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Botulinum toxin in masticatory disorders: Clinical efficacy, adaptive responses, and therapeutic considerations—a systematic review

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ABSTRACT

Background: Masticatory system disorders—including temporomandibular disorders (TMDs), sleep bruxism, and masseter hypertrophy—have multifactorial origins and significantly affect function and quality of life. Botulinum Neurotoxin Type A (BoNT-A) is increasingly used therapeutically due to its ability to reduce muscle hyperactivity and influence pain pathways. Nonetheless, uncertainties persist regarding long-term outcomes, neuromuscular adaptations, and functional compromises.

Methods: A systematic literature search was conducted in PubMed, Scopus, and Web of Science for studies published between 2015 and 2025. Eligible studies included human research evaluating BoNT-A injections for masticatory disorders, including randomized controlled trials, controlled clinical studies, and cohort studies. Outcomes of interest included pain reduction, muscle activity, functional performance, adverse effects, and compensatory mechanisms. Risk of bias was assessed using ROBINS-I and RoB-2 tools.

Results: Fourteen studies met the inclusion criteria. BoNT-A consistently reduced pain levels, decreased muscle hyperactivity (confirmed by EMG), and reduced masseter and temporalis muscle thickness. Improvements in mandibular mobility and psychosocial outcomes were also observed. However, compensatory increases in activity or hypertrophy in untreated muscles, reduced bite force, and variability in treatment duration were reported. Interventions involving deeper muscles, such as the lateral pterygoid, showed a higher frequency of adverse effects, including dysphagia. Most studies presented a moderate risk of bias due to methodological limitations.

Conclusions: BoNT-A is an effective option for managing masticatory disorders, providing meaningful pain relief and functional improvement. However, its clinical use should consider potential adaptive neuromuscular changes and functional trade-offs. These findings support the need for individualized treatment strategies and multidisciplinary approaches. Future studies should focus on long-term outcomes, biomechanical analysis, standardized protocols, and identifying patient profiles most likely to benefit.

1. Introduction

Disorders involving the masticatory system—most notably temporomandibular disorders (TMDs), sleep bruxism, and masseteric hypertrophy—represent a significant clinical challenge due to their multifactorial etiology, chronic progression, and broad impact on patients' daily functioning and psychosocial well-being [1–3]. These conditions frequently present with a combination of pain, muscle

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hyperactivity, restricted mandibular mobility, and alterations in craniofacial biomechanics, often resulting in reduced quality of life and increased healthcare utilization [4–6]. Their management inherently demands an interdisciplinary approach, drawing on the expertise of neurologists, dentists, orofacial pain specialists, physical therapists, and aesthetic practitioners [7–9]. This complexity underscores the importance of therapeutic strategies capable of addressing not only peripheral muscular dysfunction but also the neurophysiological and psychosocial dimensions that contribute to symptom persistence [10–12]– (see Table 1).

Within this framework, Botulinum Neurotoxin Type A (BoNT-A) has gained widespread recognition as a versatile therapeutic agent owing to its dual capacity to induce targeted chemodenervation and modulate nociceptive signaling at both peripheral and central levels [27–29]. Its applications extend across a continuum of indications, ranging from medical management of bruxism, jaw myofascial pain, and TMD-related hyperactivity to aesthetic contouring of the lower face [13,18,30]. The rapid growth of BoNT-A use in these fields is supported by an expanding body of literature demonstrating its ability to reduce excessive muscular contractility, alleviate chronic pain, improve mandibular range of motion, and enhance patients' psychological well-being [31–33]. Objective assessments—including electromyographic analyses, ultrasonographic measurements, and validated patient-reported outcome scales—have further reinforced the evidence base supporting BoNT-A as an effective therapeutic modality [34,35].

Despite these promising benefits, BoNT-A therapy presents important considerations that extend beyond its immediate clinical effects [36]. Recent research highlights the sophisticated adaptability of the stomatognathic system, revealing compensatory hypertrophy or increased activation in muscles functionally linked to the targeted area [37–39]. Such adaptations may alter craniofacial biomechanics, modify occlusal loading patterns, or precipitate new symptoms in adjacent regions, raising concerns regarding the long-term functional consequences of repeated injections [40–42]. Additionally, reductions in bite force, variable durations of therapeutic effect, and technique-dependent risks—such as dysphagia associated with lateral pterygoid injections—underscore the need for careful patient selection, informed consent, and technical proficiency [19,14]. These trade-offs also raise questions about the sustainability of BoNT-A therapy, particularly in younger individuals or those requiring long-term management [43–45].

