Review Article

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Botulinum Toxins in Temporomandibular Joint Disorders

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ABSTRACT

Background: Temporomandibular joint disorders (TMDs) are arguably a common disease and because of the complex nature of temporomandibular joint it is often very difficult to treat. Botulinum Toxin (BTX) is a neurotoxin that is produced by the bacterium that is responsible for Botulism. The neurotoxin works by weakening the muscles and stopping them from contracting. Current medical recommendations favor invasive and non-invasive treatments including the injection of BTX into masticatory muscles. This article elaborates the effectiveness of BTX in the treatment of TMDs.

Keywords: Temporomandibular joint, Temporomandibular Joint disorders, Botulinum Toxin.

INTRODUCTION

The Temporomandibular joint (TMJ) is a hinged synovial joint located on both sides of head at the point where the jawbone meets the skull. The TMJ is one of the few synovial joints with an articular disc and it functions as both hinge joint and a sliding joint.TMJ is used during talking, eating, swallowing, and other everyday activities. If this joint becomes displaced or is overworked through excessive teeth grinding, a person may suffer severe tension headaches, as well as sharp pain in the jaw.

Temporomandibular disorders (TMDs) are a non specific term used to describe orthopedic and myofascial disorders that affect the TMJ. The prevalence of TMD is between 30% and 44% with up to 25% of the population seeking professional care [1]. There are 2 types of TMDs in general: articular and muscular, sometimes combined. Muscular TMD is associated with pain from hyperfunctioning muscles of mastication leading to chronic myositis. In contrast articular TMD is associated with intracapsular pathology with pain at the level of joint itself.

DIAGNOSIS

The diagnosis is mainly based on history and physical findings. Patients should be asked about bruxism, jaw soreness, headaches, use of orthodontic appliances, history of trauma, and personal habits [2]. Clinically atleast one of the three cardinal signs must be present as represented in the French acronym ***"BAD"*** [3] –

"B"- Bruit: clicking, popping and crepitus sound noise during jaw movement.

"A"- Algie: facial pain modulated by jaw function,

"D"- Dyskinesia, or abnormal jaw movements.

It is more prevalent in women (11.3% to 12.7%) as compared to men (6.5%). [4, 5] while the cause is not precisely known researchers are looking into hormonal causes. Imaging studies are used only when there is dysfunction of articular disc and or disorders that may complicate the diagnosis like rheumatoid arthritis, osteoarthritis or trauma [6]. OPG is usually the initial imaging modality with CT

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or MRI of TMJ obtained when a more detailed anatomical examination is necessary.

TREATMENT

There are varieties of treatment options ranging from nonpharmacological therapy, conservative therapy to surgery. The purpose is to reduce the impact of pain and associated functional limitations. In many cases, people can successfully treat TMDs at home. Self-care and lifestyle changes may be enough to handle mild to moderate symptoms. This could involve avoiding chewing gum, eating only soft diet, avoiding clenching or tensing the jaw. Gentle exercise such as massaging the affected muscles around the jaw may also help. For TMDs that are caused by pre-existing conditions, more specific treatment is required like TMDs associated with bruxism a night guard may help to ease the symptoms. In cases where TMD is caused by degenerative conditions, such as osteoarthritis, steroid injections may be used. Short term over the counter pain medications can reduce discomfort temporarily. In more extreme cases surgery may be required. The interpositional arthroplasty in TMJ-ankylosed patients, using either a temporalis muscle and facial flap or a dermal graft, yielded a comparable and satisfactory outcome [7-8]. Despite the effectiveness of analgesic pain medications, response to opioid therapy is often incomplete with approximately three quarters of patients suffering from persistent pain [9]. Hence, Botulinum toxin (BTX) has become an adjuvant and attractive choice in patients who do not achieve a complete response with conservative therapy and pharmacotherapy.

BOTULINUM TOXIN AS ADJUNCTIVE THERAPY

Botulinum toxin is an exotoxin of a gram-positive aerobic bacterium called *Clostridium botulinum* with eight different types [10]. *C. botulinum* elaborates eight antigenically distinguishable exotoxins (A, B, C_1, C_2, D, E, F and G). Type A is the most potent toxin, followed by types B and F toxin. Types A, B and E are commonly associated with systemic botulism in humans.

The first time BTX was used for treating pain in patients treated for hyperfunctional lines who reported reduced frequency and severity of headache [11]. Soon thereafter, pain relieving effect of BTX was reported during the treatment of oromandibular dystonia and cervical dystonia [12-15]. Tintner *et al*. used toxin injections to cure the hyper-tonicity of Lateral Pterygoid muscles and its consequent bruxism [16]. The use of this toxin in the treatment of joint sounds was reported in 2005 with no recurrence in one-year follow-up period [17]. In another study conducted in 2004, injections of BTX for patients with articular disc displacement resulted in pain relief and return of the normal movements of the mandible. The treatment was effective and stable up to 6 weeks [18]. Nowadays, use of BTX has been established in many conditions such as migraine, tension headaches and myofacial TMD [19-20].

Mechanism of action: All botulinum neurotoxins are produced as relatively inactive, single polypeptide chains with a molecular mass of about 150 kDa with a high degree of amino acid sequence homology among the toxin types. The polypeptide chain consists of a heavy (H) chain and a light (L) chain of roughly 100 and 50 kDa respectively, linked by a disulfide bond [21]. The botulinum toxin neurotoxin complex is also associated with various other nontoxic proteins, which may also have hemagglutinating properties [22]. All the serotypes interfere with neural transmission by blocking the release of acetylcholine, which is the principal neurotransmitter at the neuromuscular junction. Intramuscular administration of botulinum toxin acts at the neuromuscular junction to cause muscle paralysis by inhibiting the release of acetylcholine from presynaptic motor neurons [23]. Botulinum toxin induces weakness of striated muscles by inhibiting transmission of alpha motor neurones at the neuromuscular junction. This has led to its use in conditions with muscular overactivity, such as dystonia [24].

