified neurotoxin complex is a novel treatment produced from bacteria called, Clostridium ***Botulinum.*** Produced in strictly controlled laboratory conditions and given in extremely small therapeutic doses, botulinum toxin is generally well -tolerated and an effective treatment for many conditions associated with hyperactive muscle disorders.

Botulinum Toxin Type A ***is*** one of seven different types of botulinum toxins (A,B,C,D,E,F,G). Each has different properties and actions. No two toxins are exactly alike. There is only one BOTOX®.

How does BOTOX® work?

Normally your brain sends electrical messages to your muscles so that they can contract and move. The electrical message is transmitted to the muscle by a substance called acetylcholine. BOTOX® works to block the release of acetylcholine and, as a result, the muscle doesn't receive the message to contract. This means that the muscle spasms stop or are greatly reduced after using
BOTOX®, providing predictable and reliable relief from symptoms, including -pain and muscle stiffness.

For more than 15 years, BOTOX® (Botulinum Toxin Type A) has been used worldwide, and has been

proven effective in the treatment of hyperactive muscle disorders. BOTOX® is not a cure. For many patients, however, its effects have been dramatic - symptoms usually begin to dissipate within a few days and the effects can last for more than three months.

Why is BOTOX® used in the treatment of Cerebral Palsy?

BOTOX® has been proven effective for use in the treatment of other hyperactive, overactive spastic muscle conditions and has been studied in Cerebral Palsy to treat muscle stiffness in children/youth.

Today BOTOX® is used in the treatment of dynamic equinus foot deformity due to spasticity in Cerebral Palsy for the following reasons:

- Significantly improved gait pattern
- Improvement in ankle position
- Reduction in equinus
- The improved gait pattern enables patients to perform daily personal activities more independently
- Decreased pain in stiff muscles
- Reduction in spasticity makes patient care easier
- May help delay surgery until the child/youth is older

Which children/youth are best suited to BOTOX® treatment?

- Over two years of age
- With muscle stiffness interfering with function
- Where calf length maintenance is required
- Who require early, conservative treatment
- Where improvement in gait is desired (toe walkers)
- Supported by a physiotherapy program

How is BOTOX® administered?

To get the best effect from BOTOX® the doctor will inject BOTOX® into the gastrocnemius using a very fine needle. The doctor may use an EMG device for guidance to help determine the site to inject. The amount of BOTOX® given will depend on how much the child/youth weighs. Most children/youth can be treated with BOTOX® on an outpatient basis.

Does the treatment hurt?

Injections of any kind can cause discomfort that is usually temporary. Anxiety about the injection can worsen the discomfort. When BOTOX® injections are given to children/youth, all efforts are made to minimize anxiety and discomfort. Sometimes, a cream is rubbed on the skin and left there for about an hour to help numb the area to be injected. The child/youth may be given a mild medication to help relax about half an hour before the injection. There are other relaxing techniques that can help keep the child/youth relaxed and calm during the procedure like calming music, a favourite stuffed toy, etc.

How will BOTOX® help with overall treatment?

BOTOX® can help provide relief from stiff muscle pain and can provide sustained improvement in both control and function of some muscle movements. A benefit of BOTOX® is that it can help make daily care easier for the parent.

When does it start to work?

BOTOX® can help by reducing the overactivity of the muscles very quickly. In fact, most people begin to see results within the first two weeks.

How long does the effect last?

Usually, BOTOX® provides relief of spasticity in the injected muscle for over three months (12-14 weeks). Then patients begin to notice a gradual fading of its effects over several weeks. At this point the doctor can give another treatment.

BOTOX® treatment may be required three or four times a year. It is not given more frequently than every three months. Cerebral Palsy is never the same for any two children/youth. The severity of symptoms will vary, so how much relief and how long it lasts will also vary from person to person. Talk to your doctor, who has special knowledge about how to get the best possible results with BOTOX® in Cerebral Palsy.

How long can BOTOX® be used in the treatment of Cerebral Palsy?

Safety for patients using BOTOX® for many years has been proven. There are a number of things that can affect how long BOTOX® is used in an individual. These include:

1. Knowing what to expect - after the first injection some children/youth show dramatic improvement. The second injection will ensure that the child/youth does not lose the improvement. Therefore, patients should not expect to see another dramatic change.

2. Determining the best dose - the doctor will adjust the dose based on each individual child's/youth's response to treatment.

3. Reducing the amount of neurotoxin protein that the child/youth gets - when people are exposed to large quantities of neurotoxin protein they can build antibodies against the protein. That is why BOTOX® has only 5 ng of neurotoxin complex proteins per vial, which may help reduce the chances of losing response to the botulinum toxin.

Are there any side effects?

All medications have some side effects. With BOTOX®, side effects are usually transient a and mild to moderate in nature. Some children/youth may notice weakness of muscles, pain at the injection site, or falling due to change in walking pattern (gait) or ankle position. Side effects are usually temporary, and BOTOX® is generally well tolerated.

