BOTULINUM TOXIN-A INJECTIONS INTO FACIAL MUSCLES FOR THE TREATMENT OF TEMPOROMANDIBULAR DISORDERS AND BRUXISM:

A SYSTEMATIC REVIEW

LIBRARY DISSERTATION

152004006 (2020 – 2023)
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STRUCTURED ABSTRACT

Background: Currently it has been shown that botulinum toxin is effective for a wide variety of medical conditions, and can be applied for therapeutic purposes as cosmetic. In recent years, there has been a growing trend in the use of this drug substance to control the muscular overactivity of bruxism. The objective of this study was the use of botulinum toxin type A (BTX-A) than traditional methods, by conducting a systematic review of randomized clinical trials (RCTs) published in the health sciences literature.

Materials and Methods: An electronic search was made in the databases of PubMed, Cochrane Library, Google Scholar and LILACS from Jan 2016. Studies that were included were of patients suffering from bruxism and/or TMD, older than 18 years where BTX-A tests were performed on the masseter and / or temporal muscles and the control systems were injections of placebo (saline) or the use of traditional methods for the treatment of bruxism. such as occlusal splints, other medications or cognitive behavioural therapy.

Results: Of the 62 articles sourced, 6 fit the inclusion criteria. These studies show that BTX-A injections can reduce the frequency of bruxism episodes, decrease pain levels and maximum occlusal force generated by this pathology, offer superior efficacy in the treatment of bruxism compared to control groups who were treated with placebo or with traditional methods for the treatment of bruxism.

Conclusion: Infiltrations with BTX-A are a safe and effective treatment for patients with bruxism, so its use is justified in daily clinical practice, especially in patients diagnosed with severe bruxism.

INTRODUCTION

Bruxism is a repetitive activity of the masticatory muscles characterized by tightening or grinding of the teeth and which may have two distinct manifestations: sleep bruxism (SB) or awake bruxism (AB). It is a common condition with an adult prevalence ranging between 8 and 31%, which has acquired considerable clinical relevance due to its association with tooth abrasions and mobility, fracture of dental restorations, hypertrophy of the masseter muscle and myalgia or arthralgia characteristic of temporomandibular disorders (TMD), among other signs and symptoms. Although etiological factors have been proposed, such as emotional stress, neurological disorders, certain drugs and occlusal interferences, the aetiology and pathophysiology of bruxism are still unclear, although it seems to have a multifactorial origin mediated by nervous systems: central and autonomous.

Various modalities of treatment for the management of bruxism have been investigated, such as: occlusal splints, drugs such as benzodiazepine or L-dopa and cognitive-behavioural therapy, but they have not been shown to be completely effective, since their effect does not seem to solve the cause of it and serves mainly for the management of the signs and symptoms of patients, helping to limit the destructive effects of bruxism on anatomical structures. At present, it has been shown that botulinum toxin is effective for a wide variety of medical pathologies, used both for its therapeutic effect and for aesthetic medicine; It is a neurotoxin produced by a Gram-positive aerobic bacterium called Clostridium botulinum. There are seven different types of exotoxins, botulinum toxin type A (BTX-A) is a biological variant that temporarily inhibits skeletal muscle by hindering the production of acetylcholine and inactivating calcium channels in nerve endings. In recent years, there has been an increasing trend in the use of this drug to control the activity of bruxism.

The purpose of this systematic review, is the further explore the usage of Botulinum Toxin, for the management and treatment of Temporomandibular Disorders and Bruxism.

AIM

The aim of this systematic review was to analyse the existing literature on the use of Botulinum Toxin A injections into Facial Muscles for the treatment of Temporomandibular Disorders and Bruxism

STRUCTURED QUESTION

Does injecting Botulinum Toxin A into the Facial muscles lead to a reduction in Pain in individuals with Temporomandibular Disorders and Bruxism?

PICO Analysis

P – Individuals with Temporomandibular Disorders and/or Bruxism

I – Botulinum Toxin A injection into Facial muscles

C – Traditional methods

O – Pain

MATERIALS AND METHODS

INCLUSION CRITERIA

The planning and preparation of this study has followed the guidelines established by the PRISMA declaration for the preparation of systematic reviews and meta-analysis.

- Randomized controlled clinical trials (RCTs) involving bruxism patients older than 18 years in which the effect of botulinum toxin in the treatment of bruxism compared with traditional therapy is analysed. (Up to 2016)

Types of studies:

Randomized controlled trials

Clinical trials.

Types of Participants:

Patients suffering from TMD and/or bruxism

Types of Intervention:

The use of Botulinum Toxin injection into the facial muscles

Types of Comparison:

Traditional methods

Types of Outcome Measures:

Pain

EXCLUSION CRITERIA

- Randomized controlled clinical trials (RCTs) involving bruxism patients older than 18 years in which the effect of botulinum toxin in the treatment of bruxism compared with traditional therapy is analysed. (Before 2016)
- Studies in which bruxism was caused by psychological or neurological disorders and those who used this therapy aimed at the treatment of other diseases were excluded.
- Descriptive studies
- Observational studies
- Reviews

SOURCES USED

The Databases of PubMed Central, Cochrane, LILACS, Google Scholar.

