

An Open Study of Botulinum-A Toxin Treatment of Idiopathic Trigeminal Neuralgia

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ARTICLE INFO	ABSTRACT
<p>Article type: Original Article</p> <hr/> <p>Article history: Received: 22-Oct-2014 Accepted: 11-Nov-2014</p> <hr/> <p>Keywords: Trigeminal neuralgia Botulinum neurotoxin type A Facial pain</p>	<p>Introduction: Trigeminal Neuralgia (TN) is a unilateral, recurrent, sharp facial pain disorder that is limited to the distribution of divisions of the trigeminal nerve. The aim of this study was to evaluate the efficacy of Botulinum neurotoxin type A (BTX-A) for alleviating the frequency and severity of TN pain.</p> <p>Materials and Methods: This trial was performed as a before and after study. We treated 31 patients (15 male and 16 female) with mean age of 52 year old that their diagnosis was made at least 4.5 years before. We injected BTX-A in various parts of face and particularly in the origin of mandibular and maxillary branches of trigeminal nerve. Injection volume was determined by the necessity and pain intensity measured with visual analog scale up to 100U. Patients were evaluated before and after the injection and were followed after week, and each month, for a three months period. Other related variables were recorded such as: toxin complications, pain status variations by brushing, chewing, cold weather and patient's satisfaction with their therapy.</p> <p>Results: showed that after injection, pain intensity and frequency decreased after tooth brushing, chewing and cold weather ($P<0.0001$). Median of pain intensity decreased from 10 to 2 in all cases. Only 6% of patients affected to transient asymmetry and other complications were not observed. After 3 months of injection 71% of patients were inclined to reinjection.</p> <p>Conclusion: BTX-A could be used as an effective and safe treatment method for drug resistant TN. Also it can be used in patients who are not satisfied with oral anticonvulsants.</p>

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Introduction

Trigeminal Neuralgia (TN), as described by the International Association for the Study of Pain (IASP), is a unilateral facial pain disorder that is described by brief, sharp, paroxysmal lancinating pains that are recurrent, and limited to the distribution of divisions of the trigeminal nerve (1). The prevalence of this disorder is approximately 1 in 25000, and it is a little more common in women than in men. It also affects middle-aged or older people more frequently (2).

In the latest classification of the International Headache Society, a distinction was made between classical and symptomatic TN: Classical TN (CTN) includes idiopathic cases in addition to those with

vascular compression of the fifth cranial nerve; Symptomatic TN (STN) is detected in cases secondary to multiple sclerosis, tumors, and structural abnormalities of the skull base (3). The pain attacks can be either spontaneous, or precipitated by specific coetaneous stimuli within specific "trigger zones," leaving some patients unable to eat, drink, brush their teeth, or shave their faces (4).

Diverse interventions have been tried to decrease the pain and reduce the frequency of pain attacks in TN.

Anticonvulsive pharmacotherapy remains the first-line treatment. Carbamazepine is often used for pain control (5).

Botulinum neurotoxin type A (BTX-A) has been successfully utilized to treat pains such as migraine and occipital neuralgia. BTX-A has recently gained popularity in treating patients with TN, more specifically TN refractory to medical and surgical interferences (6-12).

These patients had been previously labeled surgical candidates; however, BTX-A treatment offer a less invasive option for pain alleviation with good results and minimal side effects.

The history should definitively rule out other causes of facial pain. Because of the association with multiple sclerosis, patients should be asked about neurologic symptoms (e.g., dizziness, focal weakness, ataxia, vision changes) and other atypical symptoms that might lead to another diagnosis.

The recognition and treatment of trigger zones on the face will provide the most benefit to the patient. Wide variations have been published in the literature, with one case report documenting the administration of 100 U to a single trigger site (3).

Frequency of administration also needs to be individualized. Duration of effect in the literature ranges from weeks to six months. Initial treatments should be accompanied by a pain diary, which enables the patient and physician to track the waning and waxing of symptoms with treatment.

Side effects of BTX-A injections are generally a result of its effect on motor synapses, including the possibility of facial weakness and asymmetry after treatment. Facial edema, erythema, and hypesthesia been reported (4). We designed an open label trial to study the efficacy of BTX-A for decreasing the TN pain.

Materials and Methods

During 24 months 34 patients who met the inclusion criteria (idiopathic TN on oral pharmacotherapy and refractory painful attacks), were included in the trial among them three patients excluded because of multiple sclerosis (two patients) and vascular loop (one patient) etiology in study period so 31 patients completed the study.

The neurologist performed a careful head and neck examination, with emphasis on the neurologic feature.

An otologic, oral, and Temporomandibular Joint (TMJ) examination was done to look for other causes of facial pain. Facial nerve function and facial symmetry documented prior to the injections in the neurologic head and neck examination.

Magnetic Resonance Imaging (MRI) of the brain performed for all patients presenting with trigeminal neuralgia.

The history definitively ruled out other causes of facial pain and oral therapies was continued before and after injection. The patients were refractory to conventional medical therapy and they had attacks despite oral pharmacotherapy.

Subjects with a known hypersensitivity to the toxin,

and diseases that might interfere with neuromuscular transmission, such as myasthenia gravis, Eaton-Lambert syndrome, amyotrophic lateral sclerosis, patients taking aminoglycosides, and patients with facial skin infection or pregnant or lactating women excluded from trial.

After their inclusion in this open label study by signing in an informed consent form, botulinum toxin type A (Dysport®) was injected intradermal in the painful region, particularly in the trigger zones.

