ISSN- O: 2458 - 868X, ISSN –P: 2458 - 8687

International Journal of Medical Science and Innovative Research (IJMSIR)

IJMSIR : A Medical Publication Hub

Available Online at: www.ijmsir.com

Volume – 3, Issue –1, January - 2018, Page No. : 134 - 140

The Effectiveness of Botulinum Toxin in the Treatment of TMJ Disorders: A Systematic Review

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Type of publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Introduction

The mandibular jaw is connected with the temporal bone of the skull by a joint called temporomandibular joint (TMJ). This joint helps in many functions such as: swallowing, breathing and speaking. It can be affected by some pathological disorders which adversely will affect its structures and its functions. These disorders might be of orthopedic or myofascial origin which nearly the same as those described conditions of the other joints in the body [1, 2]. However, the nature of the temporomandibular joint as both joints in both sides moves simultaneously at the same time and the location of this joint as it is in the proximate of other facial and cranial structures may provoke the complications of the temporomandibular disorders (TMD) or even mimic the sources of the pain in the head and neck [3, 4]. TMD can be considered as the main cause of non-dental pain in the orofacial region [5].

The symptoms associated with TMD include the following: headaches which might be chronic; hearing impairment or pain in the ears; difficulty in speaking, eating, and sleeping; dysfunction of the jaws (hyper- or hypomobility); and orofacial pain. The most common symptom is the pain particularly at the TMJ. The diverse nature of TMJ disorders with different signs and symptoms which are similar to those of head and neck pain makes the differential diagnosis difficult and more complex [6, 7]. Additional diagnostic aids might be required such as X-ray radiography, cone beam computed tomography, and magnetic resonance imaging. Moreover, there is no globally accepted classification available for these conditions [8].

The primary treatment options should be aimed to be minimally invasive, reversible, and conservative. These options include jaw exercises, oral appliances, drugs (anti-inflammatories and muscle relaxants), low-level laser, laser, or by stretching the affected muscles, infiltration with local anesthetics or dry needling [1, 3, 4]. However, some cases may be resistant to these options and the patients do not show any improvement. In such cases the botulinum toxin may be the alternative treatment due to its analgesic and antinociceptive properties [8]. This material is produced by Clostridium botulinum (a gram-positive aerobic bacterium) and found on seven different types designated from A to G. The most common used type is botulinum toxin type A (BTX-A). It has been since 1977 for the treatment of different neuromuscular disorders such as oromandibular dystonia. It works on the presynaptic endings by blocking the release of acetylcholine which becomes non-functional and inhibits the muscular contraction. The clinical effects take place after few days (1-2 days) till 1-2 weeks after administration while the complete recovery of the nerve takes about three months [9-11].

Botulinum toxin was used originally for the treatment of focal dystonias. It also has been used to relief pain in the head and neck region (migraine, tension headaches, cervical dystonia, and whiplash-associated neck pain) making its use possible for the treatment of temporomandibular disorders [12, 13]. Previously, some prospective and randomized clinical studies have reported that botulinum toxin is effective for the treatment of neurologic disorders particularly those associated with hyperactivity of skeletal muscles [10, 12]. The different groups of TMDs which have shown a positive response to the treatment with botulinum toxin include: bruxism, oromandibular dystonias, masseter and temporalis hypertrophy, and myofascial pain.

The aim of this systematic review was to explore and evaluate the published articles dealing with the effectiveness of botulinum toxin in the treatment of temporomandibular disorders.

Keywords: Masseteric Hypertrophy, Botulinum Toxin

Materials and Methods

Data Sources and search strategy

An electronic search was conducted on PubMed search engine. Keywords used for this research included; TMD, TMJ disorders, bruxism, oromandibular dystonia, myofascial pain, masseter hypertrophy, temporalis hypertrophy, tension headaches, TMJ clicking, botox, botulinum toxin, pain score, mouth opening, function disability index, and bite force.

Eligibility Criteria

All articles published in English language up to October 2017 were eligible to be included in this review. Search on the PubMed revealed 52 articles. After reading titles and abstracts, irrelevant and duplicated articles were excluded. The resulting articles were read carefully for the use of botulinum toxin in the treatment of TMD and the references lists of the resulting articles were screened for additional studies. Review articles were excluded. Therefore, the included articles for this review were 28 articles.

