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Original Article

Assessing the effectiveness of botulinum toxin injections into masticatory muscles in the treatment of temporomandibular disorders

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Abstract – Introduction: Temporomandibular disorders (TMD) are a common and invalidating disease sometimes difficult to treat. Current international recommendations favour reversible and non-invasive treatments, including the injection of botulinum toxin (BTX) into masticatory muscles. There is no strong evidence of its effectiveness. **Objective:** The main goal of this study was to assess the effectiveness of BTX six months following injection, in terms of pain, mouth opening, improvement of symptoms and duration of effect. **Materials and methods:** A retrospective study carried out at Nantes University Hospital between 2014 and 2016. **Results:** Thirty-four patients were included. The mean age was 37 years (17–76) and seventy six percents were female. Eighty percent of patients reported a significant improvement, notably in cases of arthralgia, which decreased in 8/18 (44%) patients ($p < 0.05$). The mean duration of measured efficacy was 4.2 months. **Discussion:** Significant improvement in cases of arthralgia and a tendency for improvement in cases of myalgia, with a mean duration of action of 4.2 months. Although BTX injection do not guarantee complete resolution of myofascial pain, it have been shown to have beneficial effects on some symptoms have been shown. **Conclusion:** Botulinum toxin should be considered as an alternative treatment when other conservative methods fail to yield satisfactory results. A thorough multicentre assessment is necessary in the future to scientifically validate its use.

Introduction

Temporomandibular disorders (TMD) are, after dental pain, the most common cause of orofacial pain. It may affect approximately 70–80% of the adult population between the age of 20 and 45, which makes it a public health concern [1]. A TMD is defined as a dysfunctional mandibular disorder resulting from myoarthropathy of the masticatory system. There are 2 types: articular and muscular, sometimes combined.

The diagnosis of TMDs is mainly clinical, with at least one of the three cardinal signs, represented in the acronym “BAD” in french [2]:

- “B” for Bruit : noise in the temporomandibular joints (TMJ) during jaw movements (clicking, popping and crepitus).
- “A” for Algie : facial pain modulated by jaw function.
- “D” for Dyskinesia, or abnormal jaw movements (restriction or shifting).

International cohort studies have shown that pain caused by TMDs affects between 11.3% and 12.7% of women, and 6.5% of men [3,4].

The pain is recurrent in 65% of cases and persistent in 19% of cases. Arthralgia occurs together with myalgia in 73% of cases, while in 23% of cases the patient suffers from myalgia alone [4].

The treatment of TMD has significantly changed in recent years. Current international recommendations [5,6] propose resorting to reversible, non-invasive procedures first. The purpose is to reduce the impact of pain and associated functional limitations.

To this end, the various therapies are:

- patient information and education like suppression of parafunctions such as onychophagy, chewing gum etc;
- cognitive-behavioural therapy for stress patients;

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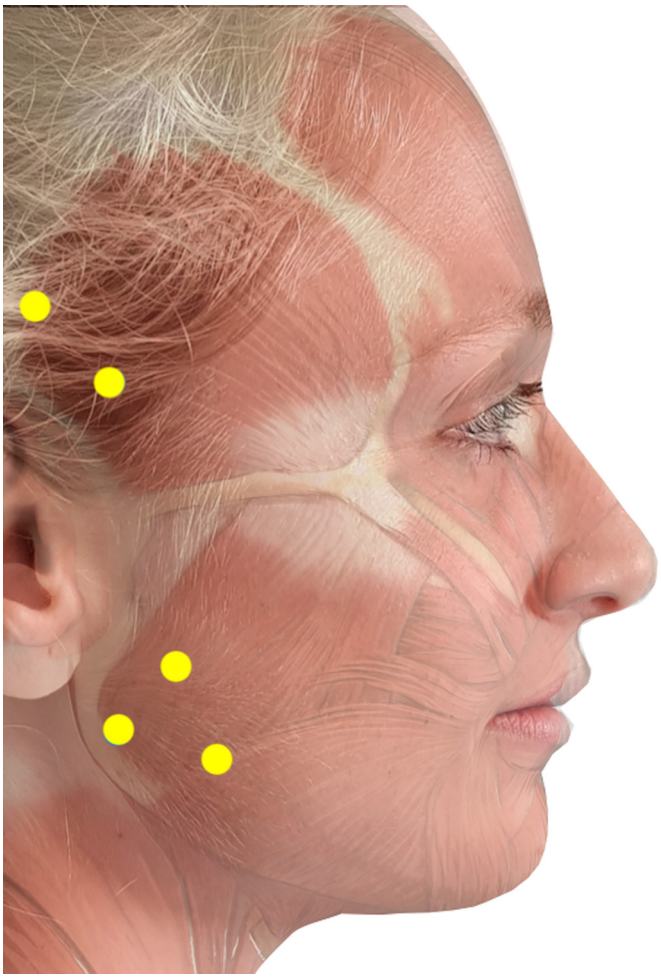

Fig. 1. Injection sites of the botulinum toxin, 3 sites per masseter and 2 per temporalis muscles.

