BOTOX THERAPY IN THE LARYNGOPHARYNX

Sam J. Cunningham, MD, PhD
Faculty Advisor: David Teller, MD
The University of Texas Medical Branch
Department of Otolaryngology
Galveston, Texas
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Overview

- Review of Botox
- Overview of uses in the laryngopharynx
- Spasmodic dysphonia
  - Types
  - Anatomy
  - Botox techniques
Clostridium botulinum

- Spore forming obligate anaerobic bacillus
- Gram + (young cultures)
- Produces a potent neuroexotoxin
- Causes the disease botulism
Botox Species

- Divided into 4 groups (I-IV)
- Produce 7 different botulinum neurotoxin serotypes

Group I: A, B, F
Group II: B, E, F
Group III: C, D
Group IV: G
Pharmacology

7 neurotoxins, serotypes A-G

- Antigenically distinct
- Similar molecular weights (~150 kDa)
- Dichain molecule (heavy and light)-active molecule
- 3 functional domains:
  - Binding domain (C terminus of H chain)
  - Translocation domain (N terminus of H chain)
  - Catalytic domain (C terminus of L chain) Zn metalloprotease
Pharmacology

- 3 steps in toxin-mediated paralysis
  - Step 1: **Binding**
    - BTX-A binds irreversibly to motor endplates
  - Step 2: **Internalization**
    - Internalized by endocytosis
  - Step 3: **Inhibition of neurotransmitter release**
Pharmacology

- After internalization: Cleaves proteins required for release of Ach vesicles (fusion or docking proteins)

- SNARE proteins:
  - N-ethylmaleimide-sensitive factor attachment protein receptor
  - Each serotype binds to a specific residue of one of the docking proteins
- SNARE proteins (i.e. fusion or docking proteins)
  - Synaptobrevin (B,D,E,G)
  - SNAP-25 (A,C,E)
  - Syntaxin (C)

- Prevents release of Ach
- Irreversible
- Results in flaccid paralysis
Pharmacology

- Paralysis is seen 24-48 hours after injection
  - presynaptic vesicles are depleted

- Recovery
  - Initially new axons sprout – 28 days
  - Return of synaptic function of the initial NMJ – 91 days

- Muscle function usually present by 3 to 4 months
Pharmacology

- Duration of neurotransmitter inhibition varies among serotypes
- Based on the cleavage of different SNARE proteins
- Different SNARE proteins, different duration of action among serotypes: $A > C_1 > B > F > E$
Pharmacology

- **Potency**
  - Determined through *in vivo* mouse assays
  - 1 U of BTX-A = median intraperitoneal lethal dose (LD50) in female Swiss-Webster mice
  - Estimated human LD50 2500-3500 Units
Botox Uses in the Laryngopharynx

- Stuttering
- Vocal tics
- Puberophonia
- Ventricular dysphonia/Dysphonia plica ventricularis
- Dysphagia
- TEP speech failure
- Prevention of posterior glottic stenosis and recurrent vocal fold granuloma
- Arytenoid Rebalancing
- Bilateral vocal fold paralysis
- SPASMOTIC DYSPHONIA
Stuttering

- Affects children and adults
- Patients often stigmatized, teased, etc
- Affects 1% of adult population
- Involuntary break in vocal fluency
- Larynx, pharynx, lips, oral cavity
- Decrease laryngeal contribution by injecting the thyroarytenoid muscles
- Return of symptoms in 12 weeks
Vocal Tics

- Tourette’s syndrome
- Repetitive dyskinetic movements of eyes, facial muscles, neck, oral cavity
- Dyskinetic movements of larynx-leads to grunts, abrupt breaks in fluency, and complex formations like screams, loud talking, repetitive word or vowel sounds, copralalia
- Botox injections into thyroarytenoid muscles have shown clinical improvements
Puberophonia

- AKA mutational dysphonia
- Men and adolescent boys
- Higher fundamental frequency of prepubescent years
- Speech and behavioral therapy
- Botox as adjunct into cricothyroid muscles
  - Enables larynx to relax and allow for lowering of pitch
Ventricular dysphonia/Dysphonia plica ventricularis

- Hyperfunctioning of supraglottic larynx
- Over adduction of false vocal folds
- Propagation of fundamental frequency from FVC’s
- Gravelly, wet, hoarse quality voice-prone to vocal fatigue
- Compensatory response after injury, cysts, sulci allowing air escape
- Botox injections into the false vocal folds
  - Aryepiglottic muscle
Dysphagia

- Cricopharyngeal dysfunction and dyscoordination
- Botox into cricopharyngeus
- Identify patients that would benefit from CPM
TEP speech failure

- Post laryngectomy if no CPM
- Patients with good TEP speech initially, then fail
Vocal fold granuloma and prevention of posterior glottic stenosis

