THE CLINICAL USE OF BOTULINUM TOXIN IN THE TREATMENT OF
MOVEMENT DISORDERS, SPASTICITY, AND SOFT TISSUE PAIN

Spasmodic torticollis (cervical dystonia), blepharospasm, and writer’s cramp are specific
types of a group of movement disorders known as dystonias. Dystonia is a neurological condition
of unknown cause. Some types of dystonia have a genetic component. Involuntary contraction
and spasms of one or more of a group of muscles anywhere in the body characterize these
disorders. This frequently involves muscles of the face, neck, arms or legs. This can cause
abnormal posturing of the head, neck, and extremities. Many different types of treatment have
been used in an attempt to control the disabling symptoms of these diseases. These have
included various types of medications as well as surgical procedures. None have proved to
provide any degree of lasting benefit. In the early 1990’s, the Food and Drug Administration
approved the use of botulinum toxin Type A (Botox) injections for the treatment of certain types
of dystonia. The FDA approved botulinum toxin Type B (Myobloc) for clinical use in early 2001.
Although not a dystonia, hemifacial spasm is characterized by episodic twitching or spasms of the
facial muscles on one side of the face. Botulinum toxin has proved to be highly effective in the
treatment of hemifacial spasm as well as spasmodic torticollis, blepharospasm, and writer’s
cramp. Newer uses of Botox include treatment of spasticity, focal soft tissue pain disorders
(myofascial pain), migraine and related headache disorders and temporal-mandibular joint
related disorders such as bruxism. Botox injections have been used successfully to cosmetically
smooth out facial wrinkles.

BOTULINUM TOXIN

Botulinum toxin is a complex protein substance produced by the bacteria, Clostridium
botulinum. It is most commonly associated with a form of food poisoning known as botulism.
Botulism poisoning is usually associated with improperly home canned foods, which can
sometimes be fatal. Botulinum toxin can be manufactured, purified, and diluted to specific
concentrations under highly controlled laboratory conditions. There are seven types of botulinum
toxin. Currently only Type A and Type B are available for clinical use (Botox and Myobloc
respectively.) Botulinum toxin can then be used to selectively inject into specific muscles. This
results in a temporary mild weakness (paralysis) of the injected muscle. The degree of weakness
can be controlled by giving varying amounts of the toxin into the treated muscles. These
selective, localized injections do not result in botulism poisoning because of the small quantities
utilized. Botulinum toxin is taken up into the nerve cells immediately in the vicinity of the
injection. These nerves are responsible for controlling muscle contraction. The botulinum toxin
then irreversibly binds to proteins inside the nerve cell. These proteins control the release of the
chemical neurotransmitter, acetylcholine. Botulinum toxin selectively blocks the release of
acetylcholine. This is the chemical messenger that allows muscles to contract. Blocking the
release of acetylcholine causes the injected muscles to relax, resulting in relief of the symptoms
of dystonia, twitching, spasticity, and pain. Maximum benefit, following injection, generally
occurs in 4-5 weeks. The clinical use of botulinum toxin is very safe when given under these
controlled conditions. There have been no reported cases of botulism poisoning in any patients
treated with botulinum toxin.
Side effects from botulinum toxin treatment are usually mild and have short duration. The most common is injection site pain or discomfort. This generally clears within minutes to a few hours after the procedure. Depending on the area treated, various degrees of weakness may occur, such as in the upper eyelid or neck. This may cause head or eyelid drooping. If the area around the eyes is treated, some patients may experience excessive tearing, dry eye syndrome, or blurred or double vision. Rarely patients with cervical dystonia have worsening of their neck pain after the procedure. Fortunately the unwanted effects of Botox are temporary, generally clearing within a few days to weeks.

**SPASMODIC TORTICOLLIS**

This condition, also know as *cervical dystonia*, results from involuntary contraction of one or more of the muscles that comprise the neck and shoulder muscle groups. This condition is initially manifested by turning or tilting of the head to one side or the other. Early on, patients can voluntarily return their head to a normal position. As the disease progresses, however, the head will assume a more fixed rotation or tilt. Head tremor is frequently present in patients with cervical dystonia. Other patients may have their head pulled backward (*retracollis*) or forward (*anterocollis*). Not only can this be socially embarrassing but also can be disabling and quite painful. Patients will frequently complain of neck pain and headaches. Functionally they may have difficulty speaking, chewing, swallowing or driving. The injection of botulinum toxin into the contracted, spastic muscles in the neck results in relief of the spasm and pain. This may allow the patient's head to return to a normal position. The therapeutic effect of these injections generally lasts two to four months. Because this is a temporary paralysis, the injections need to be repeated. Infrequently, some patients may experience temporary mild swallowing difficulty. This problem improves within two or three weeks after the injection.