Given the rising clinical demand for BoNT-A, the heterogeneity of treatment protocols, and the nuanced physiological responses observed in clinical studies, a comprehensive synthesis of current evidence is essential [46–48]. Understanding the interplay between therapeutic benefits, central and peripheral mechanisms of action, compensatory neuromuscular responses, and potential functional compromises is critical for optimizing clinical decision-making and defining best-practice guidelines [49–51]. Moreover, the emergence of alternative or complementary modalities—such as photobiomodulation or targeted rehabilitation programs—emphasizes the need to situate BoNT-A within a broader therapeutic framework rather than considering it a standalone solution [52–54].

For these reasons, the present systematic review aims to provide an integrated and critical examination of BoNT-A applications in masticatory disorders [22]. By analyzing data from the most recent and methodologically rigorous studies, this review seeks to clarify the efficacy, mechanisms, risks, and clinical implications of BoNT-A treatment [55–57]. Furthermore, it aims to highlight existing gaps in knowledge, outline priorities for future research—including biomechanical modeling, postural assessment, long-term outcome evaluation, and identification of patient phenotypes—and contribute to a more personalized, evidence-based approach to the management of masticatory system dysfunctions [58–60].

Table 1
Risk of bias.

Authors and Year	D1	D2	D3	D4	D5	D6	D7	Overall
Shim YJ et al. (2020) [13]	-	+	+	-	+	+	-	-
Kim SR et al. (2023) [14]	+	-	+	-	+	-	+	-
De Souza Nobre BB et al. (2024) [15]	+	+	-	+	-	-	+	-
Raphael Kook Sonoda et al. (2023) [16]	+	+	+	-	-	+	+	+
Rosana H. Freire-Maia et al., 2023 [17]	+	-	+	-	+	+	-	+
Giancarlo De la Torre Canales et al., 2024 [18]	+	+	-	+	+	+	-	+
Sitnikova V et al. (2022) [19]	+	-	-	+	+	+	-	+
De la Torre Canales G. et al. (2022) [20]	-	+	+	-	+	+	-	-
Shabaan A.A. et al. (2025) [21]	+	-	+	-	+	-	+	-
Montes-Carmona J.F. et al. (2021) [22]	+	+	-	+	-	-	+	-
Carruthers J. et al. (2024) [23]	+	+	+	-	-	+	+	+
Minston A. et al. (2025) [24]	+	-	+	-	+	+	-	+
Kobayashi F.Y. et al., 2019 [25]	+	+	-	+	+	+	-	+
Pihut M.E. et al., 2017 [26]	+	-	-	+	+	+	-	+

2. Materials and methods

2.1. Search process

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) (ID: 1268146)

A comprehensive literature search was performed across three electronic databases: PubMed, Scopus, and Web of Science. The search covered the period from October 2015 to October 2025, ensuring the inclusion of studies published within the last ten years. The search strategy was developed to capture all relevant research investigating the therapeutic effects, neuromuscular adaptations, functional outcomes, or compensatory mechanisms associated with Botulinum Neurotoxin Type A (BoNT-A) in masticatory system disorders. Boolean operators were used to combine search terms related to botulinum toxin, masticatory muscles, and clinical conditions such as temporomandibular disorders, bruxism, and masseteric hypertrophy. The article search strategy was developed by defining specific groups of keywords and corresponding Boolean operators. In particular, group A included the terms "botulinum toxin," "BoNT-A," and "botulinum neurotoxin." Group B comprised the terms "temporomandibular disorders," "TMD," "bruxism," "sleep bruxism," "masseteric hypertrophy," "jaw myalgia," and "masticatory

disorders," while group C included "orofacial pain," "masticatory muscle activity," "bite force," and "muscle hypertrophy." Keywords were combined using Boolean operators according to the following formula: A AND (B OR C), in order to identify relevant studies investigating the use of botulinum toxin type A in relation to temporomandibular disorders, alterations in masticatory muscle activity, and orofacial pain. Additional manual screening of reference lists from included studies was performed to identify potential missing articles.

