Effects of botulinum toxin in patients with myofascial pain related to temporomandibular joint disorders: A systematic review

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Abstract

Botulinum toxin is used as an alternative for the treatment of chronic refractory myofascial pain derived from temporomandibular disorders (TMDs). It is important to establish the benefits of botulinum toxin in this type of symptomatology. The aim of the study was to conduct a systematic review in order to evaluate the effects of botulinum toxin in patients with myofascial pain related to temporomandibular disorders. The search was carried out systematically, without limitations of language or year of publication, until February 2021. The databases searched included PubMed, Web of Science, Scopus, The Cochrane Library, and Latin American and Carribean Health Sciences Literature (LILACS). Partial gray literature was searched using Google Scholar, ClinicalTrials.gov, OpenGrey, and the reference lists of selected articles. Randomized controlled clinical trials evaluating the effects of botulinum toxin in the treatment of myofascial pain were included. The risk of bias was assessed with the Cochrane RoB 2.0 tool, and the The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to determine the certainty of the scientific evidence. A total of 900 studies were retrieved, out of which only 8 randomized clinical trials were selected. From these 8 studies, the data of a total of 314 patients, predominantly women, between the ages of 18 to 75 years was obtained. After the assessment of the studies with the RoB 2.0 tool, 7 studies showed some concerns regarding the reported results and only one was at a low risk of overall bias. The analysis of the studies has shown that low doses of botulinum toxin are effective in the treatment of refractory myofascial pain associated with temporomandibular disorders. The studies presented medium- to low-certainty evidence..

Keywords: botulinum toxin, myofascial pain, temporomandibular joint disorders

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Introduction

The American Academy of Orofacial Pain (AAOP) defines temporomandibular disorder (TMD) as a generic term that contains a series of clinical problems that affect the temporomandibular joint, masticatory muscles and associated structures.[1,2] Temporomandibular disorder has a multifactorial etiology that involves biological, infectious, hormonal, psychological, social, and emotional factors. [3–10]

Patients with TMD present with pain,[11–20] limitation of movement, dysfunction, fatigue, subjective weakness, and stiffness of the facial and chewing muscles.[21] In addition, there is a subgroup within the TMD that corresponds to musculoskeletal disorders, the most prevalent of which are localized myalgia and myofascial pain.[17] Myofascial pain can present with acute to moderate intensity and is characterized by the presence of sensitive areas called trigger points, located in bands, tendons and muscle fascicles, and generating deep and localized pain in the tense muscular band. However, pain can also occur in other areas distant from the trigger point.[17,21–23]

Different treatment approaches have been proposed including conservative therapies such as pharmacotherapy,[4,24–26] physical therapy,[14,27,28] ultrasound, transcutaneous electrical nerve stimulation,[17] occlusal therapy (occlusal splints),[29–32] and psychotherapy.[26,33–35] On the other hand, more invasive procedures such as dry needling and acupuncture are also available.[17] However, even after receiving these treatments, the symptoms may partially persist. In this chronic condition, botulinum toxin type A (BTX-A) has recently been used as the alternative for the longer relief of the symptoms of chronic refractory myofascial pain.[20,28,36,37,38]

The BTX-A is an exotoxin synthesized by a spore-forming gram-negative anaerobic bacterium called Clostridium botulinum. This powerful botulinum neurotoxin performs its action at the presynaptic junction of alpha and gamma motor neurons by blocking Ca.[35] It has a dual mechanism of action on the neuromuscular junction such as the inhibition of acetylcholine exocytosis from the nerve end plates (temporary weakening of nerve endings and consequent relaxation of muscle contraction or paralysis, depending on the dose, without any systemic effect) and the inhibition of the release of substance P and glutamate to reduce inflammatory pain.[39]

Despite the aforementioned factors, there is still a lack of unification and collection of scientific information on the benefits of BTX-A therapy. Therefore, the objective of this systematic review was to assess the effects of botulinum toxin in patients with myofascial pain related to TMD.

