Cosmetic Botulinum Toxin Injections (Fundamentals)

Tam Nguyen, MD, FAAFP
Mason Dang, MD
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Mason Dang, MD

Program Director, American Board of Aesthetic Medicine; Medical Director, Aesthetic Arts MD

Dr. Dang is board certified in anesthesiology and specializes in aesthetic medicine and anti-aging medicine in a private practice in San Diego, California. His areas of expertise include use of botulinum toxin, dermal fillers, facial contouring, laser and light therapies, chemical resurfacing, and sclerotherapy. Dr. Dang frequently lectures and teaches hands-on courses at various national and international conferences. In April 2014, Dr. Dang presented at the XI Congresso Mundial Medicina Estetica in Rio de Janeiro, Brazil. Dr. Dang has presented workshops on aesthetic medicine at FMX since 2012.
Tam Nguyen, MD, FAAFP

Physician, Washington Township Medical Foundation (WTMF), Fremont, California.

Dr. Nguyen is a graduate of Pennsylvania State University College of Medicine in Hershey. He completed his residency at Family Practice at San Jose-O'Connor Family Medicine Residency Program. He practices inpatient and outpatient family medicine at WTMF. His topics of specialty include dermatology and diabetes. Dr. Nguyen instructs physicians of various specialties on aesthetic procedures, including the use of botulinum toxin, lasers, liposuction, and nonsurgical facial reconstruction. He also consults with providers on how to establish an aesthetic practice. Dr. Nguyen believes family medicine's most critical challenge is caring for the uninsured and underinsured.
Learning Objectives

1. Choose appropriate treatment areas for desired results by practicing with saline injections.
2. Compare the uses for botulinum toxin injections.
3. Assess the clinical effects of botulinum toxin on the skin.
4. Evaluate dosages for selected patients for safe and effective treatment.
History

• Discovered in 1895

• Neurotoxic protein \( \rightarrow \) Clostridium Botulinum

• One of the most toxic substance known

• Cause of botulism food poisoning
  ◦ Ingestion of food contaminated with spores
  ◦ Perforated can \( \rightarrow \) anaerobic environment \( \rightarrow \) spore germination
• Botulinum toxin type A isolated in 1920’s

• Clinical use for > 21 yrs

• 1989 → FDA for treatment of strabismus, blepharospasm
Introduction

Cosmetic effect initially described in 80’s

◦ Jean & Alastair Carruthers
  • Ophthalmologist/dermatologist husband & wife team from Canada

◦ Wrinkles in glabellar region decrease after treatment for eyelid spasm with Btx-A

◦ Experimented on themselves & staff
Introduction

• 2002 → FDA approved Btx-A → glabellar lines
• BTX-A also approved for axillary hyperhidrosis
• Increasingly use for dystonic & spastic disorder
  – Limb dystonia
  – Lingual dystonia
  – Facial spasm
  – Migraine
Introduction

- Purified protein complex

- 7 serotypes
  - A, B, C, D, E, F & G
  - A & B serotypes $\rightarrow$ clinical use
  - Type B (Myobloc/Elan) $\rightarrow$ mostly clinical e.g. cervical dystonia
  - Type A most potent & most established for cosmetic use
    - Botox (Allergan)
    - Dysport (Galderma)
    - Xeomin (Mertz)
Mechanism

Inhibition of acetylcholine release at NMJ

⇓

Acetylcholine impulse transmission blocked

⇓

Muscular flaccid paralysis
Mechanism

- Botox is composed of light & heavy chains

  Heavy chain bind to receptor (irreversible)
  ↓
  Receptor-toxin complex internalized (endocytosis)
  ↓

  light chain cleave peptide bonds requires for
  Acetylcholine formation
Botulinum Toxin-A

• 3 types in current cosmetic use
  – Botox $\rightarrow$ Onabotulinumtoxin A
  – Dysport/ $\rightarrow$ Abotulinumtoxin A
  – Xeomin $\rightarrow$ Incobotulinumtoxin A
Onabotulinumtoxin A - Botox