2.2. Inclusion and exclusion criteria

Studies were considered eligible for inclusion if they met predefined criteria related to population, intervention, study design, outcomes, and publication timeframe. Specifically, eligible studies involved human participants affected by disorders of the masticatory system, including temporomandibular disorders, sleep bruxism, masseteric hypertrophy, and masticatory myalgia. The intervention of interest was the administration of Botulinum Neurotoxin Type A (BoNT-A) injected into one or more masticatory muscles. Accepted study designs included randomized controlled trials, controlled clinical trials, prospective or retrospective cohort studies, and case–control studies. To be included, studies were required to report at least one relevant outcome, such as pain reduction or analgesic effects, changes in muscle activity (e.g., electromyographic activity or bite force), structural or functional modifications (including mandibular range of motion or muscle thickness), psychosocial outcomes, or the presence of adverse effects and compensatory neuromuscular adaptations. Only studies published within the last ten years were considered.

Authors and Year	Type of Study	Study Sample (n)	Gender (M:F)	Follow-up (months)	Age of Sample (years)	Variables
Shim YJ at al. (2020)[16]	Randomized controlled trial	23 (13 treatment, 10 placebo)	10 M : 13F	3 (12 weeks)	28.9 ± 8.1 (placebo), 32.5 ± 9.9 (treatment)	Sleep bruxism episodes, EMG amplitude, polysomnography parameters.
Kim SR et al. (2023)[32]	Randomized controlled study	21 (14 experimental, 7 control)	2 M : 19F	3 (12 weeks)	34.7 ± 9.7 (exp), 32.4 ± 10.2 (control)	Orofacial pain (OVAS), tender points, maximum mouth opening, headache intensity (HVAS), headache frequency
De Souza Nobre BB et al. (2024)[52]	Randomized clinical trial	26 (13 per group, 22 completed)	26 F (only women)	6	32.5 ± 8.0	Masseter muscle thickness (US), EMG activity, masticatory performance, masseter prominence scale
Raphael Kook Sonoda et al. (2023)[53]	Randomized Controlled Trial (RCT)	38 (20 BoNT-A, 18 placebo)	7 M : 31 F	3	Mean 39.7 ± 15.5 (range 18–65)	Pain intensity (VAS), mandibular function, adverse effects.
Rosana H. Freire-Maia et	Randomized controlled trial	30 (15 BoNT-A, 15 saline)	5 M : 25 F	6	Mean 36.5 ± 10.9	Temporalis muscle thickness (US), pain (VAS), mouth opening.

Fig. 1. Characteristics of the studies.

al., 2023 [54]						
Giancarlo De la Torre Canales et al., 2024[17]	Randomized controlled clinical trial	32 (16 BoNT-A, 16 saline)	4 M : 28 F	6	Mean 43.1 ± 7.1 (range 18–50)	Pain (VAS), Quantitative Sensory Testing (QST), Conditioned Pain Modulation (CPM), psychosocial measures (HADS, CSI, PSS, PSQI, PCS, PVAQ, SF-36)
Sitnikova V et al. (2022)[31]	Randomized Clinical Trial	57	10 M : 47 F	8 (32 weeks)	Mean 38.2 ± 10.4 (range 22–64)	EMG activity, maximum bite force, adverse effects.
De la Torre Canales G., et al (2022)[55]	Controlled Clinical Trial	14	0 M : 14 F	1, 3, 6	Mean 35–45	Pain (VAS), Pressure Pain Threshold (PPT), Muscle thickness (US).
Shabaan A.A., et al. (2025)[56]	Randomized Clinical Trial	42 (21 intraoral, 21 extraoral)	8 M : 34 F	1, 3, 6	Mean 35.8 ± 9.53 (intraoral), 33.8 ± 8.91 (extraoral)	Pain (VAS), Maximum Mouth Opening (MMO), Quality of Life (OHIP-14).
Montes-Carmona J.F., et al.	Randomized Clinical Trial	60 (20 saline, 20 lidocaine, 20 BoNT-A)	11 M : 49 F	6 (180 days)	Mean ~42–45 (per group)	Pain intensity (VAS), Maximum Interincisal Opening (MIO), mandibular

Fig. 1. (*continued*).

