

Botulinum toxin use in children

Botulinum neurotoxin (BoNT or BTx) has been used to manage focal spasticity in children since the early 1990s and is now established as an effective treatment. The most common causes of the upper motor neuron (UMN) lesions that lead to skeletal muscle spasticity in children are cerebral palsy and acquired brain injury.

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Cerebral palsy and spasticity

Cerebral Palsy (CP) is the most common physical disability of childhood, occurring in approx 2.5/1000 live births in Western nations. CP is defined as an impairment of movement and/or posture resulting from a non-progressive cerebral abnormality arising early in development. CP encompasses a wide range of clinical presentations, all of which include abnormalities of muscle tone, with spasticity in >75% of children.

This spasticity interferes with function (e.g. causes abnormal walking pattern or impaired upper limb use), causes pain and discomfort, and can also interfere with care e.g. dressing and toileting. Spasticity also interferes with normal muscle growth; muscle under tension does not grow normally but bone continues to grow resulting in relative muscle shortening and contracture, with muscle becoming fibrotic.

Therefore, early intervention to reduce spasticity and maximise function are very important in improving long term outcome of children with CP. Decreasing spasticity allows more directed therapy to further improve function and can reduce or delay the need for orthopaedic surgery in select patients.

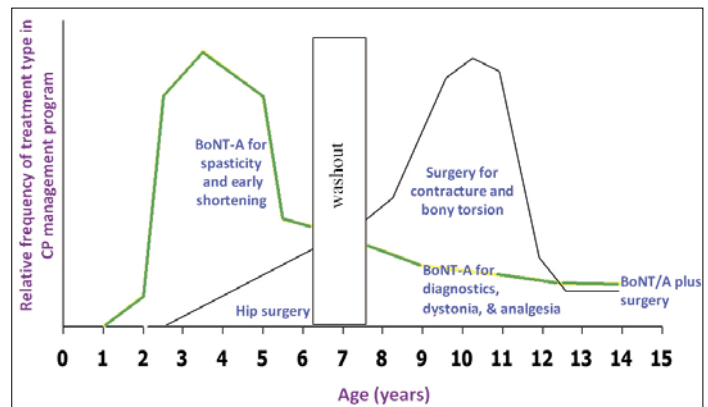
Understanding BoNT-A use

Where there is significant contracture (muscle shortening) there is little role for BoNT-A. In general, BoNT-A is largely used in children under 10 years of age and orthopaedic surgery becomes important in the older child as contracture develops (see chart).

While the pharmacological effect of BoNT-A lasts three months, the clinical effect can be seen for up to 6 months when injections are combined with physical therapy programs and orthotics. Hence the growing child will often need a series of 6-monthly injections to maintain ongoing effect and decrease the negative effects of growth on spasticity.

Multiple injection sites and 6 monthly repeats require that the child has good access to pain management – intranasal fentanyl works well for older children and younger children have access to general anaesthetic or topical lignocaine and IV midazolam.

BoNT-A dose is limited by weight; for Australian children 12-20u/kg, and a maximum 450 units per session. The dose limit means only certain muscle



■ Indicative timeline for cerebral palsy treatment [Boyd and Graham, 1997]



■ Botulinum toxin injected under ultrasound guidance

groups can be targeted in one session and it stresses the need for combined physical therapies. For children with severe spasticity, other management options include intrathecal baclofen or selective dorsal root rhizotomy.

The broader context

Spasticity is only one factor influencing function in children with CP. Other major factors include muscle strength, motor planning, sensory input and cognition. All of these must be taken into account when managing children with CP and considering if there is a role for BoNT-A.

Clearly defined treatment goals and documented clinical response by reduction in spasticity measures is important.

References available upon request.

Botulinum neurotoxin (BoNT) Profiled

- BoNT is a microbial protein purified from the toxin of clostridium botulinum. There are 7 serotypes, A through to G and Botulinum toxin A (BoNT-A) is the most clinically used.
- BoNT-A causes reversible blockade of acetylcholine at the neuromuscular junction. The reduction in release of Ach results in a decreased stretch-sensitive tonic muscle contraction and reduced spastic co-contraction, contributing to ease of stretch and lengthening of injected muscle and increases in antagonist muscle power.
- Administration is by intramuscular injection; muscle identification is by anatomical localisation confirmed with ultrasound and/or electrical stimulation of the muscle.
- BTx weakness onset is after two days, peaks in 2-4 weeks, and lasts 2-6 months or occasionally longer. Reinnervation occurs. Repeated injections are needed to maintain an effect.
- BoNT-A is considered safe. Local adverse events are low (<5%), self limiting and include haematoma, denervation pain or excess local weakness at the injection site. Generalised weakness due to systemic uptake of the BoNT-A is very low but occasional incontinence is seen. In children with swallowing difficulty, particular care must be taken with dosing and follow-up.
- BoNT-A is also used in children to manage focal dystonia, severe sialorrhoea and detrusor muscle instability in neurogenic bladder.

Clinical Examples of Use

- **A 2-year-old child** with hemiplegia who presents with unilateral toe walking would do well with BoNT-A to the gastrocnemius muscle, with an ankle foot orthosis and physiotherapy.
- **A 4-year-old child** with diplegia (bilateral lower limb spasticity) who is walking but has crouched and scissoring gait pattern, would respond well to BoNT-A to bilateral hamstring and adductor muscles in conjunction with physiotherapy treatment.
- **A 6-year-old child** with hemiplegia who has spasticity blocking upper limb reach and grasp activity would respond well to BoNT-A to upper limb muscles including brachialis, wrist flexors and pronators, combined with occupational therapy. ■