Data Extraction

Extraction of the data in relation to the required information was ensured by two reviewers. The data extraction form included: type of the study, sample size, age and gender of the participants, type of TMJ disorder, injection technique (dose, number of session, muscles involved), methods of outcome assessment, outcome of treatment (success rate, recurrence, difference between before and after, and complications (type, frequency, percentage).

Results and Discussion

A total of 28 studies were included in this systematic review. According to the type of TMD they can be divided into:

- ***Masseteric hypertrophy***

A total of 5 studies [14-18] were found in this regard. All of them were with prospective design. The number of the included subjects varied considerably from 7 subjects in the study of Ahn et al [14] to 35 subjects in the study of Freund et al [16]. Most of subjects were young adults. The dose of the injected botulinum toxin was 50 units in 3 studies [14, 15, 17], 150 units in one study [16], and 120 units in another one study [18]. Number of sessions ranged from 1 session to 4 sessions. Masseter and temporalis muscles were the targeted muscles for injection. Visual analogue scale (VAS) and/or bite force measurements were used to assess the outcome of the treatment.

Ahn et al [14] injected botulinum toxin A (50 units in total) for 7 patients. The bite force was measured before injection and then 2, 4, 8, and 12 weeks after injection. There was significant differences between before injection and 2, 4, and 8 weeks after injection. However, no

significant difference was observed with bite force before injection and 12 weeks after injection, suggesting that the bite force returned gradually to the normal range after 12 weeks from injection. As a result of bite force reduction some patients complained of masticatory difficulty when chewing hard foods. The same results were obtained by Song et al [15] and Kim et al [17], in which the bite force a decrease of bite force was observed after injection with botulinum toxin A and then an increase was recorded to the value before injection after 12 weeks. In another study, a total of 150 units of botulinum toxin A were injected in masseter and temporalis muscles on 35 patients. The outcomes were measured by VAS and bite force. All subjects reported changes in their chewing and some of them complained headache one day after injection which was resolved within 3 days. No clear conclusion could be drawn from this study despite the analgesic effect of botulinum toxin A was evident [16]. Weakness while chewing foods and decline in bite force one week after injection were seen in the study conducted by Yu et al [18]. The bite force, however, recovered completely after 3 months and all subjects reported recovery of their chewing power. The botulinum toxin was found to be effective in the treatment of widened lower facial height.

- ***Myofascial pain with/without TMJ involvement***

A total of 13 studies [19-31] were found. Out of them, 5 studies [19, 20, 22, 23, 31] were RCT, five studies [21, 25, 28-30] were with prospective design, one study [27] was non-randomized clinical trial, one study [26] was case series, and one study [24] was retrospective cohort study. The number of the recruited samples ranged from 10 subjects in the study of Nixdrof et al [31] to 30 subjects in the study of Guarda-Nardini et al [19]. The injected dose was 50 units in three studies [21, 24, 27], 60 units in one study [25], 90 units in one study [26], 100 units in two studies [20, 22], 150 units in three study [28, 29, 31], 300 units in one study [19], and 500 units in another two studies [23, 30]. Number of sessions of injections was one or two sessions. Masseter and temporalis muscles were the most targeted muscles of injection. VAS and/or jaw range motion or mouth opening were used to assess the outcome of therapy.

In the study of Guarda-Nardini et al [19] it was found that fascial manipulation was slightly superior in pain relief while BTX-A was slightly superior in increasing jaw range motion. Some minor discomfort during chewing were reported by the injected patients in the first 2-3 weeks after injection. Among another studies [21, 22, 25, 28-30] the injected patients showed more improvement than the placebo groups in pain relief and jaw range motion. However, Guarda-Nardini et al [20] in another study found non-significant difference between the tested (injected) group and the placebo group which was related to the small sample size.