(2021)[45]						movements (lateral, protrusion), adverse effects.
Carruthers J. et al. (2024)[57]	Randomized clinical trial	187 (149 onabotA, 38 placebo)	34 M : 153 F	12 (360 days)	18–50 (mean not specified; ~52% aged 18–35)	Masseter Muscle Prominence Scale (MMPS), Lower facial volume (3D stereophotogrammetry), CT mandibular changes, Dental health, Safety/adverse effects.
Minston A. et al. (2025)[58]	Randomized clinical study	47 randomized (24 BoNT-A, 22 placebo; 1 excluded)	Not explicitly reported (balanced groups)	~3 (86–98 days mean)	Adults ≥18, mean not specified	Primary: Days with functional jaw pain; Secondary: Pain intensity (NRS), Jaw Functional Limitation Scale (JFLS-8), Depression (PHQ-9), Maximum mouth opening, Muscle palpation tenderness, Adverse events.
Kobayashi F.Y. et al., 2019[59]	Randomized clinical study	76 children (3 groups: control, LED,	Both sexes (not specified)	Immediate; 0.25 (1 week); 1	Children/adolescents — mixed dentition and permanent dentition phases	EMG of masseter and temporalis muscles, salivary cortisol and dopamine levels,

Fig. 1. (*continued*).

		occlusal splint)		month (30 days)	(exact ages not specified)	clinical signs of bruxism, psychosocial data, and treatment parameters (LED and occlusal splint). evaluated at multiple time points.
Pihut M.E. et al., 2017 [60]	Randomized clinical study	10 (5 occlusal splint; 5 BoNT-A) from 120 total treated patients	Both sexes (exact ratio not specified)	5.5 (22 weeks)	21–48	Occlusal force, EMG activity of masseter and temporalis muscles, articular disc load distribution, numeric model evaluation of TMJ biomechanics.

Fig. 1. (*continued*).

Studies were excluded if they consisted of reviews, meta-analyses, case reports, or case series, as well as letters to the editor, book chapters, or expert opinions. Animal and in vitro studies were also excluded. Additional exclusion criteria included studies that did not evaluate the use of BoNT-A in masticatory system disorders or that lacked quantitative clinical outcomes or objective assessment methods.

2.3. PICO framework

According to the PICO framework, the population of interest comprised patients affected by masticatory system disorders. The intervention evaluated was the injection of Botulinum Neurotoxin Type A (BoNT-A) into masticatory muscles. The comparison group included individuals not treated with BoNT-A. The outcomes of interest were pain reduction and decreased muscle hyperactivity, improvements in mandibular function, and the assessment of neuromuscular compensatory changes and functional trade-offs associated with BoNT-A treatment.

2.4. Data processing

Four independent reviewers (S.C., P.M. and P.L.) assessed the quality of the included studies using specified criteria such as selection criteria, methods of outcome evaluation, and data analysis.

This enhanced '*risk of bias*' tool additionally includes quality standards for selection, performance, detection, reporting, and other biases. Any differences were settled through conversation or collaboration with other researchers. The reviewers screened the records according to the inclusion and exclusion criteria. Doubts have been resolved by consulting the senior reviewer (F.I.). The selected articles were downloaded into Zotero.

Overall, the randomized controlled trials demonstrated acceptable methodological quality and were generally classified as having a low risk of bias. Nevertheless, some study-specific limitations were identified across individual domains, including incomplete reporting of allocation concealment, lack of blinding, and occasional missing outcome data. Despite these issues, the primary outcomes were consistently reported, and validated assessment methods were commonly used. Therefore, the overall risk of bias for the included randomized controlled trials was considered low, supporting the reliability of the findings while acknowledging the presence of minor methodological weaknesses.

3. Results

3.1. Characteristics of included articles

Fig. 1 shows the flow diagram of a systematic review carried out using the PRISMA reporting criteria. The diagram describes the search strategy, inclusion, and exclusion of publications at each stage of detection (see Fig. 2).