Dystonia may affect different parts of the body other than the head and neck. An arm or leg can be affected (*focal dystonia*) and rarely patients may have generalized dystonia. Patients with focal forms of dystonia obtain tremendous benefit from Botox therapy. Functional use of the extremity is frequently restored with Botox.

**BLEPHAROSPASM**

Involuntary, forceful contractions and spasms of the eyelid and brow muscles characterize this type of focal dystonia. This results in intermittent or prolonged closure of the eyes. Blepharospasm can be very disabling. Blepharospasm may result in a functional blindness due to uncontrollable closure of the eyes. Affected patients frequently have difficulty reading and are unable to drive. Blepharospasm is frequently accompanied by spasms of other facial muscles around the nose and mouth as well as the neck and laryngeal muscles. This clinical syndrome is known as *Meige's syndrome*. Botulinum toxin injections into the affected eyelid and facial muscles provide excellent control of these spasms. Seventy to ninety percent of treated patients have significant improvement. Most patients can resume driving and are able to read. Their quality of life is dramatically improved. Clinical improvement generally lasts two to four months. Side effects may include blurred vision, drooping eyelid, double vision and increased tearing. All of these are self-limited and will spontaneously resolve. Botulinum toxin is considered the treatment of choice for blepharospasm because of its proven safety and effectiveness.
WRITER’S CRAMP

This is one of the more common forms of focal dystonia. It is also some of the most occupationally disabling. Affected individuals generally have symptoms only when performing specific tasks with their hands. These individuals experience spasms in their fingers and hands and they are unable to continue their routine activities. This can be completely disabling for people with jobs requiring a high degree of manual dexterity such as musicians, typists, jewelers, hair stylists or any other job requiring fine, coordinated hand movements. Injection of botulinum toxin, under EMG guidance, into selected muscles in the hand and forearm has been shown to be effective in controlling this form of dystonia. Many patients have noticed transient, mild hand weakness, but this is generally well tolerated and is much less disabling than the hand cramps.

OROMANDIBULAR DYSTONIA

This rare type of focal dystonia involves the muscles responsible for opening or closing the jaw. The muscles in the lower part of the face as well as the muscles of the tongue can be involved. There are two main types of oromandibular dystonia: jaw-closing and jaw-opening type. Jaw-closing dystonia can result in forceful involuntary closure of the mouth and teeth grinding (bruxism). Affected individuals can have marked difficulty eating and speaking. Injection of botulinum toxin into the jaw closure muscles results in good functional improvement of the symptoms. Botulinum toxin injections are considered safe and effective for this type of oromandibular dystonia. Injection of botulinum toxin for jaw-opening dystonia is more complicated. This disorder involves the muscles in the front part of the neck. These muscles are located next to some of the muscles involved in swallowing. Treatment of oromandibular dystonia requires a great deal of skill from a clinician very familiar with this particular disorder and advanced Botox (or Myobloc) administration techniques.

HEMIFACIAL SPASM

This disorder is not a form of dystonia, although it can be equally disabling as well as socially embarrassing. Patients with hemifacial spasm have involuntary twitching and contractions of the facial muscles on one side of the face, particularly around the eye. These spasms may occur at any time throughout the day and can progressively worsen. The spasms can become almost constant. This can impair an individual’s ability to read, watch television or drive. The cause of this condition is usually attributed to irritation of the facial muscle nerve as it exits the brainstem. This is usually due to a blood vessel rubbing against the nerve. Certain brain tumors can also cause symptoms of hemifacial spasm. A magnetic resonance image (MRI) brain scan should be performed on all patients with hemifacial spasm (HFS), at the time of initial diagnosis to exclude the possibility of brainstem abnormalities.

Various treatments have been utilized for HFS. Oral medications have been tried to alleviate the symptoms. The medications most effective are in the family of anti-seizure drugs. These include carbamazepine (Tegretol, Carbatrol), Dilantin (phenytoin) and Klonopin (clonazepam.) These medications can, in some cases, provide limited benefit. Neurosurgical decompression of the facial nerve is frequently successful in providing patients with relief. This procedure, however, requires brain surgery and is associated with certain risks.
Botulinum toxin is highly effective in the treatment of hemifacial spasm. This provides an excellent, safe alternative to surgery. Selective injections into specific facial muscles provide relief in almost all patients. Clinical improvement generally lasts five months, which is a longer period of improvement than with any other of the dystonias. The primary troublesome side effect that has been reported is a temporary, mild facial weakness. This occurs in approximately one third of HFS patients treated with botulinum toxin.

