Chapter 10
Botulinum Toxin Treatment of Chronic Facial Pain: Trigeminal Neuralgia, Temporomandibular Disorders, and Dental-Related Pain

Abstract Chronic facial pain is physically and emotionally disabling. Trigeminal neuralgia, pain associated with temporomandibular disorders, and dental-related pain are some of the most common forms of chronic facial pain. Despite the advances in pharmacological therapy of these disorders, many patients with these ailments remain unsatisfied with the level of pain relief. This chapter begins with a review of clinical features, pathophysiology, and conventional treatment of these three forms of chronic facial pain. The literature in the efficacy of botulinum neurotoxins (BoNTs) in trigeminal neuralgia, pain related to temporomandibular disorders, and dental disorders is reviewed. Case reports from the author's experience are provided in selected patients. A comment page, at the end of each section, critically reviews the technical and dosage issues and provides recommendations for the design of future studies.

Currently, a significant level of efficacy for local use of botulinum toxins can be ascribed only for trigeminal neuralgia (one class I study, level B, probably effective). In temporomandibular pain, data generated from retrospective studies and observation of experienced clinicians suggesting efficacy are encouraging, but solid blinded and controlled studies are lacking and very much needed. In chronic neuropathic pain following dental procedures, the positive data on the local use of BoNTs is limited to few anecdotal observations.

Keywords Facial pain • Trigeminal neuralgia • Temporomandibular disorder • Temporomandibular joint • Dental pain • Botulinum toxin • Botulinum neurotoxin • OnabotulinumtoxinA • AbobotulinumtoxinA

Introduction

Management of facial pain is a major challenge in clinical medicine. Most facial pains reflect a form of neuropathic pain. The role of botulinum toxins in neuropathic pain (including trigeminal neuralgia) is of considerable interest (Brown et al. 2014). Facial pain is treated separately in this chapter since the pathophysiology of pain in a vast majority of cases pertains to the dysfunction of a single cranial nerve.

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Trigeminal Neuralgia

Trigeminal neuralgia is one of the most painful of human afflictions. Its incidence in the USA is estimated at 4/100,000 individuals (Katusic et al. 1990). Women are more frequently affected. The peak age of onset is between 50 and 70 years (Yoshimasu et al. 1972).

The pain is severe and often described as jabbing, stabbing, and shock-like. It involves one side of the face and may affect any branch of the trigeminal nerve, but the ophthalmic and maxillary branches are more commonly affected. The pain usually lasts for seconds, but durations of up to 2 min are also observed. Bouts of pain may occur multiple times a day and disable the patient. Facial movements, eating, speaking, chewing, and shaving often exacerbate the pain. Many patients have local trigger points in the face that upon touching provoke severe pain. In the chronic state, a high proportion of the patients live in constant fear and anticipation of upcoming bouts of pain. Table 10.1 summarizes the clinical features of TN and provides a list of differential diagnoses.

Pharmacological approaches to therapy include antiepileptic drugs such as carbamazepine, oxcarbazepine, and gabapentin that specifically block pain mediators and GABAergic medications such as baclofen (30–60 mg) which enhances inhibitory mechanisms (Fromm et al. 1981). In one blinded study, combination of carbamazepine and baclofen proved more effective than either of the two alone (Fromm et al. 1984). Unfortunately, with passage of time, patients will require more analgesics and higher doses of medications to control pain with the risk of developing more side effects (particularly among elderly). Narcotic analgesics are not usually helpful.

In many cases, trigeminal neuralgia is caused by an anomalous artery or vein impinging against the trigeminal nerve at or close to its exit point from the brain stem. This compression causes focal demyelination in the nerve which, over time, leads to generation of ectopic discharges. Hence, in recalcitrant cases, surgical intervention may prove helpful. The anomalous vessel can be surgically lifted from the nerve during decompression surgery (Brown 2014). Gamma Knife surgery is also effective; the frequency of this approach is increasing (Baschnagel et al. 2014). Both approaches are not devoid of side effects which may be substantial and include permanent ataxia, brain stem damage, and cranial nerve palsies. It is currently believed that at least half of the patients with TN are not satisfied with their medical management. Therefore, a pharmacological agent with low incidence of side effects would be welcome in the management of TN.