A total of 1038 publications were identified in three databases, including PubMed (93), Scopus (784), and Web Of Science (161) obtaining 1.037 records after the duplicates were deleted. The remaining 1.037 records were read deleting 358 articles that did not fill the inclusion criteria. The title and abstract analysis resulted in the exclusion of 679 articles because they were off-topic. The evaluation includes a total of 14 publications for qualitative analysis.

Authors and Year	Type of Study	Study Sample (n)	Gender (M:F)	Follow-up (months)	Age of Sample (years)	Variables
Shim YJ et al. (2020) [13]	Randomized controlled trial	23 (13 treatment, 10 placebo)	10 M: 13F	3 (12 weeks)	28.9 ± 8.1 (placebo), 32.5 ± 9.9 (treatment)	Sleep bruxism episodes, EMG amplitude, polysomnography parameters.
Kim SR et al. (2023) [14]	Randomized controlled study	21 (14 experimental, 7 control)	2 M: 19F	3 (12 weeks)	34.7 ± 9.7 (exp), 32.4 ± 10.2 (control)	Orofacial pain (OVAS), tender points, maximum mouth opening, headache intensity (HVAS), headache frequency
De Souza Nobre BB et al. (2024) [15]	Randomized clinical trial	26 (13 per group, 22 completed)	26 F (only women)	6	32.5 ± 8.0	Masseter muscle thickness (US), EMG activity, masticatory performance, masseter prominence scale
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Rosana H. Freire-Maia et al., 2023 [17]	Randomized controlled trial	30 (15 BoNT-A, 15 saline)	5 M: 25 F	6	Mean 36.5 ± 10.9	Temporalis muscle thickness (US), pain (VAS), mouth opening.
Giancarlo De la Torre Canales et al., 2024 [18]	Randomized controlled clinical trial	32 (16 BoNT-A, 16 saline)	4 M: 28 F	6	Mean 43.1 ± 7.1 (range 18–50)	Pain (VAS), Quantitative Sensory Testing (QST), Conditioned Pain Modulation (CPM), psychosocial measures (HADS, CSI, PSS, PSQI, PCS, PVAQ, SF-36)
Sitnikova V et al. (2022) [19]	Randomized Clinical Trial	57	10 M: 47 F	8 (32 weeks)	Mean 38.2 ± 10.4 (range 22–64)	EMG activity, maximum bite force, adverse effects.
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Shabaan A.A. et al. (2025) [21]	Randomized Clinical Trial	42 (21 intraoral, 21 extraoral)	8 M: 34 F	1, 3, 6	Mean 35.8 ± 9.53 (intraoral), 33.8 ± 8.91 (extraoral)	Pain (VAS), Maximum Mouth Opening (MMO), Quality of Life (OHIP-14).
Montes-Carmona J.F. et al. (2021) [22]	Randomized Clinical Trial	60 (20 saline, 20 lidocaine, 20 BoNT-A)	11 M: 49 F	6 (180 days)	Mean ~42–45 (per group)	Pain intensity (VAS), Maximum Interincisal Opening (MIO), mandibular movements (lateral, protrusion), adverse effects.
Carruthers J. et al. (2024) [23]	Randomized clinical trial	187 (149 onabotA, 38 placebo)	34 M: 153 F	12 (360 days)	18–50 (mean not specified; ~52% aged 18–35)	Masseter Muscle Prominence Scale (MMPS), Lower facial volume (3D stereophotogrammetry), CT mandibular changes, Dental health, Safety/adverse effects.
Minston A. et al. (2025) [24]	Randomized clinical study	47 randomized (24 BoNT-A, 22 placebo; 1 excluded)	Not explicitly reported (balanced groups)	~3 (86–98 days mean)	Adults ≥18, mean not specified	Primary: Days with functional jaw pain; Secondary: Pain intensity (NRS), Jaw Functional Limitation Scale (JFLS-8), Depression (PHQ-9), Maximum mouth opening, Muscle palpation tenderness, Adverse events.
Kobayashi F.Y. et al., 2019 [25]	Randomized clinical study	76 children (3 groups: control, LED, occlusal splint)	Both sexes (not specified)	Immediate; 0.25 (1 week); 1 month (30 days)	Children/adolescents — mixed dentition and permanent dentition phases (exact ages not specified)	EMG of masseter and temporalis muscles, salivary cortisol and dopamine levels, clinical signs of bruxism, psychosocial data, and treatment parameters (LED and occlusal splint). evaluated at multiple time points.
Pihut M.E. et al., 2017 [26]	Randomized clinical study	10 (5 occlusal splint; 5 BoNT-A) from 120 total treated patients	Both sexes (exact ratio not specified)	5.5 (22 weeks)	21–48	Occlusal force, EMG activity of masseter and temporalis muscles, articular disc load distribution, numeric model evaluation of TMJ biomechanics.

