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Adverse effects of treating bruxism and masseter muscle hypertrophy with botulinum toxin injection - a literature review

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ABSTRACT

Background Botulinum toxin injection in the masseter muscle has gained popularity for both therapeutic and aesthetic applications, such as treating bruxism, masseter hypertrophy and lower facial slimming. Despite its efficacy, adverse effects associated with this procedure have been documented. This literature review aims to analyse and summarize the adverse effects associated with botulinum toxin injection in the masseter muscle, examining their incidence, underlying mechanisms and management strategies.

Material and methods A comprehensive search of databases including PubMed, MEDLINE and Google Scholar was conducted using above-mentioned keywords.

Conclusions Masseter muscle botox injection is considered a safe procedure with low incidence rate. Although the complications are temporary, they can significantly reduce patient satisfaction and confidence. To minimize the risk of complications, clinicians should familiarize themselves with risk mitigation strategies.

Keywords: botulinum toxin, masseter hypertrophy, bruxism, complications, adverse effects

INTRODUCTION

Bruxism, a condition characterized by the clenching or grinding of teeth, and masseter hypertrophy are common issues that can lead to various adverse effects on oral health and overall well-being. In recent years, the use of botulinum toxin injections has emerged as a potential treatment option for these conditions [1,2]. This procedure showed promising results in reducing bruxism episodes, alleviating pain levels, and improving muscle balance in patients with masseter hypertrophy. The mechanism of action of botulinum toxin involves chemical denervation by blocking the release of acetylcholine at the neuromuscular junction, leading to muscle relaxation, temporary paralysis and subsequent atrophy of the muscle. Also, botox injections are shown to be effective in relieving TMD-related myofascial pain and pain-related mouth opening restriction, thus improving patients 'psychological well-being [3]. Moreover, botulinum toxin decreases inflammatory pain by inhibiting substance P and glutamate release [4]. After administering Botox injections into the masseter muscle, studies have shown a

significant reduction in muscle activity and size. Masticatory function can decline by 20-40% post-botox injection [9]. Moreover, a decrease of nearly 80% in action potentials of the masseter muscle on day 14 after injection was observed [10]. However, like all medical interventions, botulinum toxin injections carry risks of adverse effects. Understanding these risks is crucial for informed clinical practice and patient safety.

1. Bruxism in athletes

Bruxism is a prevalent issue among athletes, particularly impacting their oral health and performance. Athletes, due to the stress induced during competitions or training, often exhibit bruxism, leading to craniomandibular disorders that affect the temporomandibular joint, teeth, and surrounding muscles [54, 55]. Studies have shown a high incidence of bruxism among athletes, with elite athletes demonstrating a prevalence as high as 51.1% [56]. The habit of bruxism not only affects the temporomandibular joint and teeth but can also result in head, neck, and back muscle pain, impacting athletes' overall well-being and performance [54, 55]. Furthermore, the biomechanical aspects of sports participation can contribute to the development or exacerbation of bruxism. During resistance training, athletes often clench their teeth to enhance performance, potentially increasing the likelihood of bruxism episodes [57]. Research has highlighted that competitive sports such as basketball, handball, wrestling, boxing, karate, mixed martial arts, field hockey, water polo, and soccer are associated with a high prevalence of bruxism among athletes [58, 60]. The increased masticatory muscle activity observed in athletes can further predispose them to conditions like bruxism, tooth wear, and tooth sensitivity, emphasizing the need for tailored oral health management strategies in this population [61, 62]. Moreover, the use of mouthguards in sports, while essential for preventing orofacial injuries, may also influence the occurrence of bruxism in athletes. The design and fit of mouthguards, particularly in contact sports, can impact the biomechanics of the jaw and potentially contribute to temporomandibular joint issues and bruxism [59]. Additionally, the consumption of sports and energy drinks by athletes has been linked to oral health problems, which can further exacerbate conditions like bruxism, highlighting the multifactorial nature of oral health issues in sports [63].

2. Adverse effects

2.1 Pain

Pain around the injection site is a common side effect. The incidence rate varies from 12.5% to 59.1% [6,7,8,14].

2.2 Swelling, bruising and hematoma

Studies have reported that after injecting botulinum toxin type A into hypertrophic masseter muscles, some common side effects include swelling, bruising, pain at the injection site [11]. These complications can occur as a result of rupture of local blood vessels during botulinum toxin injection [5,6]. These side effects are typically transient and resolve on their own without long-term complications [12].

2.3 Dizziness and headache

Dizziness and headache are side effects with unclear etiologies. Headaches tend to recur after future injections in people who have experienced them before and presumably have increased individual susceptibility [5,6]. The post-injection headache often takes 2-4 days to ease [7]. The incidence of dizziness as a side effect of botulinum toxin injection in the masseter muscle is relatively low based on the available literature [11].

2.4 Masseter muscle weakness

Botulinum toxin injections in the masseter muscle can lead to decrease in masticatory strength and that is the most reported side effect. The incidence rate for this complication is around 0.9%-63.6% [8,13,14]. After weakening effect of injections on the muscle patients experienced mild fatigue after vigorous chewing and transient buccal weakness [15,16]. The reduction of mastication force starts around 1-4 weeks after treatment [18,64,65]. The bite force gradually restores in 3-8 weeks and usually returns to pre-injection strength in around 12 weeks [6,13,18,64,65].