Material and methods

Protocol and registration

The present review was carried out following The Cochrane Handbook for Systematic Reviews of Interventions,[40] and reported as suggested using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[41] Likewise, the protocol of the study was registered in the PROSPERO Centre for Reviews and Dissemination (CRD) database at the University of York (Heslington, UK), and the National Institute for Health and Care Research (London, UK),[42] under the number: CRD42020168889.

Eligibility criteria

To define the eligibility criteria, the acronym PICOS (Population, Intervention, Comparison, Outcomes and Study design) was used:

– **P**opulation – adult patients with TMD-related myofascial pain;
– **I**ntervention – botulinum toxin injection treatment for myofascial pain;
– **C**omparison – no treatment, placebo or other specific treatment including physical therapy, occlusal splints, drug therapy, or acupuncture;
– Primary **O**utcome – changes in intensity of myofascial pain due to botulinum toxin treatment;
– Effect measures – changes from baseline to last available tracking measured by visual analogue scales or similar tools; and
– **S**tudy design – randomized clinical trials (RCTs) conducted in humans.

The exclusion criteria included studies in children or adolescents, studies on craniofacial anomalies or neuromuscular diseases, literature or systematic reviews, letters to the editor, pilot studies, case report studies, in vitro studies, and animal studies.

Information sources, search strategy and study selection

The search for studies was carried out regardless of the language or year of publication in following electronic databases: MedLine (via PubMed), Scopus, The Cochrane Library, Latin American and Caribbean Health Sciences Literature (LILACS), Embase, Web of Science. Additionally, a partial search of gray literature using specific keywords was conducted up to February 2021 (the detailed data is available from the corresponding author on reasonable request), using Google Scholar, OpenGrey and ClinicalTrials.gov databases. The first 100 records were searched using

Google Scholar. Also, the reference lists of the selected articles were checked to ensure that no potential articles were lost. Articles were managed using EndNote software (Thomson Reuters EndNote X7®; New York, USA) to avoid possible duplication.

The study selection was carried out independently in 2 phases by 2 reviewers (RMRH and KJAS). In the first phase, the reviewers screened titles and abstracts identified from the results of the electronic database and additional sources. Then, studies with titles and abstracts that did not meet the inclusion criteria and duplicate studies were removed. In the second phase, full-text studies were retrieved to confirm their eligibility, according to the inclusion criteria. The reference lists of the selected articles were also evaluated. The reviewers independently selected articles for inclusion in a qualitative synthesis. Disagreements were resolved by verbal discussion and consensus was reached with the help of a third reviewer (LEAG), when necessary.

Data collection process and data elements

Two reviewers (RMRH and KJAS) independently extracted data from included studies using a standardized Excel spreadsheet. The following data was extracted: study design, sex and age of the patient, sample size, diagnosis of TMD, diagnosis of myofascial pain, muscles involved, treatment approach, area of application of botulinum toxin, number of doses, and treatment time. At the beginning of the study, we planned to include the results on the quality of life of the patients. However, this was not possible as none of the studies selected for the review assessed this variable. To clarify and resolve doubts about the studies, we contacted the authors by e-mail.

Risk of bias in individual studies

The risk of bias (RoB) assessment of the RCTs was performed using the Cochrane Risk of Bias tool (RoB 2.0; Cochrane, London, UK).[43] The following domains were considered: randomization process, deviations from planned interventions, missing outcome data, outcome measurement, and selection of the reported result. Each domain was assessed as having: a low risk of bias, some concerns or a high risk of bias. Then, an overall RoB judgment was assigned to each study as: low risk (if all domains had a low RoB), some concerns (if in at least one domain there had been some concerns) or high risk (if in one or more domains there had been some concerns).[43]

In addition, the degree of certainty of the evidence in the studies was assessed using The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach[44] according to the categories (high, moderate, low, and very low).

Both reviewers (RMRH and KJAS) independently assessed the risk of bias and the certainty of the evidence from the included studies. Discrepancies were resolved by verbal discussion and consultation with the third reviewer (LEAG).