Laser has been found to be faster in pain relief when compared with BTX-A while, no significant difference was found regarding mouth opening [23]. Another important findings can be seen in the study of Nixdrof et al [31], in which no significant difference was observed in any outcome measure except maximum opening which showed BTX-A patients opening was less wide than placebo group. On the other hand, Hartl et al [27] in their study found that BTX-A did not improve trismus and no significant objective improvement of jaw opening was observed. With different units of the injected BTX-A different prospective studies [21, 25, 28-30] showed significant improvement in the tested (injected) patients in relation to pain, particularly chronic pain, and jaw range motion although some transient difficulties were reported within the first week by some patients. A result from retrospective cohort study [24] revealed that the effect of

BTX-A combined with TMJ arthroscopy for the treatment of TMJ arthralgia and fascial pain was evident. VAS and maximum inter-incisal opening were measured. Patients in BTX-A had a significant greater reduction in VAS compared to control group. Effectiveness of BTX-A for the treatment of chronic masticatory myofascial pain was also found in a prospective case series study [26] where the pain, measured with VAS, was decreased significantly and maximum opening was also significantly increased.

- ***Oromandibular dystonia***

Three studies [32-34] were found with different designs; one cohort study [34], one prospective study [33], and one case report [32]. The number of the recruited subjects varied considerably between studies (one subject in the case report, 8 subjects in the prospective study, and 50 subjects in the cohort study). Subjects in the cohort study [34] were divided into 3 groups according to the type of TMJ disorder. In the first group 100 units of BTX-A were injected (jaw opening disorder) while, 150 units of BTX-A was used in the second group (jaw closing disorder), and another 100 units of BTX-A was used for the third group (jaw deviation/dystonia group). The targeted muscles for injection were lateral pterygoid and anterior digastric muscles for the first group; masseter, temporalis, and medial pterygoid muscles for the second group; and temporalis and lateral pterygoid muscles for the third group. The effect of BTX-A could take place after 16 weeks after first injection with 75-80% of pain reduction. Some adverse effects such as mouth dryness and dysphagia were reported.

In the case report study of Yoshida et al [32] injection of BTX-A in the pterygoid muscles for the treatment of jaw opening dystonia has shown great effect after few weeks but, adversely, the symptoms as before injection was reported to gradually begin to return. However, the patient showed no TMJ dislocation or any further airway collapse. In contrast to these results, Moscovich et al [33] in their study reported much improvement of their patients after injection of BTX-A in pterygoid muscles.

- ***Bruxism***

Among the screened published articles there were 7 studies [20, 29, 35-39] dealing with bruxism. One of them was prospective [29], one was retrospective [37], two were RCT [20, 35], and three were case reports [36, 38, 39]. The number of subjects and the injected BTX-A varied accordingly. Most of the studies used VAS as a method to assess therapy outcome. The majority of the studies showed good improvement of the included subjects. However, in the retrospective study done by Austay et al [37] the loss of effectiveness was reported 4 months after the first injection.

Chronic myofascial pain may result from chronic inflammation and localized muscular hypoxia which in turn result from chronic local muscular contracture. Botulinum toxin has a direct effect on nociceptors and parasympathetic nervous system and thus has analgesic effect and stress relief [40-42]. After 3-4 weeks from the initial dose of BTX-A another appointment should be scheduled for reevaluation and addressing any side effects. Another additional dose of BTX-A might be required based on clinical examination and patient's experience of pain. Although the typical duration of effectiveness is 12 weeks, some patients may need more to express pain relief. Moreover, patient's response to BTX-A may change over time [43, 44]. Difficulty during chewing is considered the most common adverse effect of BTX-A injection which result from weakness of the muscle and it is dose dependent. Diplopia is another side effect which may occur if the injection of temporal muscle was too close to the orbit. Dry mouth may also occur if the injection was directed toward the parotid gland [40, 45, 46].

It can be noted from the results of the current review that the significant evidence of the evaluation of using BTX-A in the treatment of TMD is limited and most of the treatments focus on the myofascial pain. This arises the need for longitudinal randomized clinical trials to evaluate the treatment of the different types of TMD by using BTX-A.

Conclusion

Despite the reported effectiveness of BTX-A in treating TMD, no clear evidence for long-term effect is exist. Further clinical trials with long term follow-up system is highly needed.

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