Anatomy and Physiology of Trigeminal Sensory System

Sensations from the face, gums, inner part of the cheeks, and teeth are conveyed to the central nervous system via three branches of the trigeminal nerve, namely, the ophthalmic, maxillary, and mandibular. The ophthalmic branch innervates the skin

Table 10.1 Diagnostic criteria of trigeminal neuralgia (TN) and how these compare with other entities in the differential diagnoses

Symptom	TN	Pulpitis	TMD	Neuropathic trigeminal pain	SUNA/SUNCT	Paroxysmal hemicrania
Character	Shooting, stabbing, sharp, electric	Sharp, aching, throbbing	Dull, aching, nagging, sharp at times	Aching, throbbing	Burning, stabbing, sharp	Throbbing, boring, stabbing
Site/radiation	Trigeminal distribution only, intraoral and extraoral, affects V(a) rarely	Around a tooth, intraoral	Preauricular, radiates down the mandible, temple area, may be postauricular or neck	Around tooth or area of trauma/dental surgery or facial trauma	Periorbital but can affect maxillary division	Orbit, temple
Severity	Moderate to severe	Mild to moderate	Mild to severe	Moderate	Severe	Severe
Duration	1e60 s refractory period	Rapid but no refractory period	Not refractory, lasts for hours, mainly continuous, can be episodic	Continuous soon after injury	Episodic 5e240 s	Episodic 2e30 min
Periodicity	Rapid onset and termination, complete periods of remission weeks to months	Unlikely to be more than 6 months	Tends to build up slowly and diminish slowly, lasts for years	Continuous	Numerous, can be periods of complete remission	1e40 a day, can be periods of complete remission
Provoking factors	Light touch, non-nociceptive	Hot/cold applied to teeth	Clenching teeth, prolonged chewing, yawning	Light touch	Light touch	Nil
Relieving factors	Keeping still, drugs	Avoid eating on that side	Rest, decrease mouth opening	Avoid touch	Nil	Indometacin
Associated factors	Local anesthetic placed in trigger area relieves pain	Decayed tooth, exposed dentine	Muscle pain in other parts of the body, limited opening	History of dental treatment or trauma in the area	Often restless	May have migrainous features

From Zakrzweska and Mc Millan (2011), reprinted with permission
SUNA short unilateral neuralgiform pain with autonomic symptoms, *SUNCT* short unilateral neuralgiform pain with conjunctival tearing, *TMD* temporomandibular disorder

of the forehead and top of the head and provides corneal sensation. The ophthalmic sensory branch to the cornea is the afferent arm of the corneal reflex, one of the most informative reflexes used in clinical medicine. The ophthalmic branch enters the cranium through the superior orbital fissure, travels with the maxillary branch in the cavernous sinus, and then along with the maxillary and mandibular branches converges into the trigeminal ganglion (Gasserian ganglion), located in the middle fossa.

The maxillary branch of the trigeminal nerve innervates the middle part of the face, cheek, upper teeth, and mucosa of the nasal cavity, soft and hard palates, and the pharynx. Innervation of the nasal mucosa is the basis for sternutatory reflex (unilateral grimacing after gently putting a Q-tip inside one nostril) that tests the integrity of the maxillary branch of the trigeminal nerve. The maxillary nerve leaves the face through the inferior orbital fissure and enters the skull via the foramen rotundum.

The sensory part of the mandibular nerve (third division of trigeminal nerve) carries information from the skin of the lower face, side of the face and head, lower teeth, anterior two thirds of the tongue, and mucosa of the mouth and cheeks. The mandibular nerve enters the skull via the foramen ovale and ends in the inferior part of the trigeminal ganglion.

Many major pain mediators, specific pain receptors, and pain-activating voltage-gated sodium channel are highly expressed in the neurons of trigeminal ganglia and trigeminal nerve endings. Cultured trigeminal neurons, within days, release large amounts of calcitonin gene-related peptide (CGRP), a major inflammatory pain mediator (Durham et al. 2004). Transient receptor potential vanilloid 1 (TRPV1), a cation channel, is recognized as a major contributor to nociception since its activation releases CGRP. TRPV1 is highly expressed in a large number (≥90 %) of trigeminal neurons (Meng et al. 2009). More recently, the role of endothelins (A and B) has been investigated as pro-nociceptives in the trigeminal system (Chichorro et al. 2010).

Botulinum Toxin Treatment of Trigeminal Neuralgia

Since 2002, a total of eight studies have reported on the efficacy of BoNT treatment in trigeminal neuralgia (Borodic and Acquadro 2002; Turk et al. 2005; Bohluli et al. 2011; Piovesan et al. 2005; Zuniga et al. 2008; Wu et al. 2012; Shehata et al. 2013; Wang et al. 2014). One study was prospective and double blind (class I) (Wu et al. 2012). Of the remaining seven, one was single blind and prospective (Shehata et al. 2013), while the six were retrospective. All used type A toxin and reported various degrees of pain relief with no serious side effects. In the retrospective studies, some did not mention the exact type of A toxin or the number of injections. The two blinded studies are described in some detail here.