Search method for the identification of studies:

To identify the studies to be included for detailed evaluation in systematic review, following search strategy were developed for each database searched:

1. PubMed Central – Randomised Controlled Trial (published till Jan 2016)
2. The Cochrane Central Register of Clinical Trials - Randomised Controlled Trial (published till Jan 2016)
3. LILACS - Randomised Controlled Trial (published till Jan 2016)
4. Google Scholar - Randomised Controlled Trial (published till Jan 2016)

Fig 1. – PubMed Search Terms

History and Search Details

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Search	Actions	Details	Query	Results	Time
#11	•••	>	Search: **(#6) AND (#7)** Filters: **Free full text, Randomized Controlled Trial, in the last 5 years**	28	11:42:58
#10	•••	>	Search: **(#6) AND (#7)** Filters: **Free full text, Randomized Controlled Trial**	65	11:42:46
#9	•••	>	Search: **(#6) AND (#7)** Filters: **Randomized Controlled Trial**	228	11:42:40
#8	•••	>	Search: **(#6) AND (#7)**	1,725	11:42:29
#7	•••	>	Search: **(pain) OR (healing)**	1,134,140	11:41:17
#6	•••	>	Search: **(#4) AND (#5)**	9,041	10:53:05
#5	•••	>	Search: **(((((((face) OR (facial)) OR (muscle)) OR (facial muscle)) OR (masticatory muscle)) OR (masseter)) OR (digastric)) OR (pterygoid)) OR (myofascial)**	1,594,544	10:52:55
#4	•••	>	Search: **((((((botox) OR (botulinum)) OR (botulinumtoxin)) OR (botulinumtoxinA)) OR (botulinum toxin)) OR (botulinum toxin A)) OR (BTX-A)**	24,755	10:48:57
#3	•••	>	Search: **(#1) AND (#2)**	1,360	10:47:32
#2	•••	>	Search: **(((((temporomandible) OR (temporomandibular)) OR (TMJ)) OR (TMD)) OR (temporomandibular disorder)) OR (temporomandibular joint)**	38,358	10:47:10
#1	•••	>	Search: **(((((((brux) OR (bruxism)) OR (grind)) OR (grinding)) OR (tooth grinding)) OR (teeth grinding)) OR (night grinding))**	19,661	10:46:16