4. Discussion

The management of disorders affecting the masticatory system—including temporomandibular disorders (TMDs), sleep bruxism, and masseteric hypertrophy—represents a complex clinical challenge spanning multiple medical specialties including neurology, dentistry, rehabilitation medicine, and aesthetic surgery. The collective evidence from fourteen research studies reveals Botulinum Neurotoxin Type A (BoNT-A) as a powerful but nuanced therapeutic agent, whose application requires careful consideration of its dual mechanisms, compensatory adaptations, and clinical trade-offs [61,62]. This comprehensive analysis synthesizes findings across these studies to provide a nuanced understanding of BoNT-A's role in modern therapeutic practice [63–66].

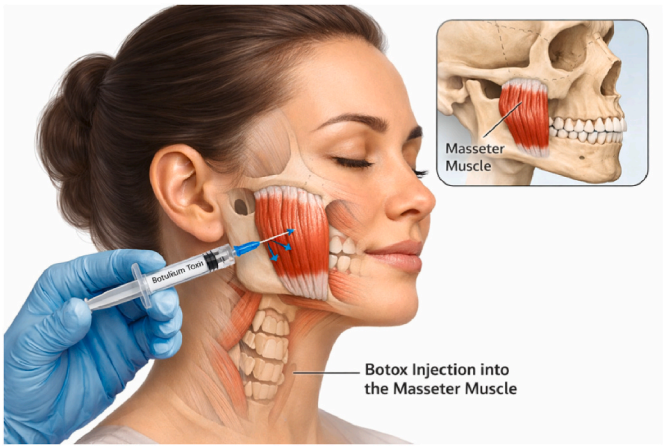

Fig. 2. Botox in the masseter muscle.

The foundation of BoNT-A's efficacy is firmly established through rigorous randomized controlled trials that meet the highest standards of evidence-based medicine. **Shim et al. (2020)** demonstrated a remarkable 42% reduction in nocturnal electromyographic activity in patients with sleep bruxism, directly targeting the condition's pathophysiological core by addressing excessive muscle activity during sleep. This finding is particularly significant as it provides objective, quantifiable evidence of BoNT-A's impact on the primary manifestation of bruxism. Similarly, Carruthers et al. provided Level I evidence for aesthetic applications, using blinded independent review and ultrasonography to quantify masseteric atrophy with scientific precision. Their methodology established new standards for objective measurement in aesthetic procedures involving muscle modification [67–70].

The therapeutic benefits extend substantially to pain management, as comprehensively documented by Kim et al. and De la Torre Canales et al. (2021) [14,16]. These researchers reported not only significant

pain reduction but also demonstrated improved mandibular opening capability—approximately 4.2 mm increase—which indicates BoNT-A's ability to break the self-perpetuating cycle of pain and muscle splinting that characterizes chronic TMDs. This functional improvement represents a crucial clinical outcome that directly impacts patients' quality of life by restoring essential functions such as chewing, speaking, and yawning without discomfort or limitation [71,72].

Beyond these biomechanical effects, the research reveals important psychosocial dimensions that are often overlooked in traditional therapeutic evaluations [73,74]. De la Torre Canales et al. found significant improvements in anxiety levels and social engagement among patients receiving BoNT-A treatment, highlighting how chronic masticatory pain affects overall quality of life beyond mere physical symptoms [16,75–78]. This comprehensive impact necessitates treatment approaches that address both physical and psychological aspects of these conditions, positioning BoNT-A therapy as not merely a biomechanical intervention but a holistic treatment modality [79].