Wu et al. (2012) enrolled 42 patients with trigeminal neuralgia in a 13-week, randomized, parallel design, double-blind, placebo-controlled study. Forty patients, 21 in the BoNT and 19 in the saline (placebo) group, completed the study. Botulinum toxin A (Chinese toxin from Lanzhou Institute) was diluted in 1 cc of normal saline and injected, using a 16 mm-long needle, either between the epidermis and dermis

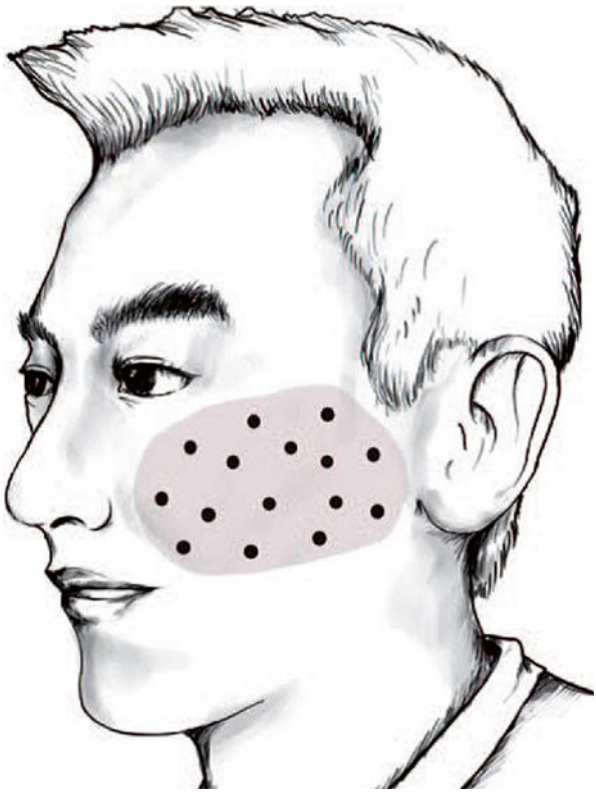

Fig. 10.1 The area of facial pain (highlighted in *gray*) in trigeminal neuralgia and the sites of injections (From Wu et al. (2012), © 2012 SAGE Publications reprinted with permission from SAGE)

or submucosally in the areas affected by pain (Fig. 10.1). Subjects in the BoNT group received 25–75 units, and a comparable volume was administered to the subjects in the saline group. Patients remained on the same dose of their medications (carbamazepine, gabapentin, and pregabalin) during the study.

The primary outcome was a significant change in pain frequency and intensity (VAS) compared to placebo. Secondary outcomes were patient global impression of change (PGIC) and proportion of responders defined as 50 % or more compared to baseline. Both primary outcomes and all the secondary outcomes improved significantly in the BoNT group compared to the placebo ($p<0.001$). Side effects were noted in the subjects who received BoNT; seven developed mild facial asymmetry which disappeared after 7 weeks, and three developed local facial swelling which subsided in a week.

In the single blind study of Shehata et al. (2013), 20 subjects with TN were randomized into BoNT and placebo groups. In the BoNT group, the subjects received subcutaneous injections of 40–60 units of onabotulinumtoxinA into 8–12 points (five units per point) in the face. Primary outcome was a decrease in pain intensity at 12 weeks measured by VAS compared to the placebo. At 12 weeks, the onaA group demonstrated a reduction of 6.5 points in the VAS compared to three points in the placebo group ($p=0.0001$). As a secondary outcome, quality of life also improved significantly, and more patients in the BoNT were able to reduce the number of their pain medications.

Case Report 10-1

A 41-year-old woman was referred to the Yale Botulinum Neurotoxin Treatment Clinic for consideration of BoNT therapy for a disabling trigeminal neuralgia. She began to have severe left-sided face pain and headaches following a car accident 20 years earlier. The pain was dull and deep at first but gradually transformed into bouts of sharp and jabbing pain lasting 15–20 s. Many factors provoked pain especially exposure to cold environment. She reported several trigger points close to the nose and corner of the mouth, making application of the makeup difficult. In "bad days," pain affected the region around the left eye and made it "twitch."