***Technique*:** Temporalis, Masseter and lateral Ptrygoid are the most commonly affected muscles. The temporalis muscle and masseter muscle are almost always involved and usually manifest as direct muscle pain. Lateral pterygoids involvement usually manifests as buccal pain, lateral jaw deviation or bruxism [16]. Botulinum toxin is injected into affected muscles or glands using a 30-gauge 1-inch needle. Doses are tailored according to the mode of use and individual patients, and the dose depends on the mass of muscle being injected: The larger the muscle mass the higher the dose

required. However, lower doses may be required in patients with preexisting weakness and in females. There is no consensus of optimal doses.

Alexis kahn et al [25] in his study injected a total dose of 100 units with 100µL at 10 sites: 3 sites per masseter and 2 per temporalis. They injected the masseter muscle 1cm in front of and above the gonial angle. The other two injection sites were 1cm in front of and 1cm above the first injection site. The temporalis musle was injected 1cm behind the hairline to avoid frontal muscle paresis, followed by 1cm behind it. Several authors have used BTX in doses ranging from 100 to 150 units per muscle.

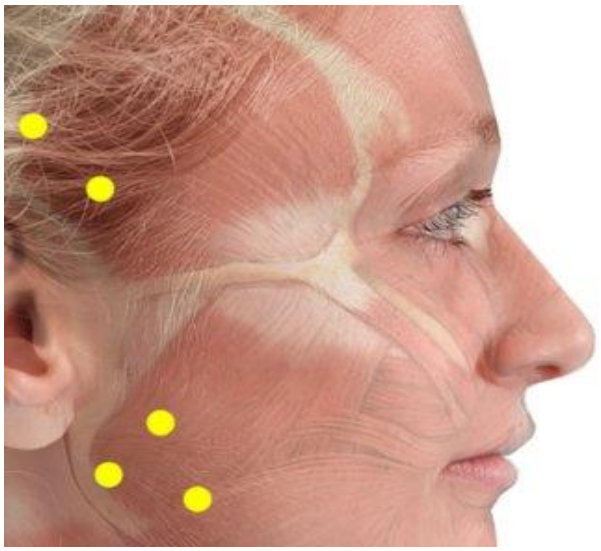

Fig 1: Various sites for BTX injection, 3 sites per masseter and 2 per temporalis muscles. Reproduced from [25].

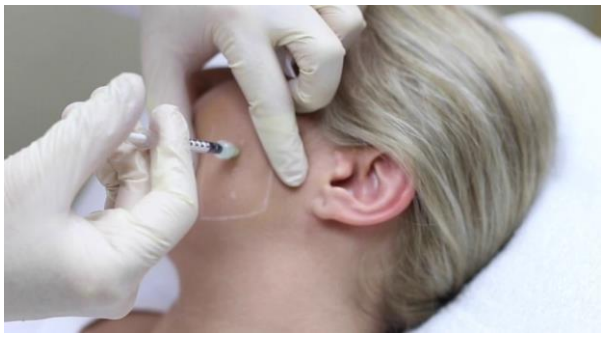

Fig 2: Injection site for masseter muscle. (Image source: Google.com)

Many authors performed injections under the guidance of Electromyography (EMG) using a 27-gauge electrode injection needle [2]. The temporalis and masseter muscle are injected transcutaneous. Identification of the lateral pterygoid muscle is done intraorally with the EMG needle placed between the pterygoid plate and the coronoid process of mandible. BTX diffuses to about 1 cm at each injection site. To avoid an inadequate diffusion and incomplete response, use of lower concentrations at multiple sites with larger injection volumes is advocated.

Contraindications: Botulinum toxin is contraindicated in patients afflicted with a preexisting motor neuron disease, myasthenia gravis, Eaton-Lambert syndrome, neuropathies, psychological unstability, history of reaction to toxin or albumin, pregnancy and lactating females, and infection at the injection site. Careful monitoring should be done in children as it might alter cell functions such as axonal growth [26].

Side Effects: If given in relative low dosing profile, adverse effects are uncommon and often mild. Difficulty in chewing is the most common adverse effect. Higher doses of BTX increase the risk of diffusion of toxin to nearby areas which may cause brow ptosis, blepharoptosis or diplopia if the toxin is injected too close to orbit. Facial asymmetry may result if the masseter muscle is injected too close to zygomaticus major [27-29]. Dry mouth may occur if BTX is injected into parotid gland. Flu like symptoms may occur. Majority of studies have reported symptoms such as dysphagia, muscle weakness, transient speech disorder.

CONCLUSION

BTX injection has recently become a popular treatment modality for cosmetic corrections, oromandibular dystonia, myofascial pain with or without TMDs, masseter hypertrophy, and migraine, etc. It is a safe and minimally invasive procedure that may be performed under local anesthesia, without sedation on an outpatient basis and its main purpose is to alter the muscular activity by inhibiting the release of acetylcholine at the motor nerve-end plates. Adverse effects are uncommon, mild and transient making it an attractive option for adjunctive therapy for myofacial TMD in patients who have failed initial conservative therapy and systemic pharmacotherapy. In future, the development of new potent toxins with increasing effectiveness and duration of effect will further aid this expanding and

interesting field of chemodenervation. The fate of the BTX used as an alternative treatment modality in refractory TMDs patients, whether it has been effective or not is an issue which is attracting a lot of debate.

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

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