The effects of BOTOX® may be increased with the use of certain antibiotics or other drugs that interfere with neuromuscular transmission. Ensure your doctor is aware of any current medications you are taking. If you have any questions regarding the use of BOTOX® treatment, please consult your doctor.

Where can I get more information on BOTOX®?

Check the BOTOX® patient web site at www.botox.com or call 1-800-668-6424.

BOTOX® for CEREBRAL PALSY

BOTOX® is indicated for the treatment of pediatric Cerebral Palsy patients with dynamic equinus foot deformity due to spasticity in patients two years of age or older.

BENEFITS OF TREATING WITH BOTOX®:

- significantly improved gait pattern
- improvement in ankle position
- reduction in equinus
- the improved gait pattern enables patient to perform daily personal activities more independently
- decreased pain in stiff (spastic) muscles[2]
- reduction in spasticity facilitates patient care
- may help delay surgery until the child is older[2,3]

BOTOX® may be used in conjunction with serial casting to stretch the muscle and help enhance the effect of BOTOX®

EXCELLENT SAFETY PROFILE:

Side effects are generally transient and well tolerated. The most common side effects with an incidence <10% are:

- temporary leg (local) weakness: usually a result of the expected effect of BOTOX®
- temporary general weakness
- falling: may be attributable to a change in ankle position, gait pattern, or local weakness
- leg pain: localized pain may be associated with the injection

CHILDREN/YOUTH BEST SUITED TO BOTOX®:[3]

- over the age of two
- with muscle stiffness interfering with function
- where calf length maintenance is required
- who require early, conservative treatment
- where improvement in gait is desired (toe-walkers)
- supported by a physiotherapy program

ONSET AND DURATION:

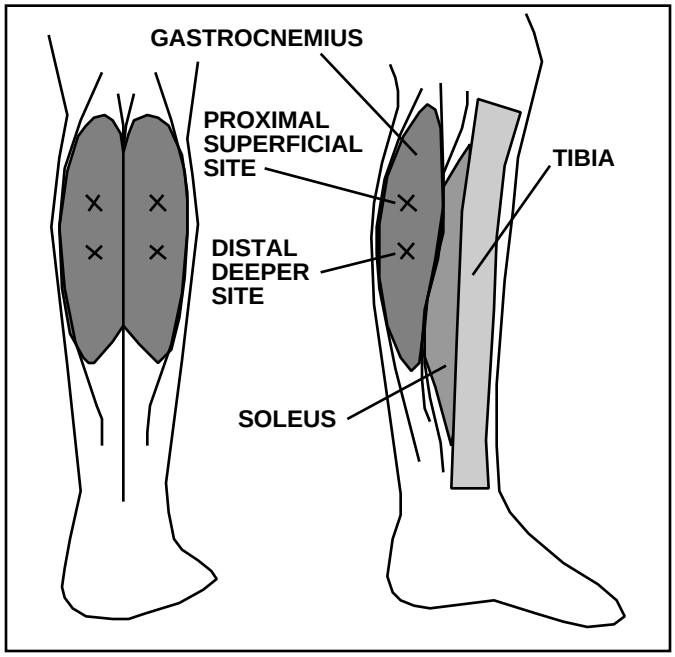
- Clinical improvement is generally seen within two weeks after injection
- The average duration of the therapeutic effect is over 3 months[†]
- Repeat doses should be administered when the clinical effect of a previous dose diminishes (not more frequently than 3 months) prescribing information available on request.

ADMINISTRATION:

Example: gastrocnemius muscle

Two sites in the medial and lateral heads of the gastrocnemius muscle of the affected lower limb(s).

INJECTION SITE EXAMPLES:



Caution should be used when BOTOX® is used in the presence of inflammation at the Proposed injection site. Ensure proper storage, handling, dose selection. reconstitution, administration techniques, muscle selection (may use EMG to assist), and have epinephrine available in case of anaphylactic reaction.

BOTOX® is a treatment of focal spasticity that has only been studied in association with usual standard of care regimens, and is not intended as a replacement for these treatment modalities. BOTOX® is not likely to be effective in improving range of motion at a joint affected by a fixed contracture.

† Dependent upon the patient's individual symptoms and responses.

Please consult prescribing information for complete dosing and safety information.

Prescribing information available on request.

Safe and effective use depends upon proper storage, dosage selection, and proper reconstitution and administration techniques.

1. Mall V., ***et al***. Treatment of cerebral palsy with botulinum toxin A: functional benefit and reduction of disability. Three case reports. ***Pediatric Rehabilitation*** 1997;1(4):235-237. 2. Koman L.A., ***et al***. Neuromuscular Blockade in the Management of Cerebral Palsy. ***J Child Neurol 1996;*** 11(Suppl 1):S23-S28. 3. Boyd R. and Graham H.K. Botulinum toxin A in the management of children with cerebral palsy; indications and outcome. ***European Journal of Neurology*** 1997:4(Suppl 2):S15-S22.