The patient had tried multiple medications for the pain including beta-blockers, antiepileptic drugs, calcium channel blockers, nonsteroidal anti-inflammatory drugs, oxycodone, and acupuncture. She had had three surgical procedures in the past: decompression surgery via retro-mastoid craniotomy for relieving pressure upon the trigeminal nerve, exploration for possible CP angle pathology (second surgery), and cortical stimulation for pain relief. None of the three procedures relieved her pain. Patient described constant daily background facial pain with superimposed bouts of sharp pain. Past medical, family, and social history disclosed no issues of concern.

On examination, several trigger points were identified on the left side of the face close to the nose and corner of the mouth. A total of 30 units of onaA was injected subcutaneously in 20 sites (1.5 units per site) into the V2 distribution. In addition, another 10 units (4 points) was injected into the left frontalis (2.5 units, 4 sites) and 5 units into the anterior temporal region (2.5 units, 2 points) (Fig. 10.2).

After 2 weeks, patient reported marked reduction in severity of pain (from level 9 in VAS to 2) and in the frequency of sharp pains (90 % less). This response lasted for 5 months at which time the severity of pain returned and required another injection that produced a similar effect. No side effects were reported. Patient described her experience as very satisfactory in patient global impression of change.

The Mechanism of Action of BoNT-A in Trigeminal Neuralgia (TN)

The data from cell culture and animal studies explains some of the mechanisms through which administration of BoNTs relieves pain in trigeminal neuralgia. Addition of onaA to the cultured trigeminal neurons results in marked reduction of CGRP release from stimulated trigeminal neurons (Durham et al. 2004). In acute infraorbital nerve injury that causes significant local allodynia in the rat, subcutaneous injection of onaA improved allodynia and reduced release of pain mediators from disconnected trigeminal neurons (Kitamuaraet al. 2009).

Addition of A/E chimera of botulinum toxin (which specifically targets sensory neurons) to the trigeminal cell culture inhibits the release of CGRP secondary to activation of TRPV1 (Meng et al. 2009). Furthermore, subcutaneous injection of 0.25 and

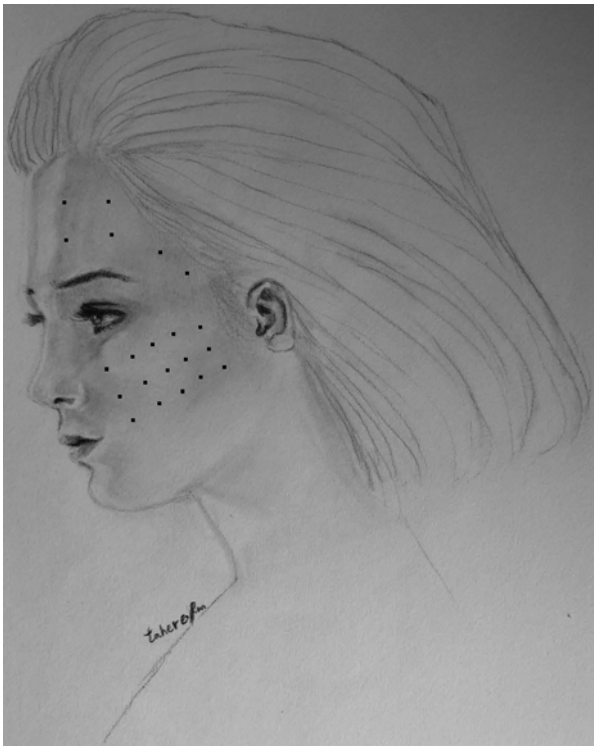

Fig. 10.2 Case report 10-1, trigeminal neuralgia. The dose is two units per site for injections in the V2 distribution and 2.5 units per site in V1 and other sites (Created by Tahereh Mousavi; published with kind permission from © Bahman Jabbari 2014. All Rights Reserved)

0.5 ng/kg of botulinum toxin A (onaA) into the rat's face markedly reduces the expression of TRPV1 in the trigeminal neurons within 2 days (Shimizu et al. 2012).

Matak et al. (2011) maintain the view that the analgesic effect of the BoNT-A in experimental trigeminal neuralgia of rats (formalin injection into the whiskers) results in a large part from a direct central effect of the toxin. In this model, after BoNT-A administration, the authors have detected presence of truncated SNAP25 in the sensory trigeminal nucleus in the medulla. The analgesic effect of the toxin was blocked by injection of colchicine into the trigeminal ganglia which blocks and prevents the toxin from reaching the CNS.