- physical methods such as physiotherapy and kinesiotherapy (massages, transcutaneous electrical nerve stimulation, ...);
- pharmacotherapy to relieve pain and inflammation (analgesics, nonsteroidal anti-inflammatory drugs, myorelaxants, ...);
- arthrocentesis or joint aspiration;
- occlusal orthopedic devices to stabilise the joints, protect the teeth, redistribute occlusal forces, relax masticatory muscles, and treat bruxism.

The French Association for Stomatology, Oral and Maxillofacial Surgery (*Société Française de Stomatologie, Chirurgie Maxillo-Faciale et Chirurgie Orale*, SFSCMFCO) includes this strategy in its good practice recommendations [7].

If usual therapeutic interventions fail, patients may be offered a botulinum toxin injection into their masticatory muscles.

Botulinum toxin (BTX) is a bacterial metalloproteinase produced by Clostridium botulinum. This neurotoxin specifically blocks the release of acetylcholine in the presynaptic membrane of neuromuscular junctions [8]. BTX A is injected into masticatory muscles (masseter and temporalis) to treat trismus, bruxism, masticatory muscle myalgia, temporomandibular joint disorders or muscle hypertrophy [9] with a Ib evidence level [10]. The first studies on temporomandibular dysfunction (TMD) were conducted by Freund *et al.* in 1998 and 1999 [11,12].

There is currently no formal proof of its efficacy with the indications mentioned above. In fact, many monocentric studies have shown significant efficacy [11,13–16], but a recent review paper [17] based on randomised, placebo-controlled trials concluded that there was no consensus regarding the therapeutic advantages of BTX for TMDs.

The purpose of this study was to assess the global efficacy of botulinum toxin injections into masticatory muscles for patients with TMDs whose treatment had failed. Unlike other monocentric studies, this study aimed at evaluating also the BTX effect on the specific TMD symptoms that impair the quality of life such as mouth opening, myalgia, arthalgia, and headache.

Materials and methods

Data collection

We conducted a retrospective study involving every patient who had received at least one injection of botulinum toxin into masticatory muscles was conducted and whose treatment was carried out at the Stomatology and Maxillofacial Surgery department of the Nantes University Hospital between 2014 and 2016. Patients who were enrolled in the study had been suffering from TMD for more than six months. BTX was used after failure of non-invasive therapies. Patients were informed of the use of their medical records. The study obtained the approval of the regional Ethics Committee (no. 2016/41).

All patients answered a series of questions about the history of their disease. The "NFD" criteria were assessed during the clinical examination: myalgia and its location, joint pain and noises, mouth opening range and kinetics.

BTX injection protocol

The main four masticatory muscles, the two masseters and the two temporalis muscles, were regularly injected, regardless of whether the symptoms were unilateral or bilateral. These injections were performed by experienced specialists who were familiar with the anatomical identification technique.

The injection was performed using a 1 mL insulin syringe and a 26G needle, at a dilution of 10 U/mL physiological injectable saline.

A total dose of 100 U was injected with 100 µL at 10 sites: 3 sites per masseter and 2 per temporalis muscles (Fig. 1). The dose was increased to 150 U in the event of insufficient response after many injections, or reduced to 50 U for patients who experienced pain relief.

After removing the anaesthetic lidocaine hydrochloride cream patches (applied 1 h earlier in the masseter area) and disinfecting the skin, the masseter muscle was first injected 1 cm in front of and above the gonial angle, which usually corresponds to the "trigger point". The other two injection sites

were 1 cm in front of and 1 cm above the first site of injection. After that, the temporalis muscle was injected 1 cm behind the hairline to avoid frontalis muscle paresis, preferably in the painful area, followed by 1 cm behind it. If possible, injections were preferably applied at the "trigger points".

Clinical evaluation

An intraoral examination was perform to assess the dental occlusion and teeth and periodontal damage caused by bruxism or parafunction. The existence of dentoskeletal dysmorphosis was also evaluated. The initial and follow-up reports identified 3 main TMD symptoms: joint pain, myalgia and headache/cervicalgia.

A clinical evaluation of efficacy and tolerance was performed at 3 and 6 months after the injection. Patients were re-examined to assess the mouth opening, the symptom release, and the BTX effect duration.

The primary endpoint was patient satisfaction, based on the improvement of the initial symptoms (myalgia, arthralgia, and headache).

The secondary endpoints were based on a comparison of mouth opening, progression of TMD symptoms (myalgia, arthralgia, and headache/cervicalgia), and the average duration of the BTX effect.

Statistical analysis

A Wilcoxon test was performed to evaluate differences between mouth openings. Data relating to symptom improvement before and after the BTX injection were compared using a Chi-square test.

The analyses were performed using Excel (Microsoft) and Systat 13 software.

For every comparison, the null hypothesis was a lack of difference between the measurements made before and after the BTX injection. Statistical significance was defined as $p < 0.05$.

Results

Epidemiological data

Our study included 40 patients. Among them, 34 answered all the questions. Six patients were not followed up. The group was made up of 76.5% of women ($n = 26$) with a mean age of 37 (17–76) at the first injection (Tab. I). The male/female ratio was 3 females for every male.