Summary measures

Primary outcome measures were based on quantitative data (efficacy of botulinum toxin therapy in TMD-related myofascial pain after botulinum toxin injection). Mean differences and 95% confidence intervals (CIs) for changes were assessed based on patient responses, using a visual analogue scale (VAS).

Synthesis of the results

The data collected from the included studies was synthesized and analyzed in a description table. After the evaluation and taking into account the differences between the botulinum toxin injection protocols, the sample size, the doses, and the follow-up periods, it was considered that the methodology of the studies was not homogeneous. For this reason, a meta-analysis was not performed.

Results

Study selection

In the first phase of the search strategy, a total of 787 studies were identified in the electronic databases (570 in PubMed, 5 in Scopus, 24 in LILACS, 15 in Embase, 60 in Web of Science, and 113 in the Cochrane Library). Furthermore, 113 studies were found during the partial search of the gray literature (100 on Google Scholar, 13 on ClinicalTrials.gov) published from 2008 to 2020. No studies were retrieved from OpenGrey or reference lists. A total of 890 studies were eliminated for being duplicated and not meeting the eligibility criteria after reading the titles and abstracts. Ten studies were obtained for full-text assessment according to the inclusion and exclusion criteria. Two studies were excluded, of which 1 was excluded for not specifying the diagnosis of TMD and the other because it could not be obtained in full text.[45,46] Finally, 8 studies were included in this systematic review. The sequence and complete search are detailed in the PRISMA flow chart (Fig. 1). All 8 studies were RCTs.[20,47–53] Table 1 shows the characteristics of the included studies.

Table 1. Evidence for the effects of botulinum toxin (BTX-A) in patients with myofascial pain related to temporomandibular disorder (TMD)