Comment

The efficacy of botulinum toxin treatment for trigeminal neuralgia is supported by a single controlled, double-blinded study (Wu et al. 2012). Using the criteria of the Assessment Subcommittee of the American Academy of Neurology (Appendices 3.1 and 3.2), this study qualifies as a class I study. The level of evidence for one class I study is defined as level B; BoNT-A is probably effective in trigeminal neuralgia. In a more recent study (Zhang et al. 2014), have shown that a dose of 25 units is as effective as 75 units in trigeminal neuralgia (using Wu's method and toxin).

Much remains to be established regarding the correct type of toxin, technique, dose, and number of injections. A dose of 30–40 units, injected into 15–20 sites, per side seems reasonable, but focal injections with a large dose such as 100 units in zygoma in two sites (Turk et al. 2005) probably run the risk of unacceptable facial weakness. The type of toxin reported in the blinded study of Wu et al. (2012) is the Chinese toxin that is unfamiliar to most researchers and clinicians in the West. How the units of this toxin translate to the more commonly used type A toxins (ona-, abo-, and inco-BoNT-As) or the B toxins is still a matter of debate. In our clinic, we have been successful in using 30–40 units of onaA (per side) in a half dozen of patients with trigeminal neuralgia.

Despite limitations, the current data in botulinum toxin treatment of TN is welcoming news since even with new analgesics (gabapentin and pregabalin), at least half of the patients with TN remain unsatisfied with their pain management. The persistent pain is often severe and the cause of significant emotional and psychosocial distress. Botulinum toxins, when effective, usually provide prolonged relief (3 months or longer) and in general are safe and well tolerated. The study of Wu et al. (2012) and the positive data derived from it has opened the door for refinement of the technique and better definition of optimum dosage through future controlled and blinded studies.

Temporomandibular Disorders (TMDs)

Temporomandibular joint disorders are a group of conditions related to pathological processes which affect the jaw and muscles of mastication (Song et al. 2007). Temporomandibular disorders may be myogenic or arthrogenic depending on the source of pathology. The former arises from myofascial involvement of the masseter, lateral pterygoid, and temporal muscles, while the latter originates from pathology of the temporomandibular joint. The prevalence of TMD in general population is hard to define due to overlap of clinical symptomatology with other facial pain disorders. Manfredini et al. (2011) reported the following prevalences in TMD based on the underlying pathology: disc disease 25 %, myofascial masseter pain 12.9 %, and inflammatory pain of the temporomandibular joint 8.9 %. The underlying pathology is difficult to discern with certainty in a majority of patients.

Pain is a major symptom of TMDs. It can be localized to the temporomandibular joint with local tenderness at palpation, or it may be felt over the masseters as a myofascial pain syndrome. Some patient presents with limitation of jaw opening often associated with disturbing jaw pain. In case of a dislocated joint, the patient often experiences a clicking sound at the region of the joint upon jaw movements. Associated headache is not uncommon and could take the form of tension or migraine headaches. Schiffman et al. (2012) indicated a sensitivity of 89 % with specificity of 87 % ($p<0.001$) for the following two criteria in TMD headache: (1) temple area headache that changes with jaw movement and (2) provocation of that headache by temporalis muscle palpation or jaw movement. Limitation of jaw

opening can be confused with dystonia of jaw opening—a form of focal dystonia which also may cause pain. Additional forms of facial pain in OMDs also occur which at times take the form of sharp and fleeting pains and can be confused with trigeminal neuralgia. The differential diagnosis also includes other common conditions such as pain of sinusitis or root and muscle pain related to cervical osteoarthritis. The condition is often difficult to diagnose due to the overlap of symptomatology with the aforementioned facial and neck pain disorders. Graff-Radford and Bassiur (2014) suggest that clinicians should highly consider the diagnosis of TMD if at least three of the following four features exist: (1) pain in the preauricular and temporal region brought on by functions such as chewing; (2) pain on palpation over the TMJ; (3) joint noise such as clicking, popping, or crepitus; and (4) limited range of motion of the TMJ.

Treatment

The first line of treatment includes noninvasive measures such as massage, warm compresses, and physical therapy. Physical therapy encompasses posture training exercises, joint mobilization, orthotic devices, and splint therapy. Other modes of treatment such as electrotherapy, ultrasound, laser therapy, and acupuncture have also been employed, but their efficacy is in question (Graff-Radford and Bassiur 2014). Pharmacological agents such as nonsteroidal anti-inflammatory drugs, muscle relaxants, tricyclic antidepressants, and antiepileptic analgesics (gabapentin, pregabalin) may provide partial relief. Opioid analgesics are used for recalcitrant pain, but significant relief occurs only in half of the patients with non-cancer-related pain (Zenz et al. 1992). Surgical intervention is considered the last resort and, depending on the pathology of TMD, consists of disc repositioning, repair of disc perforation, disc recontouring, lysis of adhesions, and discectomy (Vallerand and Hall 1991).