Among the identified TMD risk factors, 53% ($n = 18$) had a class II deformity. Among them, 17.6% ($n = 6$) were class II.2. Bruxism was identified in 26.5% ($n = 9$) of patients.

Regarding TMD symptoms, 19 (56%) patients were suffering from myalgia, 18 (53%) from arthralgia and 13 (38%) from headached or cervicalgia. Five patients were followed in a pain treatment centre.

Masticatory muscle hypertrophy was observed in 26.5% ($n = 9$) of patients.

Table I. Age distribution of patients.

<20	4
21–29	6
30–39	10
40–49	8
50–59	3
60–69	2
70–79	1

Table II. Number of injections of botulinum toxin per patient.

Number of injections	Number of patients
1	17
2	5
3	4
4	2
5–10	5
>10	1

As part of treatment before the BTX injections, 76.5% of patients ($n = 26$) used occlusal splint to prevent bruxism, 57.7% ($n = 15$) did not report sufficient pain relief.

Ninety injection sessions were performed on the whole population. Fifty percent of patients ($n = 17$) received only one injection, 14.7% ($n = 5$) received two, and the average was 2.6 injections per patient (Tab. II).

Functional results

Subjective clinical improvement was observed in 80% of patients. Regarding TMD symptoms, myalgia decreased in 8/19 (42%) patients ($p = 0.0507$), Arthralgia decreased in 8/18 (44%) patients ($p = 0.0487$), and headaches or cervicalgia decreased in 3/13 (23%) patients ($p > 0.05$). the average mouth opening was 34 mm before and 36 mm after the injection ($p = 0.15$) (Tab. III). The mean duration of measured efficacy was 4.2 months [1–12]. One case of transient facial paresis (at smile) was observed and resolved after 3 months.

Discussion

BTX injection is described as an alternative treatment of TMD when other non-invasive treatments give unsatisfactory results. The first study on botulinum toxin for the treatment of TMD was conducted by Freund in 1998 [12] but to date there is no clear consensus regarding the efficacy of this treatment.

Table III. Symptom progression before and after the injection of botulinum toxin.

Symptoms	Before the injection (*n*)	After the injection (*n*)	*p*
Myalgia	19	11	0.0507
Arthralgia	18	10	0.0487*
Headache	13	10	0.4419

* $p < 0.05$.

We decided to perform injections was performed with anatomical identification only, favouring the "trigger points". This reproducible technique was used for several reasons. Freund [18] injected areas with significant muscle volume and significant activity detected during the electromyogram (EMG), which were not necessarily trigger points. However, numerous studies highlight the advantages of injecting BTX into trigger points [16,19,20].

Although the use of EMG is growing rapidly, most authors use anatomical identification (3/5 in studies by Chen *et al.* [17]). The injections were bilateral to avoid muscular imbalance, which could worsen the symptoms.

A 100-U dose of BOTOX® (Allergan) was injected per patient, with 30 U per masseter and 20 U per temporalis muscle. In literature [17], BOTOX® is used in doses from 100 to 150 units for every muscle. The injection is always intramuscular in 2–4 sites in each muscle. The efficacy of the injected dose depends on muscle mass and symptom severity, and there is no consensus on the optimal dosage [17].

During the follow-up period, the patients were examined after 3 and 6 months to assess the efficacy of BTX. In literature, patients are generally controlled after 1 month. Three months seems to be a suitable interval: at that point, BTX has disappeared completely, muscle strength is fully recovered, and it is the minimum period before re-injection [9], to reduce BTX resistance caused by the production of antibodies [16].

In the present study, 80% of patients reported a significant improvement of their symptoms. There was a significant improvement of arthralgia, as well as a tendency for myalgia improvement. However, there was no significant difference in mouth opening 3 months after the first injection. Sidebottom *et al.* [20] showed that clinical improvement was not related to mouth opening improvement.

This is the first study that indicates the rate improvement for each symptom. Results are therefore difficult to compare to the literature data.

Nevertheless, BTX efficacy for symptoms that cause TMD is thoroughly described. Numerous studies have shown the beneficial effects of BTX for masseter hypercontraction [15,16], bruxism [21], tension headache [13,14] as well as pain and myalgia [12–14,18].

The most recent reports related to randomised, multicentre studies comparing facial manipulation [15] or placebo to BTX injections were contradictory [16,19,22].

Theses studies had significant biases [17]: performance and detection biases for the study of Guarda-Nardini *et al.* [15], selection and reporting biases for studies of Kurtoglu *et al.* [19] and Von Lindern *et al.* [16].

Conclusion

This study shown that BTX should be considered as an alternative treatment for TMD when other conservative methods fail to yield satisfactory results. Randomised clinical studies with high-quality descriptions of all aspects of the methodology and results should be conducted in the future by emphasizing the effect of BTX on different symptoms and adapting treatments.

Conflicts of interests: The authors declare that they have no conflicts of interest in relation to this article.

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