Author (year)	Study design	Sample and features	Muscle evaluated	Concentration of BTX-A	Dosage and administration	Follow-up	Relevant findings
Ernberg et al. (2011)	randomized clinical trial	21 patients Control group: isotonic saline solution	masseter	100 U of BTX-A in 1.0 mL of saline solution maximum: 100 U per patient and 50 U in the masseter muscle Control group: 1.0 mL of saline solution	1 dose, 3 administration points on each muscle Control group: 1 dose	1 week before, 1 month after and 3 months after	No significant differences in pain reduction were found between BTX-A injection and saline injection in patients with persistent myofascial pain.
Guarda-Nardini et al. (2012)	randomized clinical trial	30 patients: 22 females and 3 males (range: 20–71 years) Control group: fascial manipulation technique	temporal masseter	150 U of BTX-A for each side	1 dose of BTX-A, multiple administration points on muscle Control group: multiple 50 min sessions, 150 min in total	treatment initiation, 1 h after and 3 months after	Both treatments are equally effective in reducing pain in a follow-up of up to 3 months. The increase in mandibular range of motion was slightly bigger after BTX-A injections.
De Carli et al. (2016)	randomized clinical trial	15 patients: 13 females and 2 males (mean age: 38 years) BTX-A group (n = 7); Control group: low-level laser therapy (n = 8)	temporal masseter	500 mL of BTX-A in 1.1 mL of 0.9% saline solution 30 U in the first session 15 U in the second session	2 doses, 2 administration points in the masseter muscle and 1 administration point in the temporalis muscle	before and after the treatment	Both treatments were effective and there was no difference between them regarding pain reduction. The low-level laser effect was faster (12 days) than BTX-A (30 days).
Kütük et al. (2019)	randomized prospective study	40 patients: 29 women and 11 men (mean age: 33.8; range: 20–60 years) Study group (n = 20); Control group: dry needling technique (n = 20)	temporal pterygoid	500 mL of BTX-A 10 cc 0.9% NaCl 25 UA 150 U per patient 25 (0.5 cc) at each trigger point	Study group: 1 dose; Dry needling group: the trigger point is injected from 8 to 10 times	treatment initiation and 6 weeks after the treatment	Pain relief at rest was more effective with the use of dry needling technique after 6 weeks. Both treatments produced significant pain relief and improved function in patients with myofascial pain.
Kurtoglu et al. (2008)	randomized prospective study	24 patients Study group (n = 12; mean age: 29.6 years; range: 16–53 years): 10 females and 2 males; Placebo group (n = 12; mean age: 23.4 years; range: 20–34 years): 10 females and 2 males	temporal masseter	100 U of BTX-A per patient Study group: BTX-A with 2 cc saline solution; Placebo group: 2 cc saline solution	1 dose, 3 administration points in the masseter muscle and 2 administration points in the temporal muscle (10 U each)	beginning of the study, 14 days after and 28 days after	Pain relief and improvement of psychological state after the BTX-A injections and until the 28th day.
Montes-Carmona et al. (2020)	randomized clinical trial	60 patients (range: 18–75 years) BTA group (n = 20); Lidocaine group (n = 20); Placebo group: saline solution (n = 20)	temporal masseter pterygoid	BTA group: 100–150 U 50 U of BTA in 1.25 mL of saline solution to obtain 4 units of BTA per 0.1 mL of the injection liquid; Lidocaine group: 2% lidocaine with vasoconstrictor; Saline solution group: 0.9% saline solution	1 dose in all groups, 3 administration points in the temporal muscle, 3 administration points in the masseter muscle, 1 administration point in the lateral pterygoid muscle	before the treatment and 7, 14, 28, 60, 90, and 180 days after the treatment	BTX-A significantly reduced pain compared to saline and lidocaine. The effects lasted up to 6 months and were more intense in patients with localized myofascial pain than in patients with referred remote pain.
De la Torre et al. (2020)	randomized clinical trial	100 female patients (mean age: 36.8 ±5.6 years) Low BoNT-A group (n = 20); Medium BoNT-A group (n = 20); High BoNT-A group (n = 20); Positive control group: oral administration (n = 20); Negative control group: physiological serum (n = 20)	temporal masseter anterior	BoNT-A group: 100 U of botox diluted in different concentrations with 0.9% sterile saline solution; Saline solution group: 0.9% sterile saline solution	1 dose of 1 mL in all BoNT-A and saline groups, 5 administration points in each muscle. Oral administration group: use during the night	before the treatment and 7, 14, 21, 28, 90, and 180 days after the treatment	BoNT-A (Regardless of dose) was more effective in the reduction of persistent myofascial pain than saline solution and as effective as the occlusal appliance after 14 days and up to 6 months of follow-up.
Gupta et al. (2016)	randomized clinical tria	24 patients (range: 20–50 years) BTX-A group (n = 12); Control group: placebo (n = 12)	temporal masseter anterior	10 U of BTX-A at 10 points 30 MU for the masseter muscle; 20 MU for the anterior temporal muscle Control group: isotonic saline solution	1 dose, 3 administration points in each masseter muscle, 2 administration points in each temporal muscle.	before the treatment, 14 days after and 28 days after the treatment	Statistically significant reduction of pain and improvement in function after the administration of BTX-A compared to the placebo that did not present a significant change in a follow-up of up to 8 months.

BTX-A – botulinum toxin type A; BoNT-A – botulinum neurotoxin type A.