Fig 2. – PubMed Search Results

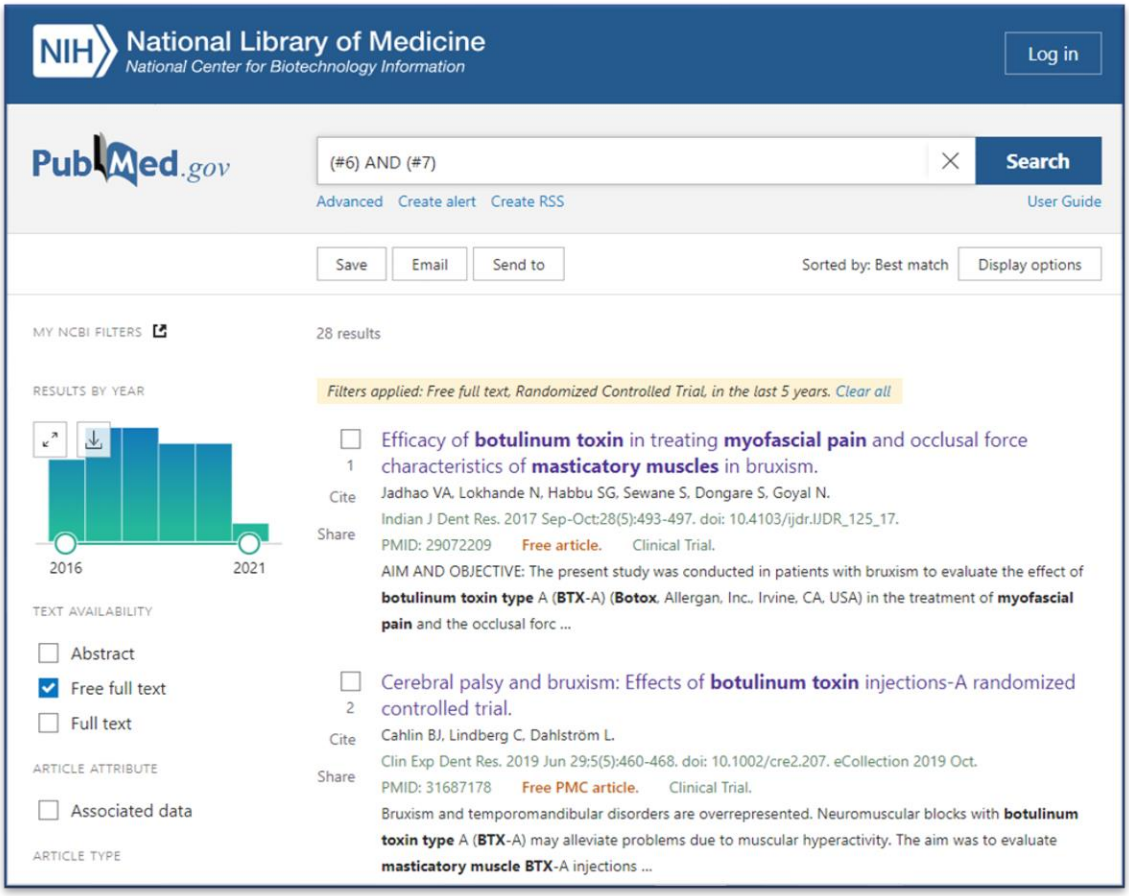


Fig 3. – Cochrane Search Terms

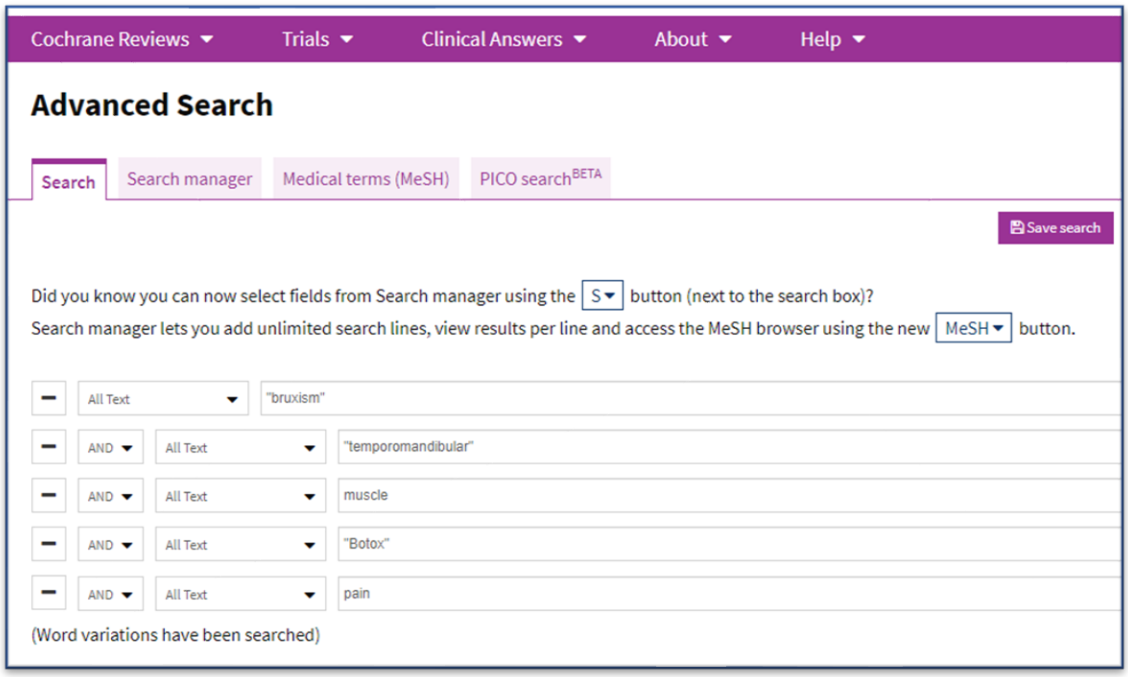


