

For the Healthcare Professional: A Reference Guide to Newer Treatments in Cerebral Palsy

Overview

Cerebral palsy (CP) is the most common childhood disability in the United States, with an incidence of two per 1000 births. A symptom complex with a primary disorder of movement and posture, CP may also affect speech, perception and cognitive development. It is due to a non-progressive lesion of the brain during early development and may occur before, during or after birth. An infant with CP will become a child, an adolescent, an adult, and eventually an elderly person with CP. All of these stages present different challenges and needs for the individual, family, and caregivers.

Until recently, the options for improving function in persons with CP have been physical, occupational and speech therapy, orthoses, wheelchairs and walking aids. Orthopedic surgeries are often performed to prevent and correct deformities. Early intervention continues to be the best opportunity to maximize function. Despite the use of conventional therapies, spasticity often interferes with the patient reaching his or her full potential. Today, newer treatments are available to address the spasticity and dystonia of CP. As with any intervention, knowledge of the indications and benefits along with patient selection are key to successful results.

This booklet is designed for pediatricians, orthopedists, neurologists, physiatrists, physical therapists, occupational therapists, and other healthcare practitioners working with children or adults with CP. The purpose is to provide a brief overview of three newer treatments for persons with CP. The treatments are botulinum toxin, intrathecal baclofen pump and selective posterior rhizotomy. This information will assist the practitioner in identifying patients for whom these treatments may be appropriate. The end of this booklet contains additional resources as well as information on educational opportunities in these treatments.

Botulinum Toxin

Description: Botulinum toxin (BTx) is produced by anaerobic bacteria *Clostridium Botulinum*. There are seven antigenically distinct varieties, labeled Botulinum Toxin A through Botulinum Toxin G. Botulinum Toxin A, known by the trade name Botox® (Allergan), has been used widely to decrease unwanted muscle activity in patients with cervical dystonia, multiple sclerosis, stroke, traumatic brain injury and cerebral palsy as well as for a variety of other conditions. Botulinum Toxin B (BTxB), known by the trade name MyoBloc® (Elan) recently received FDA approval. To date, reports on the use of BTxB and cerebral palsy are anecdotal.

Physiological effects -When injected into the muscle, BTx interferes with the release of the neurotransmitter acetylcholine at the neuromuscular junction. It's action on the myoneural junction denervates and weakens the muscle while leaving sensation intact. The drug is dosed according to body weight. When injected into the bulk of the muscle, BTx diffuses rapidly,

remaining in the muscle injected; changes in spasticity begin within one to three days. The drug's peak effect occurs six to eight weeks after injection; the effects continue for approximately four to six months. Injections may be repeated with no long-term cumulative or permanent effects. Side effects, which are transient and rare, include dysphagia, local muscle atrophy, generalized fatigue and pain at the injection site. Antibody formation has been reported, however, it is rare and is avoided by a minimum of three months between doses and the avoidance of booster injections.

Indications - Botulinum toxin A (BTxA) is most effective in reducing dynamic spasticity, or spasticity that is present without muscle contracture. Examples of its use include injection into the gastrocnemius to eliminate toe walking, the hamstrings to decrease knee flexion and scissoring gait, and the biceps brachii to improve upper extremity function or posturing. Injections are often followed by serial casting to allow for sustained stretch of the newly weakened muscles.

Patient selection - Botulinum toxin A has been used successfully in patients where spasticity or dystonia is limited to a few muscles which interfere with function. Pediatric patients with mild to moderate dynamic spasticity are the best candidates. Patients with contractures can be treated successfully with BTxA, however, they often require serial casting over a four to six week period for optimum results. Adults with spasticity and children and adults with dystonia may also benefit from BTxA. In some cases, gait analysis, including kinematic and EMG data, may be indicated to determine the muscles to be injected. Botulinum toxin A is not considered a generalized treatment for full-body spasticity or dystonia, but is effective in treating selected culprit muscles.

Evidence - In randomized, double-blind, placebo-controlled studies looking at the effects of BTxA on the gait of children with cerebral palsy, BTxA improved initial foot contact^{12,23} and increased peak ankle dorsiflexion in both stance and swing²¹. Active dorsiflexion and composite Physician Rating Scale scores were also improved following BTxA¹². Other investigators have reported BTxA to be beneficial in improving upper extremity function^{3,4}, delaying or preventing orthopedic surgery¹³, and improving daily care and hygiene¹⁰.