- Allergan
- Bacterial strain → Hall
- Molecular wt → 900 kD
- 100 u BTX-A, 0.5 mg HSA, 0.9 mg NaCl
- Complexing protein 5 ng/100U
- USA, Canada, South America, Asia, Europe
Abotulinumtoxin A - **Dysport**

- Ipsen (UK), Medicis (US)
- Ipsen strain
- **300-500 kD**
- 300 or 500 U BTX-A, 0.125 mg HSA, 2.5mg Lactose
- Complexing protein $\rightarrow$ **2.5 ng/100 U**
Incobotulinumtoxin A - Xeomin

- Merz pharmaceutical, Germany
- Hall strain
- 150 kD
- 100 U BTX-A, 1 mg HSA, 5m sucrose
- Complexing protein → none
  - Possible less allergic potential
Botulinum Toxin-A

- Unit potency $\rightarrow$ mouse intraperitoneal injection assay
- 1 U activity $\rightarrow$ dose which causes death in 72hrs in 50% of mice assessed (Ld 50)
- Assay protocols varies among manufacturers
- 1 unit Botox = 2 units of Dysport
- Lethal dose 2500-3000 units or 30 bottles (70 kg person)
• Diffusion differ due to proteins clustered around active molecule

  – Botox $\rightarrow$ 900 kD

  – Dysport $\rightarrow$ 300 – 500 kD

  – Xeomin $\rightarrow$ 150 kD (no protein!)

  – Spread: Botox < Dysport < Xeomin
Anatomy

• KNOW YOUR ANATOMY!
  – Complications usually due to inappropriate placement
Anatomy

• Muscle responsible for frown lines to forehead

  – *Frontalis*

• Not continuous but 2 separate bands

• Opposes depressor muscles of glabellar complex & brows
Anatomy

• Muscles responsible for frown lines between the eyes
  ◦ *Glabellar Complex*
    • *Corrugator* bilateral
    • *Procerus* medial
  • Depressor complex → opposes elevator muscles of the frontalis
  • Brow adduction & brow medial inferior movement
  • Angry or worried appearance effects
Anatomy

• Muscles responsible for crow’s feet (lateral canthus area)
  – Lateral Orbicularis Oculi
  • Closure of eyes & depression of brows and eyelids
Cosmetic Usage for Botulinum Toxin A

- Glabellar frown lines
- Forehead lines
- Crow’s feet
- Excessive sweating (hyperhydrosis)
- Lines and bands in neck
- Lines on chest
- Perioral wrinkles
- Facial contouring
Patient Selection & Evaluation

- Expectation realistic?
- Past medical history
- Past treatment & outcome
- Location & severity of treatment site
- Pretreatment Asymmetries
  - Ptosis
  - Lid laxity
Contraindications

- Pre-existing neuromuscular disease
  - Amyotrophic lateral Sclerosis (ALS), Myasthenia Gravis, ....
- Pregnancy
- Breast feeding
- Infection at injection site
- Unrealistic expectation
Contraindications

• Relative
  – Marked asymmetry
  – Moderate to severe ptosis
Preparation

• Botox
  – Labile protein
  – Lyophilized vials (100 Units / vial)
  – Vacuum should be presented upon dilution
  – Inject saline slowly to minimized bubble.
  – Gently swirl vial. No vigorous shaking
  – Dilution range 1-4 ml
  – Recommended dilution
    • 2.5 ml or 4 units/0.1 ml
Preparation

• Dysport
  – Lyophilized vials (300 Units / vial)
  – Same preparation as Botox
  – Vacuum should be presented upon dilution.
  – Recommended dilution
    • 3 ml or 10 units / 0.1 ml
• Xeomin
  – Lyophilized vials (100 Units / vial)
  – Same preparation as Botox
  – Vacuum should be presented upon dilution.
  – Recommended dilution
    • 2.5 ml or 4 units / 0.1 ml
Preparation/Techniques