Fig 4. – Cochrane Search Results

Fig 5. – LILACS Search Terms

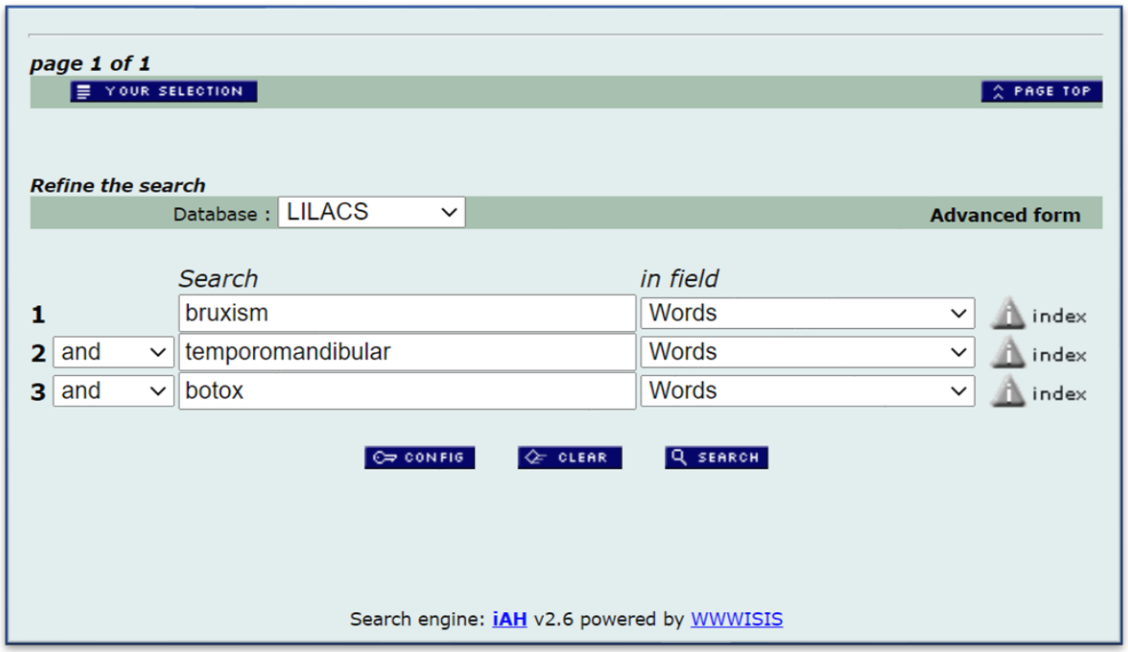
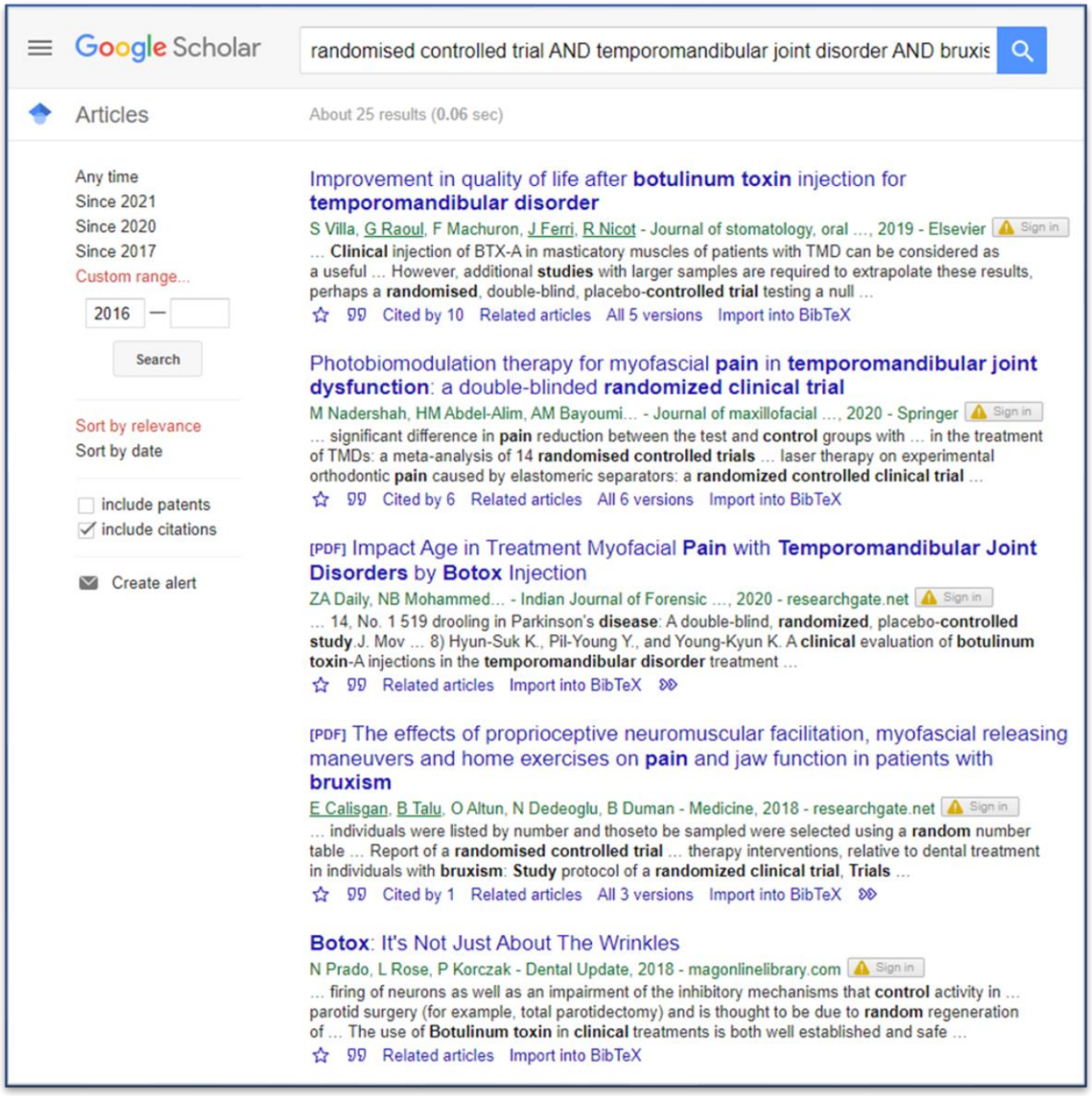