Intrathecal Baclofen Pump

Description – Oral baclofen has been widely used to treat spasticity in persons with spinal cord injury, stroke, multiple sclerosis and cerebral palsy. An intrathecal baclofen (ITB) pump delivers small amounts of the drug directly into the cerebral spinal fluid (CSF) via an implanted, programmable pump. This method of drug delivery allows for the benefits of the medication to be achieved at a much smaller dose. Refills of the pump and dosage adjustments are accomplished through routine office visits.

Physiological effects - Baclofen is an analog of GABA, an inhibitory neurotransmitter. It is understood to decrease spasticity by inhibiting reflexes at the spinal level. Only a fraction of oral baclofen passes the blood brain barrier. This limitation often does not provide relief for many patients; higher doses frequently produce unwanted side effects. By introducing the drug directly into the intrathecal space, effective levels of concentrations are reached in the CSF with one-

hundredth the dose given orally. Side effects of ITB, which have reported to be manageable, include hypotonia, somnolence, headache, nausea, seizures, vomiting and dizziness^{8,16}.

Indications - For person with cerebral palsy, ITB has been used both in cases of sustained spasticity and dystonia. Dystonia is characterized by unwanted, involuntary movements which interfere with mobility and activities of daily living and may cause pain. Until now, there were few options available to treat patients with these conditions.

Because of the complex nature of the ITB pump, appropriate candidates undergo a screening trial. The trial is designed to determine whether the patient's movement disorder responds to intrathecal baclofen. A bolus injection via lumbar puncture is done for patients with spasticity. This is done during an overnight hospital stay. Patients with dystonia require placement of a catheter in the intrathecal space under general anesthesia. Following catheter placement, the dosage of baclofen is slowly titrated over a three to four day in-patient stay.

During the trial, the patient's spasticity and dystonia are carefully monitored to determine if they are mitigated by baclofen. If the trial is successful, the patient is scheduled for pump implantation. This typically requires a four to six day hospital stay.

Following pump implantation, the patient is followed closely to titrate the dosage of the baclofen. During the first six months, frequent office visits are needed to monitor the patient's response and adjust the dosage as needed. As spasticity or dystonia are lessened, movement patterns may change and weakness may become apparent. Intensive physical and occupational therapy can strengthen muscles and assist the patient to learn new, more efficient movement patterns.

Patient selection - The use of an ITB pump is recommended in patients over the age of four with spasticity or dystonia that is not amenable to other interventions. Success of the ITB pump is contingent upon clear functional goals. These are identified by meeting with the patient, family and caregiver during the evaluation process. During this process, members of the team clarify the patient's goals and expectations to assure compliance with the ITB program. Common goals for ITB are improved upper extremity function, increased independence in activities of daily living, decreased energy cost during walking and increased ease of care.

The pump is placed in the abdominal wall, therefore, the patient must have sufficient body mass to support an implanted pump. Patients with an ITB pump require careful monitoring and frequent refills. Both the patient and the family or caregiver must have access to and be supportive of continuous and on-going assessment. Immediately after implantation, weekly re-evaluations are often needed. Once stable, pumps are typically refilled every eight to twelve weeks.

Evidence – Investigators have reported that ITB significantly reduced spasticity and dystonia in patients with CP. In a randomized, double-blind study of an intrathecal injection of baclofen or placebo, patients receiving baclofen exhibited a significant decrease in spasticity, as measured by the Ashworth Scale⁸. Other investigators reported that dystonia significantly decreased in patients following the short-term infusion of intrathecal baclofen². In both of these studies,

patients who responded to the short term use of baclofen received an ITB pump. Following implantation patients had a 50% decrease in lower extremity spasticity scores⁸ and improved movement dysfunction were sustained in 75% of the patients with dystonia². These findings substantiate other reports of diminished spasticity¹⁶ and improved ambulation⁷ with ITB. The reduction in spasticity associated with an ITB pump has also been reported to decrease the need for orthopedic surgery⁶ and reduce energy expenditure¹¹.

Selective Posterior Rhizotomy

Description – Selective posterior rhizotomy (SPR) is a neurosurgical procedure done to treat severe spasticity of the lower extremities. The surgery involves dividing and cutting selected posterior lumbar and sacral nerve roots. Rootlets are selected for transection by intraoperative electrical stimulation.

