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Effect of botulinum toxin type A on Temporomandibular joint disorder and Masseter Dystrophy - A Systematic Review

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Abstract

Objectives: The purpose of this systematic review is to find out the efficacy of botulinum toxin type A in treating temporo mandibular joint disorder and Masseter dystrophy.

Materials and Procedures: To date, an electronic database search in PubMed, Google Scholar, and Embase was conducted using the keywords "Temporo mandibular Joint Disorders", "Botulinum Toxin A", "Clostridium Botulinum Toxin A", "hypertonic solutions", "Saline", "Muscular Dystrophy", and "Masseter Dystrophy". Only Human studies were included, in those who have temporo mandibular joint disorder signs and symptoms.

Results: The search strategy yielded 115 results. Following the selection of articles based on inclusion/exclusion criteria and the removal of duplicates, 7 articles are qualified for the final analysis. The studies on the effects of botulinum toxin A on Masseter dystrophy and temporo mandibular joint disorder produced widely disparate results. Some studies found that there was a significant improvement in pain management and mouth opening.

Conclusion: Botox provided a significant benefit, according to the detailed examination of studies conducted by various authors. However, the therapeutic benefits of Botox in the treatment of Masseter dystrophy and Temporo mandibular joint disorder are not statistically significant. As a result, additional research is required to demonstrate the healing benefit of Botox, as well as a large sample size, extended follow-up time, and minimal bias.

Keywords: Temporo mandibular joint Disorder, Botulinum Toxin A, Pain, Masseter dystrophy, Systematic Review.

Introduction

TMJ disorders are defined as "complex ailments involving the temporo mandibular joints themselves and associated structures"[1]. According to the National Institute of Dental and Craniofacial Research[2], the prevalence of Temporomandibular Mandibular Joint Disorders is estimated to be 5-12%. Temporomandibular Mandibular Joint Disorders impose serious health issues[3,4] such as Masseter Dystrophy, chronic orofacial pain, bruxism (tooth grinding), and conditions affecting the cervical spine and mobility, with symptoms such as clicking sounds and masticatory muscle tenderness and is not limited to temporomandibular joint disorder[5]. Thus, the management of Temporomandibular Mandibular Joint Disorders and Masseter dystrophy ranges from non-pharmacological conservative treatment to invasive surgical procedures.

There has been a shift in consensus views regarding the management of Masseter dystrophy and Temporo mandibular Mandibular Joint Disorders over the years. As a result, the use of Botulinum toxin A injections in the Masticatory muscle disorders and Temporo mandibular Mandibular Joint Disorders [6] has skyrocketed. Botox is an exotoxin produced by Clostridium botulinum[7], a gram-negative, anaerobic spore-forming bacterium with seven serotypes ranging from A to G, with serotype A (BTX-A) being the most commonly used. Botulinum toxin A's mechanism of action begins with receptor-mediated endocytosis and then cleavage of the SNAP 25 protein, which inhibits acetylcholine release and causes muscle weakness[8,9]. Botulinum toxin A has only a short duration of action, lasting 3 to 6 months. Botulinum toxin A had analgesic properties, which help to relieve masticatory muscle spasms (masseter dystrophy) and improve Temporo mandibular Mandibular Joint Disorders treatment outcomes.

With this context in mind, the purpose of this systematic review was to determine the beneficial aspects of Botulinum toxin A by answering the PICO question. Does Botulinum toxin A reduce pain in adults with Masticatory muscle disorder and Temporomandibular joint disorder?

P – Participants over the age of 19 who have temporomandibular problems.

I – BTX Intervention

C – Placebo only.

O – Outcomes, both primary and secondary.

Methodology

This study was carried out under PRISMA guidelines[10], with updated searches in three electronic databases -

PubMed, EMBASE, and Google Scholar, using the following Mesh terms: Temporo mandibular Joint, Temporo mandibular Joint Disorders, TMJ Diseases, Clostridium Botulinum A Toxin, Botulinum toxin A, Botulinum Neurotoxin A, Muscular Spasm, Masseter Dystrophy, Hypertonic Solutions, Saline, Burning Pain, Migratory Pain, Crushing Pains.

Inclusion criteria: Studies describing the full text of human studies, adults, and clinical trials related to this study published in English literature up to the date of inclusion were included.

Exclusion criteria: This study excluded studies in which patients had undergone any type of surgery for temporomandibular joint disorder or rheumatoid arthritis.

Quality Assessment

publication bias was estimated according to the PRISMA statement criteria to verify the quality of reviewed papers for clinical decision-making.