Fig 6. – LILACS Search Results

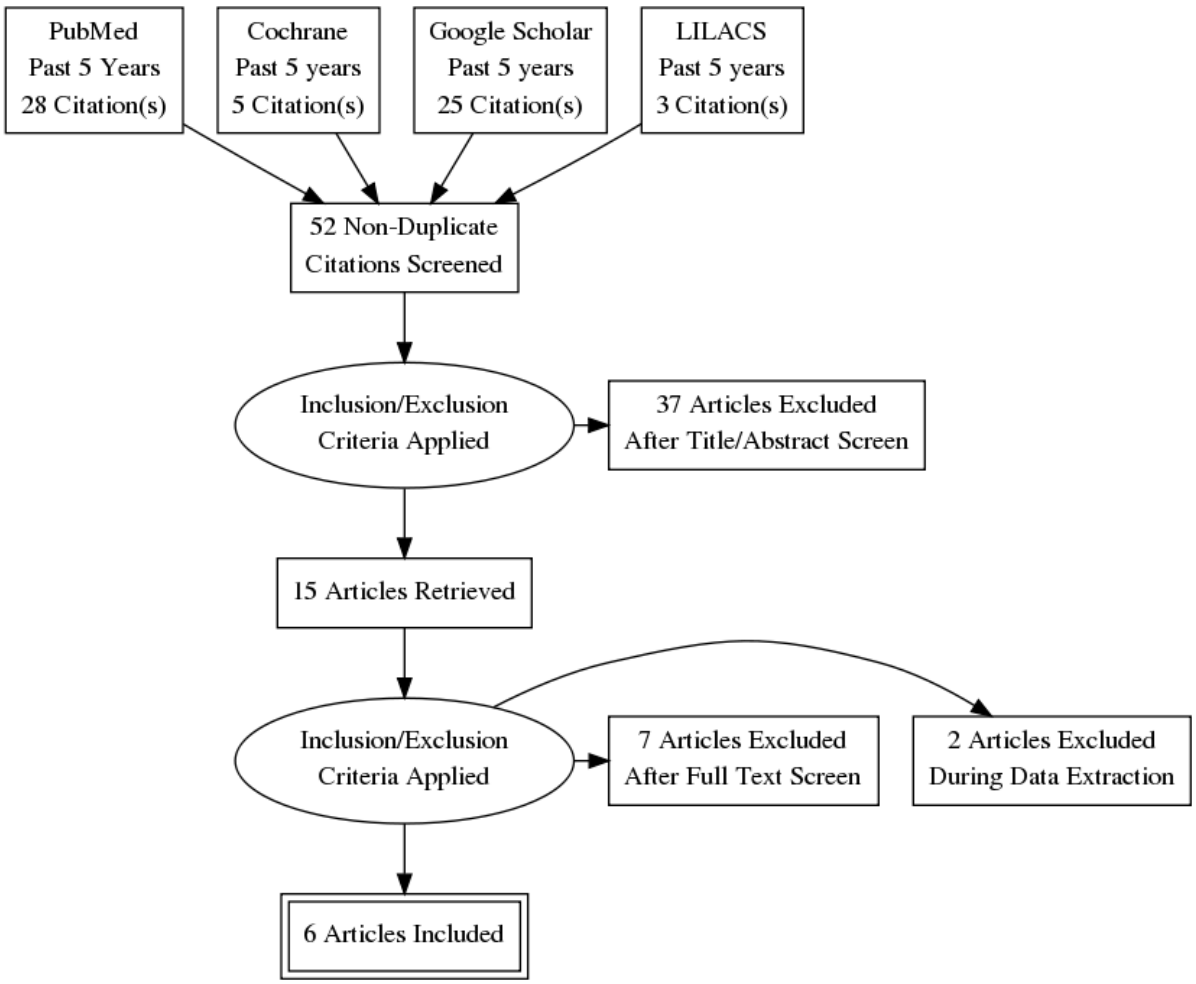
Fig 7. – Google Scholar Search Results



Electronic search was carried out using the keywords in the Search engines- PubMed, Cochrane, LILACS and Google Scholar which yielded a total of 52 articles. Based on the specific inclusion and exclusion criteria, the titles of the studies identified from the search were assessed independently by two review authors (Dr. Sabari Nathan Rajamoorthy and Dr. Hemavathy). Conflicts concerning inclusion of the studies were resolved by discussion. 37 articles were identified and excluded by reading titles, abstracts and removing duplicates. Abstracts of selected articles were reviewed independently. 15 articles were retrieved of which 7 were excluded after full text review and a further 2 were excluded during data extraction. Quality Assessment criteria to evaluate the studies were decided by two review authors in accordance with CONSORT and Cochrane Collaboration Guidelines. The risk of bias for each study was independently assessed by the review authors and conflicts concerning risk of bias were sorted by discussion.

