The Clinical Use of Botulinum Toxin in Primary Eye Care

James L. Fanelli, OD, FAAO
Cape Fear Eye Institute

Leonid Skorin, Jr., OD, DO, MS, FAAO, FAOCO
Mayo Clinic Health System in Albert Lea

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Key Points

- Botulinum at the Neuromuscular Junction
- Available Products
- Clinical Uses
  - Cosmetic
  - Therapeutic
- Administration

Mechanism of Action

- Blocks the release of Ach from the terminal end bulb
  - ‘blocking’ the neuromuscular junction
- Works at cholinergic nerve endings
  - Those that release Acetylcholine (Ach)
- Naturally produced by Clostridium botulinum
  - Gm + anaerobe
  - Broken down into several types of neurotoxins

The neuromuscular junction

- Acetylcholine is the neurotransmitter in motor neurons at the neuromuscular junction (PNS)
  - Paralysis of muscle
- Acetylcholine is also the neurotransmitter used in the autonomic nervous system (CNS)
  - Parasympathetic PRE and POST ganglionic neurons
  - Sympathetic PRE ganglionic neurons

Keep in Mind:
Neuropathic Pain

- Defined as:
  - pain caused by a lesion or disease of the somatosensory nervous system
- Mechanism of action of BoNT in neuropathic pain:
  - Inhibits release of inflammatory inhibitors from sensory neurons
  - Inhibits release of peripheral neurotransmitters from sensory neurons

**Post herpetic neuralgia**, diabetic neuralgia, spinal cord injury

Migraine Pain

- A bit more complex mechanism of action
- Meninges are innervated primarily by branches of the Trigeminal nerve
  - Trigeminal nucleus receives afferent input from INTRA and EXTRA cranial neurons
  - Meningeal pain via CN V is referred to extracranial dermatomes
- BoNT uses the ‘reverse’ pain referral:
  - Peripherally delivered BoNT → taken up by sensory afferents → transported to trigeminal nucleus → thereby preventing downstream afferent activity

Available Products

- 8 different neurotoxins
- Produced by bacteria Clostridium botulinum
- Type A – Botox (Allergan)
  - Dysport (Medicis)
  - Xeomin (Merz)
- Type B – Myobloc/NeuroBloc (Solstice)
- No direct muscle damage
- Lethal dose – 3,000 units

Botox (Botulinum - A)

- 50 or 100 units of botulinum toxin
- Reconstituted with sterile, nonpreserved 0.9% NaCl
- Use within 4 hours
- Initial effect at 3 days, 1-2 weeks
- 3-6 months duration of action

Botox vs Dysport

- Botox
  - 100 unit vials
  - 4 times more potent per unit than Dysport
  - store in freezer
- Dysport
  - 500 unit vials
  - similar clinical effect as Botox if 4 times greater dosage is used
  - store at room temperature

Xeomin (Botulinum – A)

- Unit-to-unit equivalent with Botox
- “Naked injectable” – no additives
- Less likelihood of developing antibodies
- Does not need to be refrigerated
Myobloc (Botulinum – B)

- Premixed solution
- Refrigerate up to 21 months
- 3 dosing volumes
  - 2,500 U/0.5 mL
  - 5,000 U/1 mL
  - 10,000 U/2 mL

Contraindications

- Infection or inflammation
- Pregnancy or lactation
- ALS, Lambert-Eaton, myasthenia gravis
- Aminoglycosides, antimalarials
- Allergy to egg products

Antibodies

- 5% of those treated
- Increase time between injections
- Minimize overall dose
- Change neurotoxins
- Do not develop with “naked injectables”

Cosmetic Application

- Glabellar folds
- Lateral periorcular rhytids
- Central forehead wrinkles
- Perioral lipstick lines
- Platysmal bands in neck

Injection Technique

- Localize – frown and relax
- Inject adjacent muscle – not crease line
- Inject 1 cm above bony supraorbital ridge
- Glabellar folds
  - 5 injections (20 U)
  - 2 each corrugator
  - 1 procerus
- Reduces resting tone of muscles
- Epidermis and dermis remodeled
Dystonias – involuntary sustained or spasmodic-patterned repetitive muscle contractions
- Aberrant regeneration
- Acquired nystagmus
- Spasm of near reflex

Benign Essential Blepharospasm
- Neurochemical etiology: Adrenergic variability
- Bilateral eyelid spasms
- 2/3 female, mean age 56 (50-70)
- Aggravated by stress, fatigue, glare
- Reduced by sleep
- Functional incapacitation 12%

Meige Syndrome
- Idiopathic orofacial dystonia
- BEB with lower facial involvement
- Lip pursing
- Tongue protrusion
- Involves speech
- Trismus (lockjaw)

Breughel Syndrome
- Idiopathic oromandibular dystonia
- BEB with lower facial, mandibular, cervical involvement
- Contraction of jaw
- Widely opened mouth

Segmental Cranial Dystonia
- BEB with several cranial nerves involved
Hemifacial Spasm

- Muscles innervated by facial nerve
- Unilateral
- Continues during sleep
- More common in middle-aged women
- Microvascular compression
- Jannetta procedure – 80% cure rate
- Neuroimaging required to rule out tumor

Botox: Hemifacial Spasm

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Induction of protective ptosis in cases of corneal compromise secondary to CN V or CN VII palsies, or in cases of upper lid retraction in GravesDz

Reversal of spastic inwardly turning lower lid

Intramuscular (EOM) Injection for strabismus
- Use in one muscle (eg, MR) will result in increased contractility of contralateral muscle (eg LR), resulting in more alignment of the eyes after recovery of the injected muscle

Ameliorating aberrant nerve regeneration problems, such as in:
- Bells Palsy induced facial muscle aberrations
- Aberrant regeneration to the lacrimal gland resulting in excessive lacrimation

Reducing post herpetic neuralgia
- Blocks both:
  - Release of acetylcholine for neuromuscular transmission
  - Release of nociceptive neuropeptides (pain transmitting) involved in chronic inflammatory pain response
- Surgical facial wound healing
  - Reduces tension across the scar

Usually caused by poor injection technique or excessive dosing
- Ptosis
- Reduced blink reflex
- Strabismus
- Lagophthalmos
- Ecchymosis
- Drooling

Non-Ocular Indications
- Spasmodic cervical dystonias
- Writer’s cramp, musician’s cramp
- Spasmodic dysphonia
- Spasticity of MS, CP, stroke
- Spasms of rectal sphincter
- Bladder dyssynergy
- Tremors, tics
- Palmar/axillary hyperhidrosis
• Migraines
• Tension-type headache
• Chronic daily headache
• Cervicogenic headache
• Cluster headache

Candidates for Botulinum Injection
• Headache refractory to preventive treatment
• Patient preference
• Noncompliance with oral medications
• Contraindications to standard prevention
• Adverse events from standard prevention
• Coexisting jaw, head or neck muscle spasm

Migraine Treatment

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Thank You!