The following criteria were used to classify the risk of bias

Data tabulation in this study was done for

1. Random selection of the sample,
2. Definition of inclusion/exclusion criteria,
3. Report of losses to follow-up,
4. Valid measurements,
5. Statistical analysis.

Results

Search outcome

The selection process is shown in Fig. 1. seven studies met the inclusion criteria.

Study characteristics

Tables 1 and 2 show the relevant characteristics of the studies (published between 1999 and 2019). A total of 216 patients, of whom 191 were treated by injection of BTX-A. All the patients had been diagnosed with Masseter Dystrophy and Temporo mandibular joint disorder according to specific diagnostic criteria and had symptoms.

Treatment

Botulinum toxin A was used in seven studies.

With the help of electromyogram (EMG) investigations, studies by Ernberg M et al (2011)[11], Nixdorf DR et al (2002)[12], Kurtoglu C et al (2008)[13], and Patel AA et al (2017)[14] identified the target muscle of injection site to be masseter, lateral pterygoid muscle, masseter, and temporalis (Table 2); at doses ranging from 10U to 50U, with follow-up.

Assessment of quality of methods

PRISMA statement criteria were used to verify the strength of the reviewed papers for clinical decision-making in this systematic review (Table 3).

The studies' summary results were displayed in (Table 4).

Primary outcome: efficacy of BTX-A for pain

Prospective cohort studies were done by Altaweel et al (2019), Kurtoglu et al, Freund et al. on pain assessment with the intervention of Botulinum toxin A and other methods, where there seemed to be no statistically significant difference between the botulinum and control groups according to Kurtoglu et al & Ernberg et al, whereas, in contrast to this, pain assessment to 10-point VAS was observed according to studies by Altaweel et al[15], and Freund et al.

Secondary outcome: efficacy of BTX-A on maximal mouth opening. Studies conducted to assess the efficacy of BTX-A on maximal mouth opening showed that injection of BTX-A resulted in maximal mouth opening, improvement in mouth opening after 3 months follow up according to Altaweel et al and Freund et al (indicate the reference article numbers in the superscript at the end of this sentence). In contrast to this, Ernberg et al[6] observed

no significant improvement in mouth opening with the BTX group.

Adverse effects

Table 4 lists the studies that reported on the side effects of BTX-A.

According to the Emberg et al study, the temporary and known side effects of BTX-A are headaches, weakness, increased pain, and some influenza-like symptoms that resolve later. According to Freund et al., the main reason for the majority of dropouts was these side effects.

Discussion

Apart from the wide applications of Botulinum toxin on cervical dystonia and chronic migraine[16], its effect on Myofacial dystrophies (Masseter dystrophies) and Temporomandibular joint disorder are firmly unknown. For better understanding the advantages of botulinum toxin on Myofacial dystrophies and the TMDs, a wider search has been done using the different electronic databases to procure information. The muscle-relaxing property of BTX was first reported by Schwartz, but the improvements in muscular and autogenous pain and function after topical application on 90% of patients were reported in the study by Freund[17]. Improvement in the symptoms of TMD have been reported in various case series, multiple cohort studies, and case reports using different techniques and BTX dosages[18], wherein, a direct analgesic effect on sensory nociceptive symptoms has been observed as Botulinum toxin partially antagonizes the release of substance P, glutamate, and calcitonin gene regulated peptide[19]. Four types of Botulinum toxin were observed based on its formulation and potency- on about linumtoxin A (Botox, Allergan), in cobotulinumtoxin A (Xeomin), rimabotulinumtoxinB B (Myobloc), and abobotu linumtoxin A (Dysport) – each with its individual and interchangeable potency, hence there is a necessity for further trials comparing the various formulations[20]. A published data indicated that instead of diluting with saline, usage of local anesthesia as a vehicle would provide efficient action of BTX without alteration of its clinical action[21], minimizing the discomfort.

This review focused on a total of seven studies describing the masseter dystrophies and TMD diagnostic criteria, wherein, pain assessment using VAS and behavioural scale without verbal descriptors designed on these scales. Because of the ambiguity in patients[22], by using these scales, validity and reliability of VAS and behavioural scale were analyzed. Later Conti et al[23], reported the best guide to assess the pain is a numerical scale. Even though this method was more accurate, there is a need to be cautious in analyzing the results, as there was no gold standard, hence, a standard numerical scale has been followed in subsequent trials. Myofascial pain and disc displacement with or without reduction were the other two problems associated with the secondary outcome of maximum mouth opening highlighted in this review, though the most common complaint encountered was the mouth opening.