6 Articles were chosen for analysis in this Systematic Review.

Fig. 8 – PRISMA Flowchart for Included Studies



DATA EXTRACTION

Data extraction for general characteristics of studies and variables of outcome was done:

For each trial the following data were recorded:

- Author
- Study Design
- Sample Size
- Participants and Group age
- Methodology
- Clinical Parameters Measured
- Recall period
- Statistical Analysis
- Results

Table 1: Variables of Interest

S. NO	VARIABLES OF INTEREST
1	Post-operative pain evaluated using Visual Analogue Scale

QUALITY ASSESSMENT

(Higgins and Green. Cochrane reviewer's hand book 2009)

The quality assessment of included trials was undertaken independently as a part of data extraction process. Four main quality criteria were examined.

1. Method of Randomization, recorded as
    a) YES- Dropouts were explained
    b) NO- Dropouts were not explained
    c) NONE- No Dropouts or withdrawals.

2. Allocation Concealment, recorded as
    a) YES- Dropouts were explained
    b) NO- Dropouts were not explained
    c) NONE- No Dropouts or withdrawals.

3. Outcome assessors Blinded to intervention, recorded as
    a) YES- Dropouts were explained
    b) NO- Dropouts were not explained
    c) NONE- No Dropouts or withdrawals.

4. Completeness of Follow up (was there a clear explanation for withdrawals and dropouts in each treatment group) assessed as
    a) YES- Dropouts were explained
    b) NO- Dropouts were not explained
    c) NONE- No Dropouts or withdrawals.

Other methodological criteria examined included:

a) Presence or Absence of sample size calculation.

b) Comparability of Groups at the start.

c) Clear Inclusion or Exclusion criteria.

d) Presence or Absence of estimate of measurement error.

Table 2: Description of Included Studies

AUTHOR	SAMPLE SIZE/AGE	EXPERIMENTAL GROUP	CONTROL GROUP	CLINICAL PARAMETERS EVALUATED	RECALL TIME	STATISTICAL ANALYSIS	RESULT	LIMITATION
Wayli et. Al, 2017	50 Aged 20-60	(25 participants) BTX-A 20 UI Into Masseter bilaterally	(25 participants) Traditional methods	Average pain scores using 10cm VAS	3 weeks, 2 months, 6 months, 1 year	Student unpaired t-test Wilcoxon sign rank test (P<0.05)	20 UI per side Botulinum toxin injection in the masseter muscles is an effective and safe means of intervention in cases of moderate to severe chronic myofascial and TMJ pain associated with bruxism.	No elaboration on "traditional methods" No blinding done
Guarda-Nardini et. Al, 2014	20 Aged 25-45	(10 participants) 4 Type A botulinum toxin (BTX-A) (Botox, Irivine, Allergan, Inc., CA). 30 UI – Masseter 3 x 20 UI – Anterior temporalis 100 UI – Total	(10 participants) Saline placebo injection	• Pain at rest and during chewing (VAS) • Mastication efficiency • Maximum non-assisted and assisted mouth opening • Protrusive and lateral movements • Functional limitation during usual jaw movements • Subjective efficacy of the treatment • Tolerance of the treatment	Baseline, 1 week, 1 month, 6 months	Two-sample permutation test Anderson-Darling permutation test Bonferroni-Holm method	Investigation supported the efficacy of BTX-A to reduce myofascial pain symptoms, even though differences with the placebo were not significant in some cases.	Sample size is small Unclear risk

AUTHOR	SAMPLE SIZE/AGE	EXPERIMENTAL GROUP	CONTROL GROUP	CLINICAL PARAMETERS EVALUATED	RECALL TIME	STATISTICAL ANALYSIS	RESULT	LIMITATION
Jadhao et. Al, 2017	24 Aged 20-35	(8 participants) BTX-A 20 UI Into Masseter bilaterally (8 participants) Placebo saline injection	(8 participants) No injection	• Pain at rest (VAS) • Pain at chewing (VAS) • Occlusal force analysis (Imotion occlusal force analyser)	1 week, 3 months, 6 months	Multivariate analysis of variance Post hoc Bonferroni test Students t-test ($P<0.05$)	BTX-A was effective for treatment of bruxism to reduce myofascial pain symptoms in bruxers. We also achieve that the occlusal analysis system precisely imitates the characteristics of occlusal force during treatment of bruxism. BTX-A has obvious advantages for the treatment of bruxism in terms of tumbling the occlusal force.	Small sample size
Baughman et. Al, 2014	32 Aged 18-65	(16 participants) 50 units Botox injection in masseter and temporalis muscles in the first 3 months, then second injection of normal saline at placebo in second 3 months	(16 participants) Injection of normal saline at placebo in first 3 months, then 50 units Botox injection in masseter and temporalis muscles in the second 3 months.	• Average pain score using VAS • Maximal opening at incisors • Lateral and anterior excursion • Progression to TMJ arthroscopic and arthroplasty procedures	Baseline, 3 months, 6 months	-	Primary outcome of the study is 50% reduction in pain. Secondary outcomes are 50% reduction in surgical therapy, 25% increase in maximal inter-incisal opening (MIO).	No statistical analysis present.