- Following repair of posterior glottis clefting (interarytenoid)
- Recurrent granulation/scarring
- Botox into the thyroarytenoid muscles to decrease the strength of vocal fold closure and allow more lateral position at rest
- Decreases strength of vocal fold closure to help in treatment of vocal fold granuloma (less local trauma)
Arytenoid rebalancing

- Arytenoid dyslocation following traumatic intubation or blunt trauma to anterior neck.
- Hoarseness/breathiness after surgery
- Immobile vocal cord
- EMG analysis and operative endoscopy
- Endoscopic manipulation of arytenoid back into native position
- Botox injected into interarytenoid muscle, ipsilateral thyroarytenoid muscle, and lateral cricothyroid muscle
- Weakens ipsilateral adductory muscles, allowing ipsilateral abductor to provide traction on the arytenoid allowing a more physiologic position
Bilateral vocal cord paralysis

- Botox injected into the thyroarytenoid and interarytenoid muscles
- Weakens the adductory muscles, allowing increased patency of the airway at rest and with activity
- “Rebalance” position of the paralyzed cords to a more abducted position
Spasmodic Dysphonia

- Usual onset in mid 30’s
- More common in women (63%)
- Two types: ADductor and ABductor
- Dx based on careful history and examination of the glottis during a variety of laryngeal tasks
Adductor Dysphonia

- Most common-80%
- Inappropriate glottal closure
- Produces harshness, strain, and strangled breaks in connected speech
Adductor Spasmodic Dysphonia

- Most common type
- Hyperactivity of the thyroarytenoid m. (TA)
- Inappropriate closing or tightness of the glottis
- Strained voice
Abductor Dysphonia

- Less common
- Inappropriate glottal opening
- Produces hypophonia and breathy breaks
Abductor Spasmodic Dysphonia

Posterior view

Epiglottis
Aryepiglottic fold
Cuneiform tubercle
Corniculate tubercle
Aryepiglottic muscle
Oblique arytenoid muscle
Transverse arytenoid muscle
Posterior cricoarytenoid muscle
Cricoid cartilage

Action of posterior cricoarytenoid muscles
Abduction of vocal folds
Spasmodic Dysphonia

- Treatment alternatives to Botox:
  - Surgical denervation: crush, neurolysis
  - Speech therapy (adjunct)
  - Psychological therapy

American Academy of Otolaryngology-Head and Neck Surgery endorses Botox as primary therapy for this disorder. (Policy Statement: Botulinum Toxin. Reaffirmed March 1, 1999)
Injection Strategy

Adductor spasmodic dysphonia: EMG-guided transcutaneous injections of the thyroarytenoid muscle, using equal amounts of Botox (1-1.25U initially)

Abductor spasmodic dysphonia: EMG-guided transcutaneous injection of one posterior crycoarytenoid muscle with Botox (3.75U initially)
Adductor spasmodic dysphonia: Injection Technique

- Reclined position with neck extended
- Local anesthesia unnecessary (hinder)
- Bend needle 30-45° (esp in women)
- Insert needle through skin just off midline at level of cricothyroid membrane
- Characteristic ‘buzz’ when in airway
- Advance superiorly and laterally
- Patient asked to phonate for EMG confirmation
- Botox injected
Thyroarytenoid injection
Injection for Spasmodic Dysphonia

- Supine with neck extended
- +/- Local anesthetic for TA injection
- EMG guidance

Inj. for adductor spasmodic dys.
TA injection with Botox
Abductor spasmodic dysphonia: Injection technique:

- PCA may be reached in two ways:
  - Retrocricoid (lateral) approach
  - Transcricoid (anterior) approach
Abductor spasmodic dysphonia: Lateral approach

- Thumb placed on posterior aspect of thyroid cartilage and entire larynx is rotated to expose the posterior aspect.
- Insert needle along the lower half of the posterior edge of the thyroid cartilage, traversing the inferior constrictor, and advance until the cricoid is encountered.
- Pull needle back slightly and ask the patient to sniff.
- EMG confirmation and Botox injected.
Abductor spasmodic dysphonia: Lateral approach
PCA injection with Botox (lateral approach)
Abductor spasmodic dysphonia: Transcricoid approach

- Insert needle through the cricothyroid membrane in the midline
- Characteristic ‘buzz’ in lumen
- Pass through the posterior lamina of the cricoid cartilage to either side of midline
- Topical lidocaine to prevent coughing (does not hinder)
- First electrical signal encountered is PCA
- Placement confirmed by sniffing and Botox injected
- Better in younger patients (cartilage is not calcified)
Abductor spasmodic dysphonia: Transcricoid approach
PCA injection with Botox® (transcricoid approach)
Conclusions

- Botulinum toxin therapy is an extremely useful and versatile tool in the laryngologist’s armamentarium. By chemically denervating the various laryngeal muscles, it is possible to effectively diagnose and treat a number of disorders of the laryngopharynx.
References:

References cont.