Current evidence from the studies of Freund et al, Altaweel et al and Ernberg et al is not sufficient to make definite conclusions about whether BTX -a injections would improve mouth opening, as these studies reported only the initial measurements. Hence, comparative studies on the outcomes of BTX-A injections and placebo in patients with a primary complaint of limited mouth opening would be useful. Also, the studies describing the site of injection into the various muscles like masseter, lateral pterygoid, temporalis with varying doses ranging from 10 U to 50 U proved the efficacy of BTX. All these studies, reporting the electromyographic evaluation to confirm the target muscle, included a very low sample of 140, which ultimately reduces the quality

of the study. A study by Freund and Schwartz[24] reported an initial reduction in maximum voluntary clenching, later reverting to normal base level, the reason being the axonal sprouting and reinnervation process for 8 weeks. Hence, only one study by Kurtoglu et al. stated that 28 days would be the adequate time given to determine the difference in measurement as effects of BTX are short-term lasting for 3 to six months and this would be the most suitable period for follow-up. Duration and optimal dosing frequency were the factors that impart patient-directed treatment. Thus, later on, all the patients were screened to identify the contraindications of BTX. The results from these screenings showed common findings like the inflammation at the site of injection, chronic degenerative neuromuscular disorders[25], short-term adverse effects like Localized pain, difficulty in chewing, and focal muscle weakness. BTX-A showed the development of asymmetric smile due to its paralyzing effect on the zygomaticus major. Also, BTX was compared economically with other conservative methods.

Conclusion

This review concludes that, although there were many beneficial aspects of BTX that have been assessed using various tools, study groups, and study designs, a definite method to treat myofascial dystrophies (Masseter dystrophy) TMD has not been developed. This review has moderate – to – low evidence and moderate – to – high bias. As a result, more Randomized Controlled Trials (RCT) with less bias, larger sample sizes, and longer follow-up periods are required. There is also a need to determine the best BTX target site and dosage, as well as to conduct feasibility and economic tests to determine whether the cost-benefit ratio is clinically acceptable. The results of this review showed that BTX can enhance outcomes in patients with masseter dystrophies and Temporomandibular joint disorder.

References

1. Toronto (ON): Diagnosis and management of temporo mandibular disorders. Royal College of Dental Surgeons of Ontario; 2018.
2. Bethesda (MD): Prevalence of TMJD and its signs and symptoms.: National Institute of Dental and Craniofacial Research; Accessed Aug 10, 2018.
3. Armijo-Olivo SL, Gadotti IC. Chapter 4: Temporomandibular disorders. In: Magee DJ, Zachazewski JE, Quillen WS, Manske RC, eds. Pathology and Intervention in musculoskeletal rehabilitation. 2nd ed. Maryland Heights (MO): Elsevier; 2016:119–156.
4. Vegard, Moen K, Storesund T, Rosén A. Prevalence of painful temporomandibular disorders and correlation to lifestyle factors among adolescents in Norway. *Pain Res Manag*. 2017:2164825.
5. S Mc Neal et al. Temporo mandibular joint syndrome. London (UK): BMJ Publishing Group; 2018.
6. Ernberg M, Hedenberg-Magnusson B, List T, et al. Efficacy of botulinum toxin type A for treatment of persistent myofascial TMD pain: a randomized, controlled, double-blind multicentre study. Pain2011; 152:1988–9.
7. Chen YW, Chiu YW, Chen CY, et al. Botulinum toxin therapy for temporo mandibular joint disorders: a systematic review of randomized controlled trials. Int J Oral Maxillofac Surg 2015; 44:1018–26.
8. Binz T, Blasi J, Yamasaki S, et al. Proteolysis of SNAP-25 by types E and A botulinal neurotoxins. J Biol Chem 1994; 269:1617–20.
9. Mor N, Tang C, Blitzer A. Temporo mandibular Myofacial pain treated with botulinum toxin injection. Toxins (Basel) 2015; 7:2791–800.

10. Page M J, McKenzie J E, Bossuyt P M, Boutron I, Hoffmann T C, Mulrow C D et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews BMJ 2021; 372 n71 doi: 10. 1136 / bmj. n71.

11. Ernberg M, Hedenberg-Magnusson B, List T, et al. Efficacy of botulinum toxin type A for treatment of persistent myofascial TMD pain: a randomized, controlled, double-blind multicentre study. Pain2011; 152:1988–96.