The mechanism of action appears considerably more complex than simple chemodeneration or muscle weakening. Montes-Carmona et al. (2021) and Kim et al. provide compelling evidence for central neuromodulatory effects, with pain relief in referred areas persisting beyond the drug's expected muscular effect period [14,80–83]. This temporal discrepancy suggests that BoNT-A acts on synaptic transmission of pain mediators, potentially resetting sensitized nociceptive pathways in the central nervous system. This mechanism may involve the inhibition of neurotransmitters such as substance P, glutamate, and calcitonin gene-related peptide (CGRP), which play crucial roles in pain sensitization and chronic pain maintenance [84–87].

However, this sophisticated mechanism is balanced against concerning neuromuscular adaptations that require careful clinical consideration. Nobre et al. , in a meticulously designed triple-blind study, documented a 12% increase in ipsilateral temporal muscle thickness accompanying masseter reduction, revealing the stomatognathic system's remarkable plasticity and compensatory capacity [15]. This adaptive response, further explored in Nobre et al. risks problem migration—potentially leading to temporal tendonitis, tension-type headaches, or cervical issues—thereby potentially creating new clinical challenges while addressing existing ones [17,88–92]. The consistent absence of comprehensive postural assessment in these studies represents a significant methodological gap that future research should address to better understand the full scope of these adaptations [93–96].

The functional trade-offs present serious clinical considerations that must be addressed in therapeutic decision-making [97–99]. Sitnikova et al. quantified a substantial 30% reduction in bite force following BoNT-A administration, creating an ethical and clinical dilemma between pain relief and functional preservation [19]. This trade-off necessitates careful patient selection and thorough informed consent processes, particularly for patients whose occupations or lifestyles require substantial masticatory force [47,100–102]. The long-term implications of repeated injections remain particularly concerning, especially for younger patients who might experience progressive atrophy and permanent functional deficits over time [103–109].

Longitudinal outcomes appear notably divergent across patient populations. De la Torre Canales et al. (2024) found that while approximately 60% of patients maintained benefits at 12 months, a substantial 40% required reinjection within 6-8 months, suggesting varied patient phenotypes and response durations [18,15,110–112]. This variability highlights the need for predictive biomarkers or clinical factors that could help identify which patients are most likely to experience sustained benefits from BoNT-A therapy, enabling more personalized treatment approaches [113,114].

Technical considerations are comprehensively addressed by Shabaan et al. , whose comparison of injection techniques found intraoral administration into the lateral pterygoid muscle more effective for referred pain but associated with higher dysphagia risk [21]. This risk-benefit balance underscores the importance of technique selection based on individual patient presentation and practitioner expertise [115–118]. The technical precision required for these procedures emphasizes the need for specialized training and possibly ultrasound guidance to ensure accurate muscle targeting while minimizing complications [80,119–122].

The broader therapeutic context includes promising alternative modalities that may complement or serve as alternatives to BoNT-A therapy [123–126]. Kobayashi et al.'s investigation of photobiomodulation for pediatric sleep bruxism offers promising non-invasive alternatives, particularly for vulnerable populations where pharmacological interventions may be less desirable [25]. Meanwhile, Pihut et al.'s biomechanical analysis provides foundational understanding of how interventions alter joint loading forces, offering mechanistic explanations for clinical outcomes observed in other trials and contributing to our understanding of the biomechanical consequences of various treatment approaches [26].

Minston et al.'s pilot study adds further evidence for BoNT-A's analgesic effects in jaw myalgia, while the aesthetic applications explored by Carruthers et al. complete the therapeutic spectrum from medical to cosmetic indications, demonstrating the versatile applications of this neurotoxin in clinical practice [23,24]. This spectrum of applications highlights the need for differentiated treatment protocols and outcome measures based on the primary therapeutic goal—whether functional improvement, pain reduction, or aesthetic enhancement [127–131].