Physiological Effects – The neurophysiological basis for the use of SPR in cerebral palsy is the understanding that spasticity is the result of decreased inhibition and increased excitability of the alpha motor neurons. Selective posterior rhizotomy reduces facilitatory input to the alpha motor neuron by dividing the sensory spinal nerve rootlets associated with hyperactive muscle responses. During surgery, muscles exhibiting abnormal electromyographic responses to electrical stimulation are identified. Rootlets associated with such responses are divided. The remaining rootlets are left intact to preserve sensation.

Typically, the rootlets of L₂ through S₁ are selected for transection¹⁸. While the spasticity is markedly reduced, post-operative muscle weakness is common. Modifications to the procedure have been described which confines the nerve rootlets cut to those of L₄ through S₁¹⁵. This procedure limits post-operative weakness without sacrificing clinical results^{5,14}.

Regardless of the surgical procedure performed, following SPR the decrease in spasticity typically improves passive and active range of motion and allows for more normal postures in standing and walking. Problems such as weakness and abnormal muscle firing patterns due to impaired motor control persist following the procedure. Children require post-operative physical therapy to strengthen anti-gravity muscles, maintain or increase range of motion and maximize motor control abilities.

Patient selection – Selective posterior rhizotomy is most successful in children four to ten years of age with purely spastic CP when their spasticity is a major limiting factor to gross motor progress. Children with spastic diplegia, selective motor control, good strength and balance are the best candidates, but good results have also been obtained in some children with spastic quadriplegia where clear function goals can be identified. Fixed contractures and deformities are not addressed by SPR and may require orthopedic surgery. If SPR is indicated, it may be performed first and the child re-evaluated as to the need for orthopedic surgery following SPR.

Spasticity is the only feature of CP that is effected by the SPR. Because of this, if the goal is to improve walking, surgery is most successful when children exhibit adequate underlying strength and motor control. Strength and motor control are less critical in patients with spastic quadriplegia for whom the goals are improved ease of care and hygiene. The procedure is not

recommended for children with dystonia, athetosis, ataxia, poor balance, weakness, hypotonia or primitive reflexes. Pre- and postoperative therapy is imperative to maximize the surgical result.

The child and his or her parents or caregiver must have access to on-going therapy. It is imperative that the child is motivated to participate in an intensive therapy program. Ankle-foot orthoses are recommended post-operatively to protect weakened calf muscles and provide limb stability until functional strength returns.

Evidence – The physical and functional effects of SPR have been examined extensively in the literature and the evidence is strong that SPR improves spasticity, range of motion and gait in children with spastic CP¹⁹. In randomized controlled studies comparing the effects of SPR and therapy to therapy alone, investigators reported that children receiving SPR had significant improvements in Gross Motor Function Measure (GMFM), spasticity and range of motion^{20,24} as well as improved foot floor contact patterns during gait²⁴. These results support findings of increased lower extremity range of motion during walking^{9,17,22} and improvements in gait characteristics^{1,5,14} in children following SPR.

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Education information and resources

If you would like to know more about one of the newer treatments described in this booklet, please contact the UCLA/Orthopaedic Hospital Center for Cerebral Palsy. Botulinum toxin, intrathecal baclofen pump and selective posterior rhizotomy are not the best choice for every patient. Each case of cerebral palsy is unique. Educational seminars are available to assist the practitioner in determining optimal treatment options for patients with cerebral palsy. For those practitioners interested, individual training modules are available.

Educational seminars are designed to provide practitioners with a in-depth understanding of the newer treatments in cerebral palsy. Using lecture, small group discussion and case presentation, participants will learn about patient selection, treatment implementation and post-procedure follow-up. Using an evidence-based approach, case reports and a review of the literature will address patient outcomes, special cases, side effects and complications. Arrangements may be made to present workshops at the practitioner's facility or at another location.

Individual training modules are designed for practitioners and members of their team who are interested in providing one of the newer treatments in cerebral palsy. Training module topics include providing botulinum toxin injections, implanting or refilling intrathecal baclofen pumps or performing selective posterior rhizotomy or its post-operative therapy. Team members will assist in the design of the module goals and objectives. Held at the UCLA/Orthopaedic Center for Cerebral Palsy, the modules are tailored to each team's needs and experience. Opportunities include one-on-one discussions with practitioners currently providing the treatment, participation in clinics and observation and interpretation of gait analysis data. Other experiences that will enhance the team's knowledge and ability to provide the treatment may be arranged as well. Please contact us so we can design an educational experience that meets your needs and the needs of your patient population.

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