12. Nixdorf DR, Heo G, Major PW. Randomized controlled trial of botulinum toxin A for chronic myogenous orofacial pain. Pain 2002; 99:465–73.

13. Kurtoglu C, Gur OH, Kurkcu M, et al. Effect of botulinum toxin-A in myofascial pain patients with or without functional disc displacement. J Oral Maxillofac Surg 2008; 66:1644–51.

14. Patel AA, Lerner MZ, Blitzer A. Inco botulinumtoxin A injection for temporomandibular joint disorder. Ann Otol Rhinol Laryngol 2017; 126:328–33.

15. Guarda-Nardini L, Stecco A, Stecco C, et al. Myofascial pain of the jaw muscles: comparison of short-term effectiveness of botulinum toxin injections and fascial manipulation technique. Cranio 2012; 30:95–102.

16. Bhogal PS, Hutton A, Monaghan A. A review of the current uses of Botox for dentally-related procedures. Dent Update 2006; 33:165–8.

17. Schwartz M, Freund B. Treatment of temporo mandibular disorders with botulinum toxin. Clin J Pain 2002;18(6 Suppl): S198–203.

18. Von Lindern JJ, Niederhagen B, Bergé S, et al. Type A botulinum toxin in the treatment of chronic facial pain associated with masticatory hyperactivity. J Oral Maxillofac Surg 2003; 61:774–8.

19. Aoki KR. Review of a proposed mechanism for the antinociceptive action of botulinum toxin type A. Neurotoxicology 2005; 26:785–93.

20. Chen JJ, Dashtipour K. Abo-, inco-, ona-, and rima-botulinum toxins in clinical therapy: a primer. Pharmacotherapy 2013; 33:304-18.

21. Gassner HG, Sherris DA. Addition of an anesthetic agent to enhance the predictability of the effects of botulinum toxin type A injections: a randomized controlled study. Mayo Clin Proc 2000; 75:701–4.

22. Boonstra AM, Schiphorst Preuper HR, Balk GA, et al. Cut-off points for mild, moderate, and severe pain on the visual analogue scale for pain in patients with chronic musculoskeletal pain. Pain 2014; 155:2545–50.

23. Conti PC, de Azevedo LR, de Souza NV, et al. Pain measurement in TMD patients: evaluation of precision and sensitivity of different scales. J Oral Rehabil 2001; 28:534–9.

24. Freund B, Schwartz M. The use of botulinum toxin for the treatment of the temporo mandibular disorder. Oral Health1998; 88:32–7.

25. Mor N, Tang C, Blitzer A. Temporo mandibular Myofacial pain treated with botulinum toxin injection. Toxins (Basel) 2015; 7:2791–800.

Table 1: Prisma flow chart

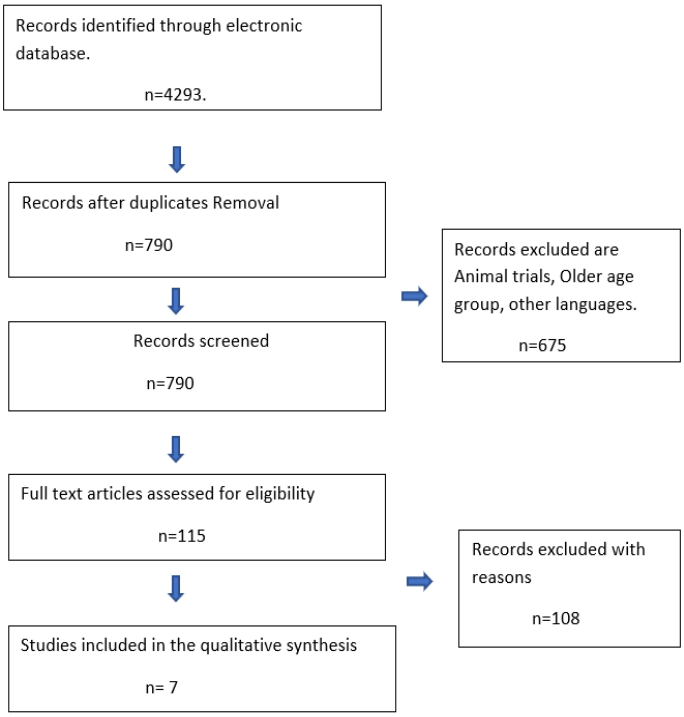

Table 2: Characteristics of the studies related to the participants.

