A New Treatment Paradigm for Trigeminal Neuralgia Using Botulinum Toxin Type A

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INTRODUCTION

Trigeminal neuralgia (TN) is a painful neuropathic condition involving cranial nerve V (CN V). It is characterized by paroxysmal episodes of intense, stabbing, electrical shock-like facial pain along the distribution of CN V, most commonly in the V2 or V3 division. It is typically unilateral in nature, but some patients may experience pain at different times on both sides of the face. Often attacks are precipitated by even mild sensory stimulation of a so-called “trigger zone” in the affected area. TN may be caused by a blood vessel or small tumor pressing on the nerve, as well as by inflammatory causes of neuropathy such as multiple sclerosis, diabetes or Lyme disease. Often, the cause cannot be identified. First line treatment is typically with anticonvulsants, particularly carbamazepine. When pharmacotherapy is not effective or not tolerated, more invasive techniques such as microvascular decompression, stereotactic radiosurgery and percutaneous procedures can be effective.

Botulinum Toxin Type A (BoNT-A) is a non-invasive therapy that has been demonstrated to be effective in a number of headache and facial pain conditions.1,2 In addition to its effect on acetylcholine at the neuromuscular junction, BoNT-A has been found to inhibit the release of several pain-related neurotransmitters including substance P, calcitonin gene-related peptide and glutamate and has been shown to be of benefit in migraine headache and other pain conditions. These properties have recently led to the investigation of BoNT-A in the treatment of TN. In our series of 17 patients with paroxysmal TN, we found that BoNT-A given intradermally and/or subcutaneously in doses of 2.5u/cm² to alldynic areas in the V1, V2 or V3 dermatome had a significant reduction in pain intensity and frequency when compared with placebo at 12 weeks, with some having relief up to 24 weeks. Similar studies have also shown significant benefit up to six months. Side effects are typically minor and include local ecchymosis and temporary paresis of facial musculature in some patients.

Conclusions: BoNT-A is an effective treatment for TN and should be considered in patients who have failed, become refractory to or are unable to tolerate first line pharmacologic treatments.

METHODS AND MATERIALS

Literature Review
A review of the current literature on BoNT-A and TN was performed using a MEDLINE search. The search terms included: Botulinum toxin, Botox, trigeminal neuralgia, tic douloureux, and facial pain. Only original research examining the use of BoNT-A in humans with idiopathic TN was included.

Our Study
17 subjects with a diagnosis of refractory trigeminal neuralgia were recruited (12 female, 5 male, mean age 57.7 years old). Patients had to have at least 3 months of stable trigeminal neuralgia refractory to a stable TN medication regimen. Patients were randomized to receive saline (placebo) or BoNT-A. The distribution of the facial pain was mapped and 2.5u/cm² of BoNT-A or the equivalent total volume of saline was injected (figure 1). Pain frequency (#attacks/day), intensity on a visual analog scale (VAS) and global percent of pain reduction was assessed at 4, 8, 12, 16 and 24 week intervals. For non-responders (<50% global pain relief) at 4 weeks, the randomization code was broken and placebo subjects were crossed over into the active BoNT-A protocol and non-responders previously treated with BoNT-A and non-responders previously treated with BoNT-A were given a booster dose of 2.5u/cm². Statistical analysis was performed using a 2-tailed Fisher’s exact test.

RESULTS

Systematic Review
A total of 6 studies examining the use of BoNT-A were identified. All of the patients in studies reviewed had been tried on medical therapy without relief. A summary of their findings as well as our study can be found in Table I.

Our Study
8 patients received placebo and nine received BoNT-A at the first treatment visit. The distribution of pain by dermatome was as follows: V1=4, V2=3, V3=3. 7 Patients had multiple affected dermatomes. 6/8 patients treated with placebo were non-responders at 4 weeks and were rolled over into the BoNT-A treatment group. 6 patients in the treatment group were non-responders and received a booster dose of BoNT-A. 5/6 patients responded after booster. 11/15 patients treated with BoNT-A had >50% global pain reduction at 4 weeks (p=0.0393).

DISCUSSION

There is a mounting body of evidence for the use of BoNT-A in the treatment of trigeminal neuralgia. The current guidelines by American Academy of Neurology and the European Federation of Neurological Societies (AAN-EFNS) recommend carbamazepine or ox-carbamazepine as first line therapy.11 They go on to state that in patients who are refractory to medical therapy, early surgical therapy may be considered. However, these procedures carry additional morbidity, such facial dysesthesia (which can be permanent and more troubling than the original symptoms) or the risks of posterior fossa craniotomy. We propose a new treatment paradigm for TN incorporating the use of BoNT-A (Figure 2).

CONCLUSIONS

BoNT-A offers a safe, effective treatment for TN and should be considered in patients who have failed, become refractory to or are unable to tolerate oral medications.

REFERENCES

6. Piovesan, et al. 2005
8. Borodic, Acquadro 2002