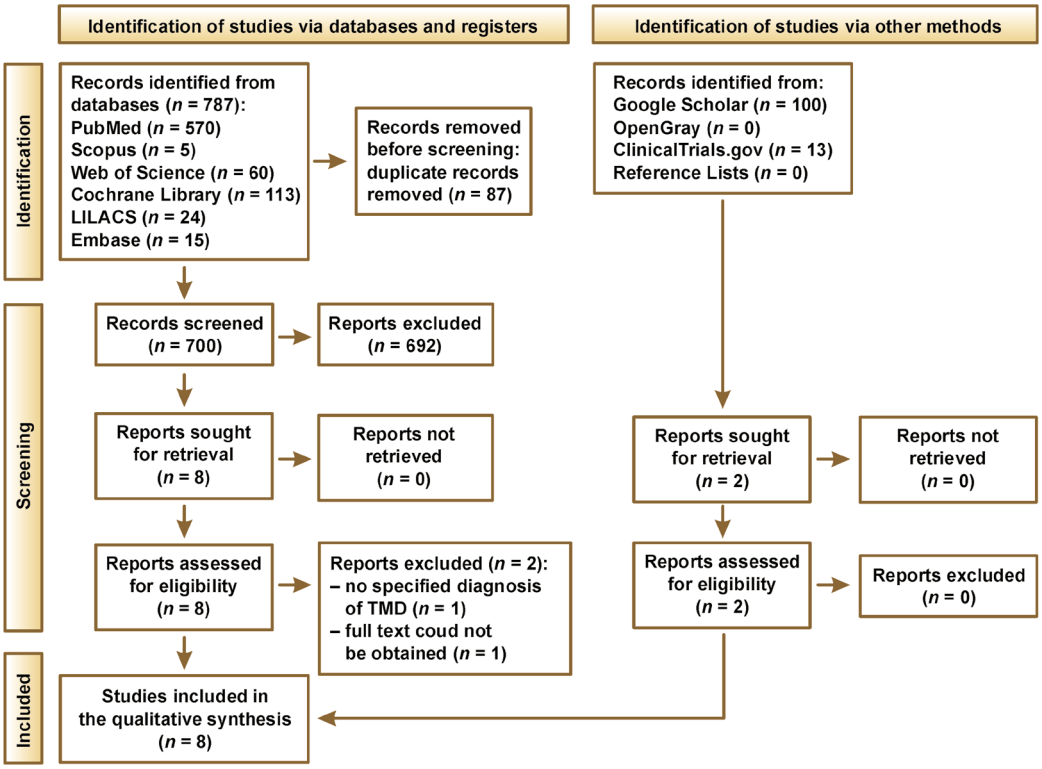

Fig. 1. PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) flow chart

Study characteristics

A sample size of 314 patients were included in the analysis, the subjects being adults between 18 and 75 years of age, predominantly female, diagnosed with TMD-related myofascial pain, without complete relief of symptoms after receiving conventional treatment for at least 6 months. The patients were treated with BTX-A in concentrations ranging from 100 U to 150 U diluted in 0.1 mL to 1.1 mL of sterile saline solution, injected into different muscles. In 6 out of the 8 studies, BTX-A was injected into the masseter and temporal muscles, whereas in only 2 studies BTX-A was injected into the masseter, temporal and pterygoid muscles. Each patient received a maximum of 25–150 U of BTX-A, with an injection of 5–50 U of BTX-A at 1, 2 or 3 sites.

Risk of bias within the study

The risk of bias assessment of the 8 included RCTs[20,47–53] was carried out using the Cochrane RoB 2.0 tool.[43] Out of the 8 studies, only one had a low risk of bias,[50] while in the remaining 7 studies some concerns have been raised, regarding the selection of the reported outcome in the studies describing multiple outcome measures (scales and time points, among others). However, not all data of the results obtained was shown in detail, evidencing a lack of information on the results.[20,47–49,51–53] The evaluation of the studies is shown in Table 2 and Fig. 2.

Table 2. Assessment of risk of bias in randomized clinical trials using Cochrane tool: RoB 2.0

Author (year)	Bias arising from the randomization process	Bias due to deviations from intended intervention	Bias due to missing data	Bias in measurement of outcomes	Bias in the selection of the reported result	Overall
Ernberg et al. (2011)	low risk	low risk	low risk	low risk	some concerns	some concerns
Guarda-Nardini et al. (2012)	some concerns	low risk	low risk	low risk	some concerns	some concerns
De Carli et al. (2016)	low risk	low risk	low risk	some concerns	some concerns	some concerns
Kütük et al. (2019)	low risk	some concerns	low risk	low risk	some concerns	some concerns
Kurtoglu et al. (2008)	low risk	low risk	low risk	low risk	some concerns	some concerns
Montes-Carmona et al. (2020)	low risk	some concerns	low risk	some concerns	some concerns	some concerns
De la Torre et al. (2020)	low risk	low risk	low risk	low risk	low risk	low risk
Gupta et al. (2016)	some concerns	low risk	low risk	low risk	some concerns	some concerns