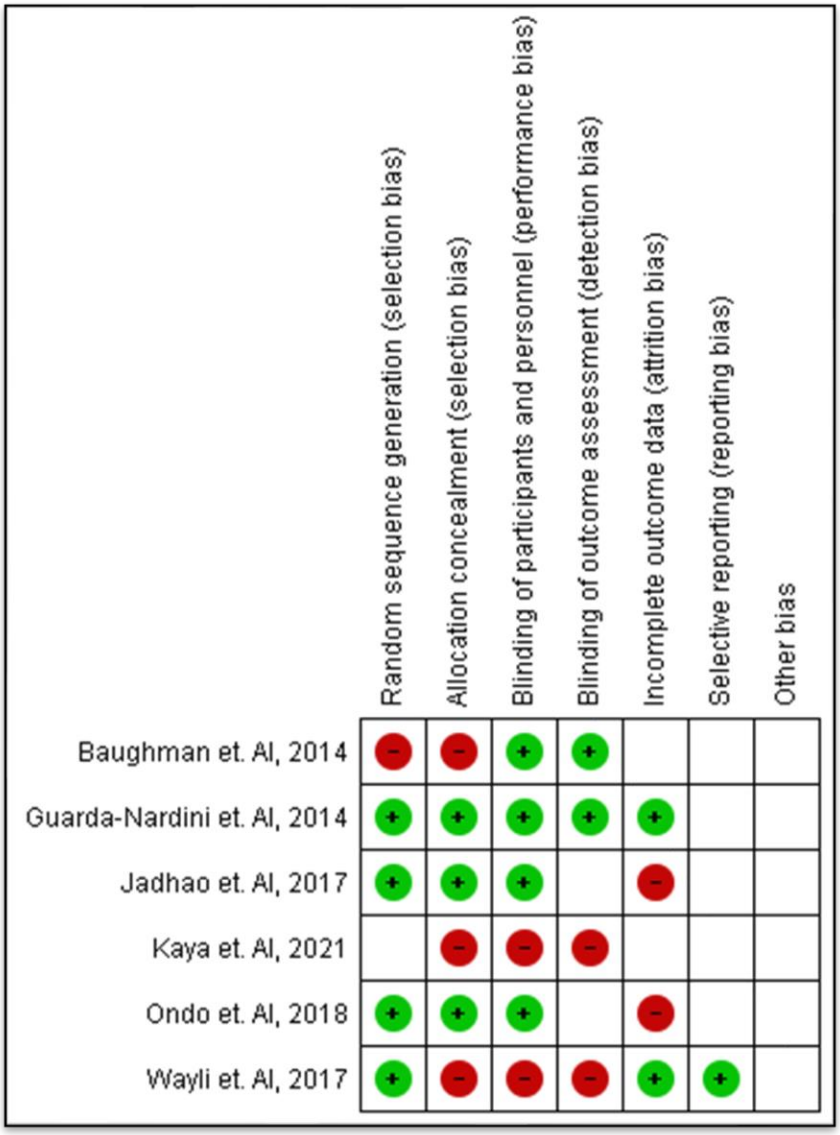
AUTHOR	SAMPLE SIZE/AGE	EXPERIMENTAL GROUP	CONTROL GROUP	CLINICAL PARAMETERS EVALUATED	RECALL TIME	STATISTICAL ANALYSIS	RESULT	LIMITATION
Kaya et. Al, 2021	40 Aged 18-45	(20 participants) BTX-A 24 UI Into Masseter unilaterally	(20 participants) Occlusal splint for atleast 8 hours a day	• Pain assessment VAS) • Maximum bite force	2 weeks, 6 weeks, 3 months, 6 months	Mann-Whitney U test Freidman test Wilcoxon test Chi-squared test ($P<0.05$)	BTX-A is a costly procedure that requires repeated dosing and is more invasive than splint applications. According to the results of this clinical study, low doses of BTX-A may be considered as an alternative treatment in patients who cannot use occlusal splints for various reasons.	Methodology vague. Difficult to monitor patients for wearing of occlusal splint for 8 hours.
Ondo et. Al, 2018	23 Aged 18-85	(13 Participants) BoNT-A 200 units (60 into each masseter and 40 into each temporalis)	(10 participants) Injection of normal saline	• Clinical global impression • Changes in pain (VAS)	Baseline, 4 weeks, 8 weeks	-	BoNT-A effectively and safely improved sleep bruxism in this placebo-controlled pilot trial. A large multi-center trial is needed to confirm these encouraging data.	No statistical analysis present. Uneven sample groups