Botulinum Toxin Treatment of TMDs

In 1997, Daelen et al. and Moore and Wood independently reported that botulinum toxin A may prevent TM joint dislocation and relieve TMJ pain in patients with TMD due to masseter and lateral pterygoid spasticity. The former authors described a 56-year-old man with multiple sclerosis and frequent dislocation of TM joint due to spasticity in whom administration of onaA into the masseter and lateral pterygoid muscles resulted in correction of dislocation and pain relief. The positive results lasted for 4 months and were reproducible with repeat injections. The patient reported by Moore and Wood (1997) received 75 units of onaA into each lateral pterygoid muscle and had similar results lasting for 10 months.

For the past 15 years, a number of retrospective studies have supported these observations (Freund and Schwartz 2003, Von Linden 2001). Similar favorable opinion regarding treatment of TMD with BoNTs has been reported by clinicians with considerable expertise in the use of BoNTs in head and neck pain disorders (Blitzer et al. 1989).

Two blinded, placebo-controlled studies, however, provided contradictory results. In one study (Kurtuglu et al. 2008), 24 patients with TMD with symptoms referable to the masseters and temporalis muscles were randomized to BoNT-A and saline groups. BoNT-A was injected under electromyographic guidance into the masseter and temporalis muscles. Patients were evaluated with a biobehavioral questionnaire that included assessment of pain and psychosocial status at baseline, 14, and 28 days after injection. Patients in the toxin group demonstrated improvement of pain and psychosocial status compared to placebo both at 14 and 28 days.

Ernberg et al. (2011) conducted a double-blind, crossover, multicenter study on 21 patients who met the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMDs) (Dworkin and Le Resche 1992). The group was heterogeneous, but most patients had myofascial pain in the masseter region. A total of 50 units of BoNT-A was injected into the masseter muscles. Subjects were tested with a variety of scales for pain, quality of life, and psychosocial effects. Regarding pain, a 30 % decrease in VAS was considered significant since this degree of pain reduction has been shown to correspond to "much improved" reported by patients in the patient global impression of change (PGIC); 50 % reduction would correspond to "very much improved" (Farrar et al. 2001). Weekly change in VAS (30 % or more) was considered as the primary outcome of the study. Both onaA and placebo improved pain by 30 % or more, but the difference between the two groups was not significant. The authors mentioned several shortcomings of the study which include small number of patients and injections limited to the masseter muscles.

Comment

Botulinum toxin treatment of temporomandibular disorders is complicated due to the variability of symptomatology which may require different injection schemes and dosage per given patient.

Recently, Blitzer's group in New York reported (Song et al. 2007) a success rate of 60 % with onaA in relieving pain of over 200 patients with TMDs. They used a dilution of 50 units/cc and injected 50 units into each masseter muscle. Masseter was injected in five points and temporalis in four points at each side. At Yale, we have had a similar experience (success rate of 50 %) in a smaller number of patients with the same dose/masseter while using a dilution of 100 units/cc. The temporalis and pterygoid muscles are also often injected.

The negative double-blind study of Ernberg et al. (2011), as the authors pointed out, had shortcomings. The injections were limited to the masseter muscles, and the injected dose was small, 25 units per masseter versus 50–100 units/masseter used by others (Song et al. 2007, Von Linden 2001). Finally, in this study, both the BoNT and placebo groups showed the targeted primary outcome—VAS improvement of 30 % or more—a finding that may merely represent a large placebo effect and would not necessarily negate the efficacy of the toxin. Another issue of concern in this study is the higher incidence of weakness in the placebo group compared to the onaA group.

We conclude that a technique that combines onaA injection of the masseter and temporalis muscles (and sometimes also the lateral pterygoid) has shown efficacy against the pain of TMD in the practice of experienced clinicians and in the open studies. Since no class II studies exists in this area (Erenberg's double-blind study is probably class III), we consider the evidence for efficacy of BoNT in TMD at this time as at U level, i.e., inconclusive (Appendices 3.1 and 3.2, AAN's subcommittee guidelines). Future, larger blinded studies are needed, which should preferably employ the technique and doses which are reported effective in open observations.