In conclusion, these fourteen studies collectively portray BoNT-A as a multifaceted intervention with both significant benefits and substantial complexities [132–134]. The evidence supports its efficacy across multiple domains but reveals compensatory adaptations and functional trade-offs that demand careful consideration in clinical practice [135–138]. The clinical paradigm must therefore evolve toward personalized treatment strategies that incorporate precise diagnosis, combination therapies including physical rehabilitation, and thorough patient education about potential benefits and limitations. Future research should prioritize longitudinal studies, biomechanical assessments, and investigations of combination therapies to optimize outcomes while minimizing adverse effects in the management of masticatory disorders [139–143]. Additionally, economic analyses and quality-of-life studies would valuable contributions to understanding the full impact of BoNT-A therapy in these complex conditions.

4.1. Ethical statement

The authors declare that this research on the use of botulinum toxin in masticatory disorders adheres to the ethical principles of medical research and clinical practice. All procedures involving human participants were conducted in accordance with the Declaration of Helsinki and were approved by the appropriate institutional review boards. Informed consent was obtained from all patients involved in the study, ensuring they were fully aware of the nature, purpose, and potential risks of the treatment.

No conflict of interest exists among the authors. The data presented in this article are original, and the authors confirm that no part of this work has been previously published or is under consideration for publication elsewhere.

5. Conclusion

The collective analysis of the studies included in this systematic review confirms that Botulinum Neurotoxin Type A (BoNT-A) is an effective and versatile therapeutic option for managing disorders of the masticatory system [144,145]. Its applications range from reducing excessive muscle activity and alleviating myofascial pain to improving functional limitations associated with temporomandibular disorders and addressing masseteric hypertrophy for aesthetic purposes. Most investigations report meaningful improvements in key clinical outcomes—pain reduction, decreased muscle hyperactivity, and enhanced

mandibular function—alongside positive effects on patients' psychological well-being and overall quality of life [146,146].

However, BoNT-A therapy is not without important considerations. Emerging evidence indicates that targeted weakening of a specific muscle may trigger compensatory activity in adjacent or functionally related structures, potentially modifying mandibular biomechanics or redistributing occlusal forces. Reductions in bite force and interindividual variability in treatment duration further emphasize the need for careful clinical assessment and tailored therapeutic planning. Additionally, injections involving deeper masticatory muscles carry a higher risk of adverse effects, underscoring the importance of accurate anatomical knowledge and operator expertise.

Overall, the literature supports the integration of BoNT-A within a broader multimodal treatment framework rather than as a standalone intervention. Combining BoNT-A with physiotherapy, neuromuscular rehabilitation, and behavioral or functional therapy appears to be the most promising approach to optimize outcomes while minimizing risks. Nevertheless, long-term, high-quality studies are still needed to clarify the consequences of repeated injections, identify patient subgroups most likely to benefit, and better understand neuromuscular adaptive responses [147–156].

In conclusion, BoNT-A represents a valuable therapeutic tool for masticatory system disorders, provided its use is guided by comprehensive assessment, individualized treatment planning, and clear communication with patients regarding potential benefits and limitations. Standardized protocols, extended follow-up, and deeper investigation of biomechanical and compensatory mechanisms will be essential to refine its role in evidence-based clinical practice.

Here is the table formatted clearly for academic use.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviation

BoNT-A	Botulinum Neurotoxin Type A
TMD/TMDs	Temporomandibular Disorders
EMG	Electromyography
VAS	Visual Analog Scale
NRS	Numeric Rating Scale
OVAS	Orofacial Visual Analog Scale
HVAS	Headache Visual Analog Scale
MMO	Maximum Mouth Opening
MIO	Maximum Interincisal Opening
PPT	Pressure Pain Threshold
QST	Quantitative Sensory Testing
CPM	Conditioned Pain Modulation
HADS	Hospital Anxiety and Depression Scale
CSI	Central Sensitization Inventory
PSS	Perceived Stress Scale
PSQI	Pittsburgh Sleep Quality Index
PCS	Pain Catastrophizing Scale
PVAQ	Pain Vigilance and Awareness Questionnaire
SF-36	Short Form Health Survey
OHIP-14	Oral Health Impact Profile
JFLS-8	Jaw Functional Limitation Scale
PHQ-9	Patient Health Questionnaire
MMPS	Muscle Prominence Scale
US	Ultrasound
RCT	Controlled Trial
TMJ	Temporomandibular Joint
LED	Light-Emitting Diode
CGRP	Calcitonin Gene-Related Peptide

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