Table 3: Evidence Level of Selected Articles

NO.	STUDY TITLE	AUTHOR	STUDY DESIGN	LEVEL OF EVIDENCE
1	Treatment of chronic pain associated with nocturnal bruxism with botulinum toxin. A prospective and randomized clinical study	Wayli et. Al, 2017	Randomised Controlled Trial	1b
2	Efficacy of Botulinum Toxin in Treating Myofascial Pain in Bruxers: A Controlled Placebo Pilot Study	Guarda-Nardini et. Al, 2014	Randomised Controlled Trial	1b
3	Efficacy of botulinum toxin in treating myofascial pain and occlusal force characteristics of masticatory muscles in bruxism	Jadhao et. Al, 2017	Randomised Controlled Trial	1b
4	Botox for Treatment of TMJ Disorder with Bruxism (TMJ)	Baughman et. Al, 2014	Randomised Controlled Trial	1b
5	Botulinum toxin treatment of temporomandibular joint pain in patients with bruxism: A prospective and randomized clinical study	Kaya et. Al, 2021	Randomised Controlled Trial	1b
6	Onabotulinum toxin-A injections for sleep bruxism: A double-blind, placebo-controlled study	Ondo et. Al, 2018	Randomised Controlled Trial	1b

RISK OF BIAS IN INCLUDED STUDIES

Risk of bias assessed using Cochrane Collaboration Tool in Revman 5.1



DISCUSSION

Botulinum toxins, purified exotoxins of Clostridium botulinum, have been used for a long period of time for Numerous neuromuscular disorders. These toxins can inhibit neuromuscular transmission, which justifies its clinical application in the treatment of bruxism, since recent scientific evidence has indicated that bruxism has a multifactorial aetiology mediated by the central nervous and autonomic systems, which regulate the motor activity of the chewing muscles. Currently, many authors support the use of BTX-A for the treatment of various conditions of the oral-maxillofacial region based on the positive results obtained in various clinical trials collected in the literature. Rao et al. made a review showing the results of several clinical trials and case reports that supported the use of BTX-A for the treatment of TMD, gingival smile correction, muscle hypertrophy and spasms, headache (migraine), trigeminal neuralgia and even after the placement of dental implants. They noted that although BTX-A could decrease muscle strength and mastication, it is temporary and normal function would return when the effect of the toxin disappeared.

GayEscoda et al. conducted a review of the literature that included clinical trials in which BTX-A was used in the salivary glands for the treatment of sialorrhea derived from different neurological disorders such as infantile cerebral palsy, the disease of Parkinson's and amyotrophic lateral sclerosis. More than half of the authors injected the product into the parotid glands, 9.5% in the submaxillary glands and 38% in both. The total doses of toxin injected varied from 10 to 100 IU of Botox® or 30 to 450 IU of Dysport® according to the different authors. A reduction in saliva production was observed after these injections, and the duration of the therapeutic effect was 1.5-6 months. Six articles (30%) described the presence of adverse effects such as dysphagia, xerostomia and difficulties to chew. The authors concluded that the injection of BTX-A in the salivary glands may be a valid treatment option in patients with sialorrhea, since it is able to improve the quality of life, however, it is important to be aware that the duration of the therapeutic effect is limited in time and usually lasts a few months. In a retrospective study carried out by Alonso-Navarro et al., the evolution of 19 patients with severe bruxism who were treated periodically with infiltrations of BTX-A in both temporal and masseter muscles, using initial doses of 25 IU per muscle, during follow-up periods of 0.5 to 11 was described; the doses were adjusted throughout the follow-up according to the degree of response observed. None of the patients presented side effects. The final dose ranges reached ranged from 25 to 40 IU per muscle and the duration of the effects ranged from 13 to 26 weeks. Based on these results, they concluded that infiltrations with BTX-A are a safe and effective treatment for patients with severe bruxism.

CONCLUSION

In conclusion, the infiltrations of BTX-A can reduce the frequency of bruxism episodes, as well as the masticatory force, and decrease the levels of pain derived from it, which translates into an improvement in the quality of life of patients. In addition, in doses <100UI it is a safe treatment with a low probability of adverse effects occurring in healthy patients. Therefore, the use of BTX-A is a safe and effective treatment for patients with bruxism that shows better clinical results than traditional methods such as occlusal splints, drugs or cognitive-behavioural therapy, so its use would be justified in daily clinical practice, especially in patients diagnosed with severe bruxism.

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