Each vial was diluted with 2 ml of standard sterile saline solution and injected in trigger zone.

A 28 gauge insulin needle was used for administration toxin in all patients and one expert neurologist performed the injections in all patients.

Initial dose was 100 units of botulinum toxin type A (Dysport®) in all of our patients. Each vial contained 500 units. We draw a grid on the patient's face in the region of allodynia or hyperesthesia. Next, 2.5 unit (U)/0.1 cc intradermal injections of BTX-A per centimeter length were administered within the grid.

The injection continued along with a line of sharp lancinating pain pathway on the face. If the trigger point was on the inner mucosa of mouth or gum, nearest point on the facial skin selected for injection.

Toxin was injected in the first visit. In patients with mandibular root involvement, a larger amount of the toxin was injected in the masseter in order to stay away from undesired cosmetic side effects.

The population was evaluated one week, one, two and three months after the injections in the clinic and pain intensity and adverse effects were asked.

Severity of pain associated with tooth brushing, chewing and cold weather was recorded based on visual analogue scale.

Friedman test was performed using the Statistical Package for the Social Sciences software (SPSS version 21, Chicago, IL). Protocol approved by the regional ethics committee of Mashhad university of Medical Sciences.

Results

Thirty one patients (15 men, 16 women) with an age average of 52 years old participated in this study with an average amount of about 4.5 years time period which had been passed since the diagnosis of trigeminal neuralgia (between one and twenty years).

Twenty nine patients (94%) were using Carbamazepine, fourteen patients were using Gabapentin and four patients were using Baclofen.

Sixteen patients (52%) were on combination therapy.

Pharmacotherapy continued after botulinum toxin type A (Dysport®) injection.

In 30 patients pain was aggravated after tooth brushing and chewing, in 27 patients pain was aggravated after cold weather exposure, median of pain severity in all categories before intervention was 10 and after BTX-A injection, median of pain severity reached two. (Table1-3).

Table1: Median pain intensity before and after one week, one, two and three month of Botulinum-A toxin injection

	Pain intensity before intervention	Pain intensity after one week	Pain intensity after one month	Pain intensity after two months	Pain intensity after three months
Total number	31	31	31	31	31
Median	10	2	2	2	2
Minimum	8	0	0	0	0
Maximum	10	10	10	10	10

Table2: Median pain intensity with brushing before and after one week, one, two and three month of Botulinum-A toxin injection

	Pain intensity with brushing before intervention	Pain intensity with brushing after one week	Pain intensity with brushing after one month	Pain intensity with brushing after two months	Pain intensity with brushing after three months
Total number	31	31	31	31	31
Median	10	2	2	2	2
Minimum	0	0	0	0	0
Maximum	10	10	10	10	10

Table3: Median pain intensity with chewing before and after one week, one, two and three month of Botulinum-A toxin injection

	Pain Intensity with chewing before intervention	Pain intensity with chewing after one week	Pain intensity with chewing after one month	Pain intensity with chewing after two months	Pain intensity with chewing after three months
Total number	31	31	31	31	31
Median	10	2	2	2	2
Minimum	0	0	0	0	0
Maximum	10	10	10	10	10

Severity of pain decreased significantly after BTX-A injection after tooth brushing, chewing and cold weather exposure ($P < 0.0001$) (Figure).

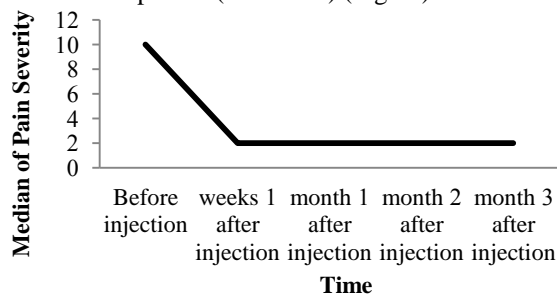


Figure: Median of pain intensity by chewing, tooth brushing and exposure to cold weather.

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Of total of 31 patients 22(71%) patients were inclined to reinjection after 3 months of follow up. Only two patients (6%) affected to transient facial asymmetry (one month duration) and other complications were not observed in our patients.

Discussion

Our findings demonstrate the beneficial effects of BTX-A in pain control in cases of idiopathic TN, which supports previous findings as well as those by Piovesan et al. and Borodic and Acquadro (6, 13).

However, many aspects remain unclear including the extremely rapid action of pain management by the toxin, within minutes of the inoculation, in some of our cases.

Alternatively, in most of our patients pain reappeared after 60 days in contrast to the motor benefit usually lasting between three and six months depending both on an individual basis and the underlying cause of muscle hyperactivity.

However, in other patients' pain improvement lasted up to three months.

BTX-A has repeatedly shown its efficacy for the treatment of headache in several clinical trials, but there still is ambiguity as to how botulinum toxin type A should be best used for treating headache, and which patients are best appropriate for this treatment (14, 15).

In addition, myofascial pain syndrome, neuropathic pain disorders, fibromyalgia, and "off" painful dystonia in Parkinson's disease, among others, have also been reported to respond to BTX-A injections (16-20).

Conclusion

Our study suggests that BTX-A characterizes a safe and effective treatment modality.

BTX-A could be a useful therapeutic method in the management of both TN and probably other similar conditions. BTX-A provides a very fast and long-term benefit, and is otherwise devoid of systemic consequences.

Additional double-blind studies including an appropriate number of patients are required to validate our findings and to explore whether higher doses provide a more sustained effect and optimize injection sites. Further studies will help to clarify ideal injection schedules and approaches.

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