• Storage
  ◦ Botox & Dysport shipped frozen on dry ice
    ◦ Placed in freezer or refrigerator upon delivery
  ◦ Xeomin shipped at room temperature
  ◦ Once reconstituted → refrigerated
    ◦ 2-8 degree Celsius. **NOT** frozen
  ◦ Allergan & Medicis recommend discarding of Botox or Dysport after 4 hrs. for sterility reason. But……
Glabellar Injection

• Pt asked to frown → corrugator and procerus are identified
• 5-6 sites
  – 2 injection sites per corrugator
  – 1 or 2 injection sites to procerus
• Injection volume
  – 0.05cc – 0.10cc per site depending on severity
• Total dose
  – 15 - 20 units
Frontalis Injection

• Injections distributed adjacent to furrow
  – “In the mountains not the valleys”

• Pt asked to furrow their forehead to determine placement

• Stay 1.5cm away from eyebrow → prevents ptosis
  – Not always possible to target lowest rhytids
Frontalis injection

- Injection site
  - 4-8 sites or more depending on severity of wrinkles

- Injection volume
  - 0.05cc (2 units) per site

- Dosage
  - 8-16 units
Crow’s Feet / Lateral Canthus

- Injection sites
  - 2-4 sites per lateral canthus
  - Usually 3 sites
  - Intradermal is effective

- Injection volume
  - 0.05 cc (2 units) per site

- Dosage
  - 4-8 units per side
Crow’s Feet / Lateral Canthus

• Pt asked to smile maximally

• Stay **1cm** lateral to orbital rim → avoid diffusion to rectus muscles

• Do not go **below zygoma** → lip ptosis

• Be aware of vessels near lateral canthus

• Crow’s feet can be
  – Evenly above & below lateral canthus
  – Primarily below lateral canthus
  – Primarily above lateral canthus
Post-Procedural Care

• Do not lie flat for 4-8 hours
• Do not bend over & pick up heavy objects for 4-8 hours
• Do not massage the area
• Work the muscles injected?
• Topical vitamin K or Arnica for bruising
• Ice for any swelling
Complications/Side Effects

- Bruising
- Pain/Redness to injection site
- Headache
- Nausea/Flu like symptoms
- Face pain
- Anaphylaxis
- Uneven result
- Unwanted muscle paralysis
Complications / Side Effects

• Eyelid ptosis
• Eyebrows ptosis
• Diplopia
• Lip ptosis
• Ectropion
• Antibody resistance
Treating Ptosis

• Avoid ptosis by not injecting closer than 1.5 cm to eye brows
  – Injection or diffusion into frontalis muscle
  – Diffusion into levator palpebral muscle of eyelid

• Treated with apraclonidine (Iopidine) eye drops
  – Allow Mueller’s muscle elevation up to 3 mm
  – 2 drops TID

• Mueller’s muscle (smooth muscle) and depends on adrenergic activity
Contraindications

• Pregnancy
• Breast feeding
• Infection in area to be injected
• Pre-existing neurological D/O (e.g. myasthenia gravis, amyotrophic lateral sclerosis, Lambert-Eaton syndrome)
• Facial palsy or pre-existing asymmetry
• Allergy to any constituent in the vial
Best Practice Recommendations

• Single treatment may not eliminate all lines & wrinkles
• **Onset in 3 days, maximum effects may take up to 2 wks**
• Complete paralysis may not provide greatest cosmetic effects
  – Relaxation not paralysis → more natural look
• Deep furrows and lines may need filler augmentation
Best Practice Recommendations

- Recovery generally begins at 3-4 months after injection
- Pts receiving regular treatment may have duration of 4-6 months
- Bruising usually resolve in 2 weeks
- Ptosis if from diffusion into levator palpebral may resolve in 2-3 wks
- Ptosis from frontalis effects last entire duration 3-4 months
Best Practice Recommendations

• SELECT YOU PATIENTS ACCORDINGLY!!!
Videos

• Forehead: https://www.youtube.com/watch?v=HePwxbnNWyo&t=3s

• Gabellar: https://www.youtube.com/watch?v=S_bcdTOYkak

• Crow’s feet: https://www.youtube.com/watch?v=DoG5OVaSJQY&t=37s