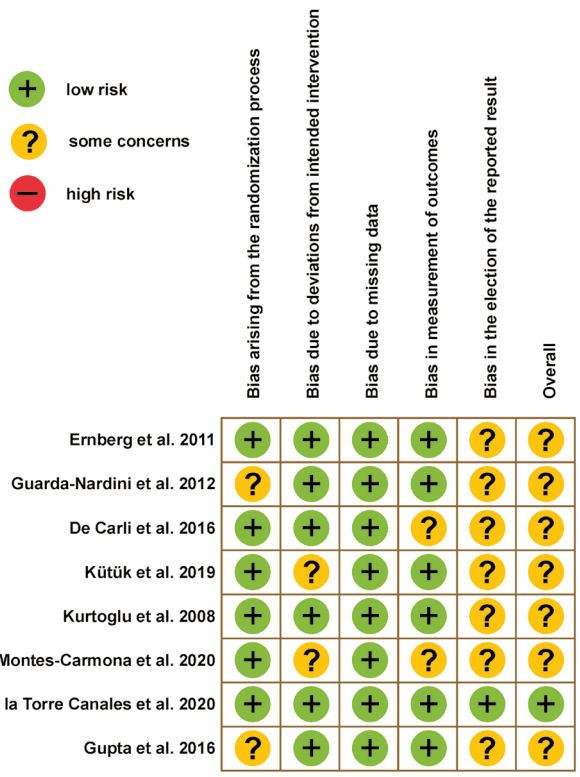

Fig. 2. Evaluation of the included studies in terms of risk of bias

Results of individual studies

All the studies included in the present systematic review evaluated changes in the range of pain intensity. Three studies compared BTX-A (study group) with saline injections (placebo group),[47,51,53] one study compared BTX-A (study group) with saline injections (placebo group) and lidocaine (control group),[49] another study compared a low-level laser (study group) with BTX-A,[48] another study compared BTX-A (study group) with the technique of dry needling (control group),[52] another compared BTX-A (study group) with the fascial manipulation technique (control group),[20] and only one study compared 3 different concentrations of BTX-A with physiological saline (negative control group) and with oral appliance (positive control group).[50]

The study that evaluated the safety and efficacy of 3 different doses of botulinum neurotoxin type A (BoNT-A) (low dose of BoNT-A (BoNT-A-L), medium dose of BoNT-A (BoNT-A-M) and high dose of BoNT-A (BoNT-A-H)) showed a significant decrease in the intensity of subjective pain in the 3 groups, regardless of the administered dose. Furthermore, no significant differences were found between the 3 groups,[50] which shows that even at low doses, BoNT-A can be equally effective up to 6 months after the administration.[49,50]

Four of the studies comparing BTX-A with saline showed that BTX-A injections were clinically effective in reducing pain[47,50,51,53] and increased the pressure pain threshold more than saline.[50]

Another study evaluated the efficacy of BTX-A in the treatment of refractory masticatory myofascial pain syndrome (MMPS) and classified myofascial pain as either localized (MP), non-localized, irradiated, or referred (PR). The results showed that the changes in pain intensity values were statistically significant for the BTX-A group (all patients showed pain reduction from day 0 to day 180, except for the saline and lidocaine groups). Likewise, when comparing the MP group with the PR group that received BTX-A, the pain reduction according to the VAS was greater in the MP group, decreasing from 6 to 2 points and from 6.5 to 4 points, respectively. Although a significant decrease in pain was observed, very low values were not reached in the PR group.[49]

After comparing the low-level laser therapy with BTX-A injections,[48] there were no statistically significant differences between the 2 treatments with respect to pain at the 30-day follow-up. This study reported a baseline VAS of 7 points in both groups, with a decrease to 2.75 on day 12 in the laser group and to 2.86 in the BTX-A group on day 30, demonstrating that both treatments were statistically effective. However, the effects of the low-level laser therapy were faster compared to BTX-A injections (the reduction observed at day 12 vs. day 30, respectively). These results should be taken into account in future studies.[48]

Another treatment compared to BTX-A injection was the dry needling technique,[52] in which the effectiveness on myofascial pain during chewing and rest was evaluated. Both treatments achieved a significant improvement in VAS scores during the 6 weeks of follow-up. However, with respect to myofascial pain at rest, the relief was greater with the dry needling technique. One of the 8 included studies compared BTX-A with the fascial manipulation technique.[20] Both treatment protocols significantly improved and decreased the intensity of myofascial pain, with no relevant clinical differences between the 2 protocols during the 3-month follow-up.