The facial nerve may be affected by other disorders, which can cause involuntary twitching of one side of the face. Bell's palsy is a condition characterized by facial paralysis. This condition most frequently heals completely. Unfortunately when the nerve regenerates some patients may be left with an involuntary facial twitching (synkinesis.) This twitching occurs every time they blink. A similar problem can develop in patients who have had certain types of brain surgery in the area of the facial nerve or in any other process that damages the facial nerve. Botulinum toxin is effective in controlling this involuntary twitching. Results are similar to those in patients treated for hemifacial spasm.

**SPASTICITY FROM SPINAL CORD INJURIES AND STROKE**

Spinal cord injuries can result from a number of causes. Trauma is the leading cause of spinal cord injury. Tumors, multiple sclerosis, spinal cord abscesses and stroke can also lead to permanent cord injury. Painful spasticity can develop as a result of cord injury in some patients. Botulinum toxin has been used successfully in controlling the pain from these spasms when other treatments have failed. In patients who have significant spasticity but not complete paralysis, the use of Botox may result in some functional improvement. The latter is particularly true for patients affected with spasticity from cerebral palsy.

Stroke is the third leading cause of death and one of the leading causes of disability in the United States. Spasticity occurs frequently after stroke. In patients who retain some function of the extremity after a stroke, they may be further disabled by the spasticity. Selective injections of botulinum toxin into the effected limb muscles, particularly in the arm, can help to relieve the pain and restore some function. It is important to note that Botox will not reverse the paralysis caused by the stroke.

**OTHER MOVEMENT DISORDERS**

Nationally, there is on-going research in the use of botulinum toxin for other neurological disorders. Patients with Parkinson’s disease occasionally can develop painful limb and hand dystonias as a result of the medications they must take. Other patients may have chronic, focal muscle pain with spasm that is unresponsive to standard medical therapy. Botulinum toxin therapy may be helpful in treating some of these patients. Tremor is another common disorder that can be difficult to treat. Patients affected with disabling tremors of the extremities can sometimes be partially helped with botulinum toxin. It is much more difficult to treat head and voice tremor, as these types of tremor frequently do not respond to any treatment. The FDA has approved the use of implantable brain stimulators for treatment of disabling tremor. This procedure requires brain surgery by a neurosurgeon trained to implant these devices.
A condition known as hyperhidrosis can be effectively managed by Botox treatment. This is not a movement disorder at all, but rather a disorder of pathologically excessive sweating. Commonly affected areas include the forehead, palms, and axillary regions. Botox can help patients affected with this socially embarrassing condition when other measures fail. The mechanism of action is the same in that botulinum toxin blocks the release of acetylcholine. This neurotransmitter directly stimulates the sweat glands. Blocking release of acetylcholine decreases sweating. Duration of therapeutic benefit is generally around five months.

**SOFT TISSUE PAIN AND HEADACHE DISORDERS**

More recently, clinicians and medical researchers have found that Botox can be helpful in treating some patients with certain soft tissue pain involving the neck and back. These are patients that have consistently localized pain and spasm in one area, despite other conservative therapies. With appropriate patient selection, adhering to specific clinical criteria, Botox may be helpful in providing patients with relief of muscle pain and spasm.

There have also been some clinical trials in using Botox for treating patients with certain refractory headache disorders. Patients suffering from headache disorders such as chronic daily headache and frequently recurrent migraine-type headaches, which do not respond to standard therapies, may be candidates for Botox treatment. The procedure involves injecting Botox into the muscles of the forehead, temples, and at the base of the skull and upper neck. Again, results are dependent on careful patient selection as well as the skill and experience of the treating physician.

In conclusion, botulinum toxin provides patients with a new safe therapy for certain types of dystonia, hemifacial spasm, facial nerve disorders, and spasticity. Patients with other disorders may be helped with selective use of botulinum toxin. These conditions were previously difficult to treat either medically or surgically. These previous forms of therapy have been associated with potential for side effects, either transient or long lasting. Drug therapy or surgery also has not been particularly effective. In comparison, botulinum toxin is safe and highly effective. When given by a trained neurologist, botulinum toxin is a safe and effective treatment for spasmodic torticollis, blepharospasm, writer's cramp, jaw dystonia, and hemifacial spasm. Current clinical investigations and results are promising for use of botulinum toxin in treatment of spasticity, tremor, soft tissue pain, headaches, and excessive sweating. Research is continuing in the use of botulinum toxin for treating various movement disorders and other clinical conditions.

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