Case Report 10-2

A 29-year-old female visited the Yale Botulinum Toxin Treatment Clinic for evaluation of jaw stiffness, tenderness over the right masseter and temporomandibular joint, and right-sided headaches. She noted the onset of her symptoms about 8 years ago. The symptoms gradually increased in severity. The headaches, in particular, became disabling occurring almost daily with marked exacerbations several times per week. During swallowing and chewing, she often heard a clicking sound bilaterally. Treatment with a variety of analgesic medications including tricyclic antidepressants, nonsteroidal anti-inflammatory agents, and antiepileptic drugs failed to relieve the pain. Her past and family history was noncontributory. She did not smoke or drink alcohol and did not use illicit drugs.

The general medical examination was normal. Opening and closing of the jaw caused discomfort. The regions of the right masseter and temporalis muscles were tender to touch. Neurological examination including assessment of cognition, cranial nerves, motor and sensory systems, cerebellar testing, speech, gait and stance, and reflexes was normal. A detailed ear-nose and throat evaluation showed no abnormality. Imaging studies of the brain and TM joints were normal.

onaA was injected bilaterally into the masseter and temporalis muscles (Fig. 10.3). The dose per masseter was 40 units (divided into two 20 unit injections at two sites), while the dose per temporalis muscle was 20 units per side (2 injections, each 10 units). A week after the injection, the patient reported marked reduction of jaw stiffness, masseter pain, and headaches reflecting a 90 %

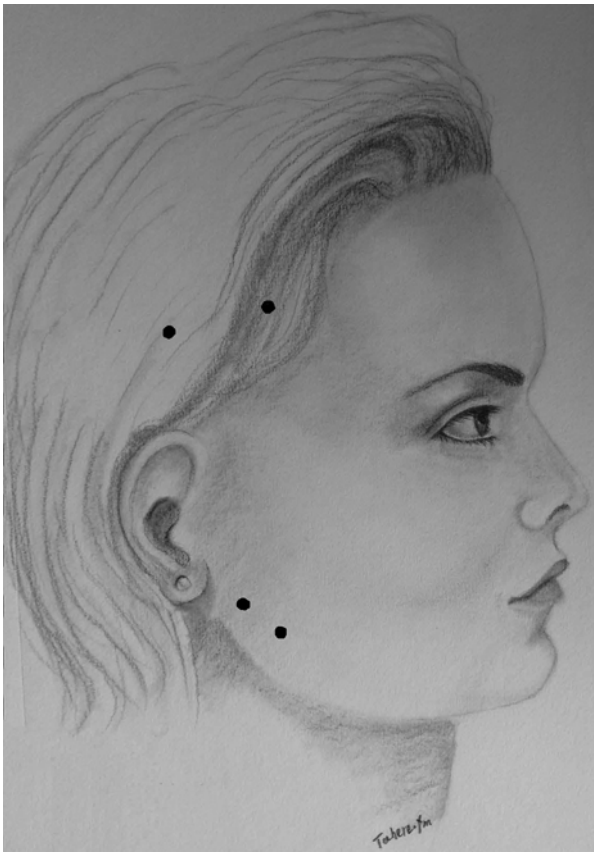

Fig. 10.3 Case report 10-2, temporomandibular joint disorder. Sites of injections: two injections 20 units each into the masseter and two injections 10 units each into the temporalis muscle on each side. Patient keeps the teeth clenched during the injections (Created by Tahereh Mousavi; published with kind permission from © Bahman Jabbari 2014. All Rights Reserved)

improvement. In patient global impression of change, her impression was "very much improved." The improvement lasted for 3 months. Repeat injections over a year of follow-up (every 4 months) had the same effect.

Pain Related to Dental Procedures

A variety of dental procedures may damage the branches of trigeminal nerve and cause chronic pain in the oral cavity. Tinastepe and Oral (2013) have recently reviewed the issue of neuropathic pain after dental procedures. Extraction of the third molar tooth can damage the inferior alveolar nerve (IAN), lingual nerve, or buccal nerve due to proximity of the tooth's root to the mandibular canal. Permanent deficits and symptoms including pain have been reported in 2 % of the patients after this procedure (Renton et al. 2005).

In dental implantation, permanent symptoms due to IAN damage occur in 1–8 % of patients due to bone removal and detachment of the mucoperiosteal flap (Ellies and Hawker 1993). The incidence of chronic pain per se is not known, however (Gregg 2000). Persistent pain has been reported in 3–13 % of the patients after root canal treatment of molar teeth (Knowles et al. 2003; Pogrel 2007), and phantom tooth pain occurs in 2–3 % of the patients with orthodontic procedures on these teeth (Reinhilde et al. 1998; Campbell et al. 1990). Procedure -related dental pain is generally treated with conventional analgesic drugs such as tricyclic antidepressants, nonsteroidal anti-inflammatory agents, and antiepileptic drugs with efficacy in neuropathic pain (gabapentin and pregabalin).