When BoNT-A (regardless of dose) was compared with the oral device, the study showed that both treatments were equally effective in treating persistent myofascial pain during the 24-week follow-up and there was no statistical difference until the last period of follow-up. However, the author also reported a reduction in muscle activity and a decrease in muscle thickness and bone volume of the condyloid and coronoid processes as dose-related adverse effects of BoNT-A (higher doses). Therefore, the BoNT-A in patients with myofascial pain should ideally be administered at low doses.[50]

A meta-analysis could not be performed due to the heterogeneity of the results (differences in botulinum toxin injection protocols, sample sizes, doses, and follow-up periods).

The assessment of the level of evidence using GRADE approach showed that the 8 included RCTs[20,47–53] presented moderate- to low-certainty evidence. A detailed description is shown in Table 3.

Table 3. Classification of the level of certainty of the evidence: The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system

Comparison	Assessment of certainty of the evidence								
	Number of studies (patients)	Studydesign	Risk of bias	Inconsistency	Indirectness	Imprecision	Publicationbias	Summary of findings	Certainty
BTX-A compared to saline injections	3 (69)	RCTs	* serious	not serious	not serious	not serious	not suspected	BTX-A had a clinically significant effect on reducing pain in the 1- to 8-month follow-up compared to the saline group that did not present a statistically significant reduction.	⊕⊕⊕○○ MODERATE
BTX-A compared to saline and lidocaine injections	1 (60)	RCT	* serious	not serious	not serious	• serious	not suspected	BTX-A significantly reduced pain compared to saline and lidocaine. The effects lasted up to 6 months and were more intense in patients with localized myofascial pain than in those with referred remote pain.	⊕⊕○○ LOW
BTX-A compared to low-level laser therapy	1 (15)	RCT	* serious	not serious	not serious	• serious	not suspected	Both treatments were effective and no difference between both treatments with respect to pain reduction was observed 30 days after starting the treatment.	⊕⊕○○ LOW
BTX-A compared to dry needling technique	1 (40)	RCT	* serious	not serious	not serious	• serious	not suspected	Both treatments showed significant pain relief at the 6-week follow-up.	⊕⊕○○ LOW
BTX-A compared to facial manipulation technique	1 (30)	RCT	* serious	not serious	not serious	• serious	not suspected	Both treatments were effective in reducing myofascial pain for up to 3 months of follow-up.	⊕⊕○○ LOW
BTX-A (3 different concentrations) compared with saline and oral apparatus	1 (100)	RCT	not serious	not serious	not serious	• serious	not suspected	BTX-A (regardless of dose) was more effective in reduction of persistent myofascial pain than physiological serum; BTX-A was also equally effective as occlusal appliance at 14 days and up to 6 months of follow-up.	⊕⊕⊕○ MODERATE

RCT – randomized clinical trial; BTX-A – botulinum toxin type A. Reasons for evaluation: * The evidence was downgraded by one level due to some limitations; • The evidence was downgraded by one level because the results were derived from a single study and few participants.

Discussion

Currently, there is no consensus on the most appropriate treatment protocol for myofascial pain. A multidisciplinary approach and first-line treatment are recommended, beginning with conventional therapy. However, some patients do not achieve complete pain relief and are diagnosed with refractory myofascial pain. Intramuscular injections with BTX-A have been proposed in the literature as an alternative treatment for these cases, since this neurotoxin induces a mechanism of action on the neuromuscular junction, inhibiting acetylcholine exocytosis from the nerve end plates and causing the relaxation of muscle contraction and pain relief.[35] Despite this, to date, the efficacy of this treatment is not very clear and therefore, the objective of this systematic review was to synthesize the current information on the effects of botulinum toxin in patients with myofascial pain related to TMDs.

