Is OnabotulinumtoxinA Good for Other Head and Face Pain?

Disclosures

BoNT/A for non-CM

- Botulinum neurotoxin (BoNT) in clinical use for headache >20 years
- Efficacy of BoNT type A (onabotulinumtoxinA, Botox) confirmed in chronic migraine (CM)
- Efficacy of BoNT for treatment of episodic migraine, cluster headache, and chronic tension-type headache (TTH) has not been examined in large controlled trials
- Lack of large studies also problem for TN, TMD, and uncommon HA/facial pain disorders
- Because BoNT is a biological product, the safety and efficacy of one BoNT formulation cannot be extrapolated to a different one, even of the same serotype.

How BoNT/A blocks vesicular transmission

- BoNT/A works by means of a three-step process, involving:

Hypothesis: BoNT-A in antinociception

- The exact mechanism of BoNT-A in antinociception has not been fully elucidated
- Animal and human studies indicate that BoNT-A inhibits the release of nociceptive mediators:
  - CGRP
  - Glutamate
  - Substance P
- Blocking release of these neurotransmitters inhibits neurogenic inflammation; this, in turn, inhibits peripheral sensitisation of nociceptive nerve fibres
- As a result, peripheral pain signals to the central nervous system are reduced and, indirectly, central sensitisation is blocked

Onabotulinumtoxin-A can decrease CGRP released from

BoNT-A® on the trigeminal/cervical
trigeminal neurons

7 **Suppressive effects of BoNT-A® on the trigeminal/cervical nociceptive system activated by injection of capsaicin to forehead**
- BoNT-A significantly reduced the capsaicin-induced pain intensity area (p=0.011)
- The suppressive effect of BoNT-A in pain reduction was observed as early as the first week
- Mean area of secondary hyperalgesia was significantly smaller in BoNT-A group than in saline group (p=0.040)
- These effects may be caused by a local peripheral effect of BoNT-A on cutaneous nociceptors

8 **BoNT-A: postulated mode of action in chronic migraine**
Initial theory...
- Pain relief achieved by reduction in muscular activity
  However...
- Pain relief often occurs before effect detected in overactive muscles
- Reduction in pain also observed to last longer than the known effects of BoNT-A on muscle
Additionally...
- BoNT-A significantly reduces pain associated with dystonia of the head and neck – an effect long considered secondary to its muscle relaxant action
- Now studies have shown...
- BoNT-A has a direct inhibitory effect on nociceptors independent of its actions on neuromuscular activity

9 **BoNT-A: postulated mode of action in chronic migraine**

10 **BoNT-A: postulated mode of action in chronic migraine**
- Pain relief and prophylactic benefits thought to be due to inhibition or attenuation of the release of various neuropeptides from nociceptor fibres so reducing the neuroinflammatory response
11 **Change from baseline, severe HA days**

12 **PREEMPT- Response by cycle**

13 **TMJ Disorders**
- Diagnosis and management is challenging
- Complex anatomical structures, function of teeth and muscles complicate specific diagnosis of TMJ disorders
- Many treatment modalities: splints, mouth restriction exercises, injection of sclerosing agents etc.
- Botulinum toxin may be effective in treatment of oro-facial pain due to muscular disorders

14 **Functional Anatomy**
- Agonist vs. antagonist
  - e.g.: lateral pyterygoid and temporalis muscles
  - Direction of muscle effects

15 **Temporal Mandibular Disorder: injection technique**
- Temporalis: anterior vs. posterior
  - 20-50 U each side
- Masseter:
  - 10 – 50 U each side

  Avoid Lateral Pterygoid

Injection sites

16 **Freund et al. (2000)***
- Open-label Trial: Chronic TMD
  - n=46 patients
  - Assessment at 2 wk intervals
  - Duration 8 wks post-injection
- Botox treatment
  - Injections
    - Masseter 50 U
• Temporalis 25 U,
• 5 sites each site

17 Freund, et al; Results
• 40/46 subjects (87%) had a reduction in subjective pain (VAS) [p<0.05]
• 44/46 subjects (96%) had a reduction in objective pain (tenderness to palpation) [p<0.05]
• 40/46 subjects (87%) had improved functional index scores [p<0.05]
• No subjects reported worsening of their condition after treatment
• No side effects were reported

18 Trigeminal neuralgia (TN)
• Unilateral, brief electric-shock-like attacks of pain
• Limited to the distribution of one or more divisions of the trigeminal nerve
• Prevalence of 0.1-0.2 per thousand
• Incidence ranging from 2 to 7.1/100 000/year up to 20/100 000/year

19 Trigeminal neuralgia (TN)
• Benefit in TN 1st mentioned by Wang and Jankovic\(^5\)
• Patient presented with hemifacial spasm and TN
• TN improved after treatment of the hemifacial spasm with BoNT-A

20 Trigeminal neuralgia (TN)
Drawbacks:
• a) shortage of double-blind trials
• b) method is operator-dependent
• c) no consensus guidelines
• d) “refractory trigeminal neuralgia” not well defined
21 Trigeminal neuralgia (TN)
   - Recent randomized, double-blind, placebo-controlled
   - Trials provide the best evidence for the efficacy of BoNT-A in TN
   - Doses range from 25-75 U
   - Typically in follow the pain fashion

22 Reduction in pain: the centripetal or shrinking pattern

23 Trigeminal neuralgia (TN)
   - Limitations are cosmetic asymmetry
   - Intra-oral injections have been associated with local infection in some cases
   - Injection across nasalis or intra-nasal well tolerated
   - BTX thus in V2 distribution

24 Nummular Headache
   - “pain in a small circumscribed area of the head in the absence of any lesion of the underlying structure.”
   - Pathophysiology of NH thought to be of epicranial origin of scalp cutaneous nerves

25 Nummular Headache
   - 4 patients refractory to NSAIDs, gabapentin, and local anesthetics
   - Injections with 25 units (U) of BoNTA divided among 10 injection sites (1-2 cm apart) in and around the circumscribed affected areas
   - 2 sets of injections approximately 14 weeks apart.

26 Nummular Headache
   - All 4 patients had reductions in pain, allodynia, and paresthesias
   - Onset 6-10 days following BoNTA treatment
   - Treatment effects lasted approximately 14 weeks on average
- No reported treatment-related AEs

27 Cluster Headache
- BoNT/A to sphenopalatine ganglion
- Single treatment under general anesthesia with transnasal approach by BrainLab
- Open label, 25 or 50 units

28 Cluster Headache

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