Botulinum Toxin Treatment of Chronic Pain After Dental Procedures

No randomized clinical trials (RCTs) are available pertaining to neuropathic pain secondary to dental procedures. The patient presented below is from the author's positive experience in a patient with chronic, severe, refractory pain after molar extraction.

Case Report 10-3

A 60-year-old gentleman, successful physicist, developed marked allodynia of the gum and bouts of severe, jabbing pain in the gum close to the site of extraction radiating to the upper lip on the left side, following extraction of the molar teeth on that side 3 years ago. His past medical history was negative. The bouts of sharp pain occurred several times daily and were rated 9 or 10 on VAS. The area of pain was sensitive, interfering with brushing of the teeth. Many different analgesic medications failed to control the pain; his current medication was gabapentin (600 mg four times daily).

On examination, areas of exquisite painful hypersensitivity to touch (allodynia) were noted over the gum at and slightly anterior to the site of extraction as well as over the upper lip on that side (Fig. 10.4). Injection of 10 units of onabotulinumtoxinA into the allodynic area of the gum, 2–3 mm below the surface (2.5 units at 4 sites), resulted in marked reduction of allodynia and cessation of the episodic pain after 1 week. The pain returned to the same level after 6 months. A repeat injection had the same effect. The patient rated his impression of change in PGIC as "very much improved."

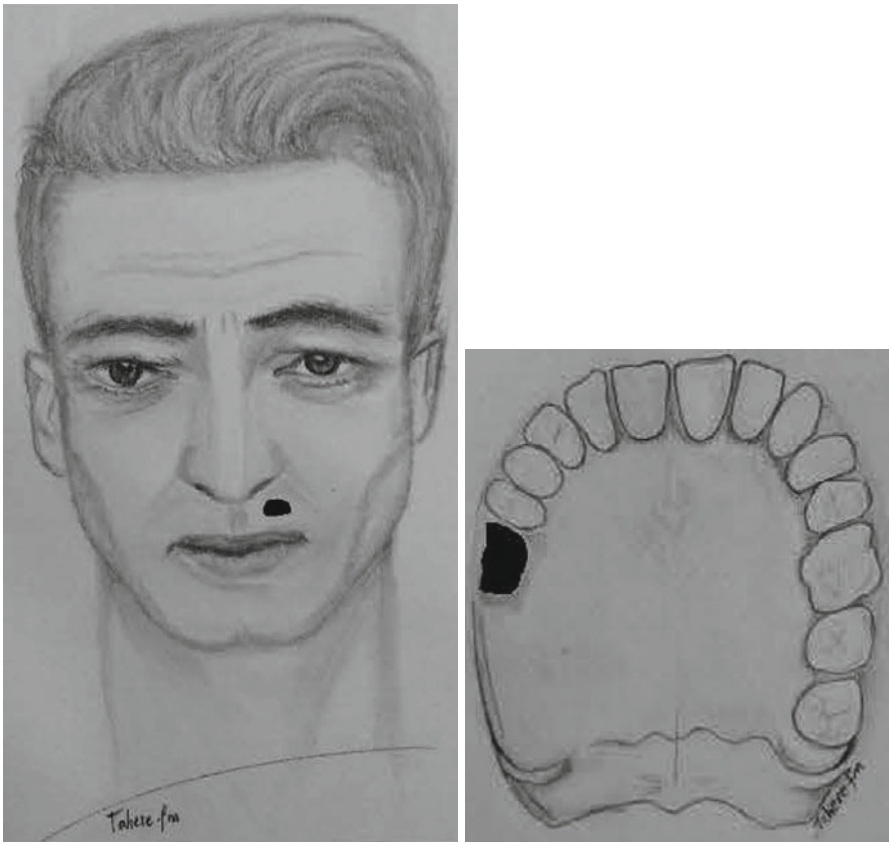

Fig. 10.4 Case report 10-3. The sites of pain on the gum around the extracted teeth and the upper lip are marked with dark ink. onaA was injected into the marked area of the gum (four 2.5 units, total 10 units) (Created by Damoun Safarpour; published with kind permission from © Bahman Jabbari 2014. All Rights Reserved)

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