In the present systematic review, BTX-A injections proved to be significantly effective in reducing the intensity of myofascial pain,[20,47–53] regardless of the dose used (high, medium, low).[50] This is evidenced in studies comparing BTX-A with placebo,[47,49–51,53] which demonstrated a reduction in pain clinically more efficient with BTX-A compared to placebo.[49,51] However, 2 studies found that the difference between the 2 treatments was not statistically significant.[47,53]

The fascial manipulation technique has been shown to be more effective in the immediate relief of self-reported pain compared to the BTX-A treatment.[20] However, the difference between the 2 treatment protocols was not clinically significant at 3-month follow-up, and both treatments were found to be equally effective in reducing pain.[20] This difference could be due to the multiple sessions (3 ±1) that patients received compared to the BTX-A treatment that was only performed in a single session. The relaxing and calming effect that the operator transmits by exerting deep digital pressure with the fingertips or elbows on the muscle areas (establishing a positive relationship) during the 50-min sessions could also have had a psychological influence, compared to the BTX-A treatment, which has a cumulative effect.[20] It should be noted that the evaluation of the immediate effect of the BTX-A cannot be compared with other therapies. Such evaluation should be performed days later when the effects appear, that is, its results should be compared in the medium and long term due to the cumulative effect of the BTX-A treatment. Similar results were obtained when the low-level laser therapy was compared to the BTX-A treatment.

From the beginning to the last follow-up of the study, lidocaine injections were not significantly effective in the treatment of myofascial pain.[49] In contrast, both the dry needling technique and the administration of BTX-A showed favorable results in the relief of myofascial pain during chewing and at rest. Furthermore, the relief of myofascial pain at rest was statistically significant with the dry needling technique.[52] Also, in a recently published study, De La Torre Canales et al. compared acupuncture therapy with BoNT-A and saline administration. The researchers found that all 3 therapies significantly reduced self-perceived pain after 1 month of follow-up. However, there was no difference between acupuncture and BoNT-A. Both therapies were effective and superior to saline.[54]

Due to its non-invasive and reversible characteristics, the oral appliance is probably the most widely used therapy aimed at reducing the symptoms of myofascial pain.[50] In our review, the oral appliance was equally effective as BoNT-A therapy. The authors of the study found no significant differences between the 2 treatments.[50] This could be due to the fact that the effect of both treatments is observed days after the start of the treatment, that is, it has a cumulative effect. Therefore, we can confirm that BTX-A compared with conventional treatments (oral appliances, fascial manipulation technique, low-level laser therapy, and dry needling technique) presents similar results. However, despite the aforementioned evidence, a definitive result cannot be established since the summary of certainty of the evidence using GRADE approach showed moderate to low certainty in the evidence of the studies (see Table 3). Moreover, the studies had limitations such as small sample sizes and short follow-up periods.

Therefore, more RCTs with larger sample sizes, longer follow-ups and the inclusion of several control groups (occlusal splints, drug therapy, acupuncture, transcutaneous electrical nerve stimulation (TENS), among others) are needed to determine the effectiveness of BTX-A in the long-term treatment of myofascial pain in patients with TMD.

Conclusions

Based on the analyzed studies, botulinum toxin appears to be as effective in controlling myofascial pain related to TMDs as conventional treatments (oral appliance, lidocaine injections, low-level laser therapy, dry needling technique, saline injections, and fascial manipulation technique).

Botulinum toxin is a useful clinical alternative adjunct to existing conservative treatments of refractory myofascial pain related to TMD.

For the control of refractory myofascial pain related to TMDs, botulinum toxin should be administered in low doses in order to avoid adverse effects related to the high-dose administration.

Ethics approval and consent to participate

Not applicable.

Data availability

All data analyzed during this study is included in this published article.

Consent for publication

Not applicable.

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