Author, year	Study design	Diagnostic criteria for TMD	Age	Sample size
Altaweel,2019	Prospective cohort study.	ADDWR.	20-35 yrs.	14
Ernberg,2010	They randomized, placebo-controlled, crossover multicentre study.	Myofascial temporomandibular disorder.	>18yrs	21
Kurtoglu,2008	Prospective, Randomized, double-blinded, placebo-controlled study.	Myofascial pain with or without functional disc displacement.	23yrs	24
Freund,2003	Prospective open-label study.	Multi-centered temporomandibular joint disorder.	17 -64 yrs.	35
Freund,1999	Prospective.	Myofascial symptoms with internal joint derangement and arthralgia. U/B.	16-75yrs	50
Alexis Kahn,2018	Retrospective study	Temporomandibular joint disorder and Myalgia	37 yrs	34
Malgorzata Pihut,2018	Prospective outcome study	Masseter muscle pain related to temporomandibular joint dysfunction.	19 – 48 yrs.	42

Table 3: Characteristics of the studies related to the interventions

Author, Year,	Intervention	BTX brand	Methods to identify target muscle	Target muscles injected	Dosage	Duration follow up
Altaweel,2019	Botulinum toxin type A	BTX-A	EMG	LPM	20IU	8 & 16 weeks
Ernberg2011	Botulinum toxin -A	BTX- A	EMG and VAS	Masseter muscle	50IU	1 &3 months
Kurtoglu,2008	Botulinum toxin -A	BTX-A	EMG and Behavioral questionnaire.	Masseter and Anterior Temporal muscle	10IU	14&28 days
Freund,2002	Botulinum toxin -A	BTX- A BOTOX	EMG and VAS	Masseter and Temporalis	50 IU	24hrs
Freund,2000	Botulinum toxin -A	BTX-A	VAS	Masseter and Temporalis	50 IU	2weeks interval for 8weeks.
Alexis Kahn,2018	Botulinum toxin - A	BTX- A	EMG	Masseter and Temporalis	50 U	3 &6 months.
Malgorzata Pihut,2018	Botulinum toxin - A	BOTOX	VAS and VNRS	Masseter bellies	21U	1 &24 Weeks.

Table 4: Assessment of the quality of the study.

Author Year	Study design	Random sample selection	Inclusion and exclusion criteria	Follow-up reported	Valid measurements	Statistical analysis	Risk of bias
Altaweel,2019	Prospective cohort study.	NO	yes	yes	yes	Yes	Low
Ernberg,2010	They randomized, placebo-controlled, crossover multicentre study.	yes	yes	yes	yes	No	Moderate
Kurtoglu,2008	Prospective, Randomized, double-blinded, placebo-controlled study.	yes	yes	yes	yes	yes	Low
Freund,2003	Prospective open-label study.	NO	yes	yes	yes	yes	Moderate
Freund,1999	Prospective.	NO	yes	yes	yes	yes	Moderate
Alexis Kahn,2018	Retrospective study	NO	yes	yes	No	yes	high
Malgorzata Pihut,2018	Prospective outcome study	NO	yes	yes	yes	yes	Moderate

Table 5: Summary outcomes of the studies at an initial follow-up appointment

First author, year, and reference	Intervention	No. of participants	Initial follow up	The primary outcome assessment tool	The secondary outcome assessment tool	Adverse effects
Altaweel,2019	Group I Botox - extraoral Group II Botox – Intraoral	Group I 10 joints Group II 10 joints	1st week	10 points pain VAS.	N/A	None
Ernberg,2010	Group I Botox – A Group II Saline	12 9	1st week	100 points pain VAS.	5-point Likert scale	Low grade of functional impairment, Transient muscle weakness, nausea, change in facial expression, difficulties in chewing and swallowing
Kurtoglu,2008	Group I Botulinum toxin -A Group II Placebo	12 12	2nd week	RDC/TMD Biobehavioural questionnaires.	Muscle clenching.	None
Freund,2003	Botox with 2 ml of unpreserved saline per 100 units.	35	2nd week	10 points pain VAS.	Bite force	3 subjects reported moderate bitemporal headaches. 1 subject reported slight bruising of the right temple area.
Freund,1999	Botox with saline 10unit/0.1ml or 5unit/0.1ml solution.	46	2nd week	10 points pain VAS.	Vertical opening and bite force.	None
Alexis Kahn,2018	Botox at a dilution of 10U /ml	34	3 months	Intra oral examination.	Intra oral examination	none
Malgorzata Pihut,2018		42	1st week	10 points pain VAS	N/A	none