2.5 Worsened jowls or sagging

Worsened jowls or sagging tend to develop in middle aged patients with a prominent zygomatic bone who received a standard dose injection [5]. It occurs when overlying skin tightening does not match the rate of muscular atrophy and volume reduction [5,17]. In order to give patient's skin enough time to contract, physicians should slow down the volume reduction process by reducing the dose and spreading the treatment out into multiple sessions. Injections of botulinum toxin in depressor muscles such as platysma can also prevent this complication [5]. The incidence rate of this side effect is around 0.2%-2.3% [5,13] and it usually takes less than 2 months to recover [6,13].

2.6 Paradoxical bulging

This side effect results from a superficial overcompensation of masseter muscle fibers in response to the weakening of the deep masseter [19]. The deep and middle layers of the masseter contract almost vertically, while the superficial layer originates more medially on the zygomatic bone, creating an oblique direction of contraction and many cases of paradoxical bulging will take this form. A tendinous structure located in the deeper part of the superficial masseter layer was discovered while examining cadaver specimens and it may block toxin diffusion from the deep layer to the superficial layer, making overcompensation more common [20]. The dose of botulinum toxin should be proportionally distributed among the superficial belly and deep belly of the masseter muscle to prevent excessive paralysis of the deep belly and compensatory hypertrophy of the superficial belly, resulting in paradoxical muscle bulging. This side effect often occurs 2-4 weeks after injection after onset [13,18], it usually disappears within a week without medical intervention [13], so it is recommended to wait for toxin diffusion before another clinical touch-up treatment. [5,6]. In cases where paradoxical bulging persists or even worsens after 1- 2 weeks, an injection of 5-10 units over the superficial layer is indicated [5].

2.7 Sunken cheeks

This term describes the appearance of volume loss around the cheeks. This complication can occur when the injection site is too high, typically in the upper part of the masseter muscle, and is more frequently observed in patients with higher zygomas and less prominent cheek fat

pads [5]. Additionally, large injection volumes, high doses, or frequent injections in the masseter muscle can also lead to sunken cheeks [22]. Furthermore, the sunken appearance of the cheeks may be due to the loss of subcutaneous fat, buccal fat pad, and elasticity of connective tissue [23]. The incidence rate is around 0.44%-26.5%.4,28,52 [6]. To prevent sunken cheeks after masseter botox injections, it is recommended to lower the injection position, avoid injecting too anterior or superiorly and properly adjust injection dose [6,24,25]. In cases where sunken cheeks do occur, the appearance may resolve over time or can be temporarily corrected with hyaluronic acid fillers [26].

2.8 Changes in facial expression

Changes in facial expression include smile limitation, asymmetric smile, unnatural smile, awkward facial appearance. It can occur if the toxin paralyzes surrounding muscles, such as risorius and zygomatic major, which happens when injections are administered in the wrong area. Changes in facial expressions become noticeable within 2-4 weeks post-injection and take around 1-2 months to recover [6]. The risorius muscle, a superficial muscle of facial expression, plays a significant role in facial movements, particularly in smiling expressions. This muscle aids in retracting the angle of the mouth during smiling. Additionally, the risorius muscle contributes to dimple formation [27]. Affecting risorius muscle by botulinum toxin leads to asymmetric smile [5,6,28,29]. Studies have shown that the risorius muscle is prone to collateral toxin effects due to its attachment to the anterior or middle part of the masseter in a majority of individuals [30,31]. Restricting the injection site within the boundaries of the masseter muscle is essential to prevent complications [12] and it should be performed approximately 1 cm away from the anterior border of the masseter [32].

It is recommended to avoid superficial injection to prevent botulinum neurotoxin diffusion to the risorius muscle [29], so the injection should be stopped at the masseteric fascia beneath the subcutaneous fat. It is also important to consider the injection volume, because it can impact the outcome and potential side effects of the procedure [25]. When a higher volume is injected, the area of diffusion seems to increase [33]. Inaccurate injection and excessive diffusion of the toxin can lead to systemic adverse effects or unwanted weakness of neighboring muscles [34]. Studies have evaluated the efficacy of low-dose Botox injections into the masseter muscle to reduce complications and achieve the desired outcomes [35,36].

Administering Botox to the masseter muscle can also potentially lead to asymmetrical smile due to its impact on the neighboring zygomatic major muscle, which is crucial for smiling

as it elevates the cheek to form a smile [37]. Improper injection can alter the balance of muscle activity involved in smiling, potentially resulting in smile asymmetry. It can happen when injections are too highly or anteriorly placed [6]

Rarely, the effects of toxins on the marginal mandibular nerve can also alter facial expressions [6]. One common symptom is an asymmetrical smile, where the affected side of the face may not move or elevate the lower lip symmetrically with the unaffected side [38]. This asymmetry is due to the paralysis of the marginal mandibular nerve, which innervates the muscles responsible for lip movement [38]. Additionally, unilateral paralysis of the marginal mandibular nerve can result in a unique lower lip deformity known as marginal mandibular lip deformity [39]. This deformity can cause a visible drooping or lack of movement in the lower lip on the affected side.

2.9 Xerostomia

Xerostomia, commonly known as dry mouth, can be a side effect of botulinum toxin injections in the masseter muscle. This side effect is attributed to the diffusion of the toxin to the parotid gland through the posterior part of the masseter muscle [40]. Xerostomia is a well-known complication that may require the use of sialogogues to manage the dryness in the mouth [40]. The physician can avoid injecting the gland, by injecting the muscle deeply while keeping a one-centimeter buffer from the masseter's posterior edge [5].

2.10 Neurapraxia

Neurapraxia is a remarkably rare complication and is caused by paralysis of the marginal mandibular nerve [5,6]. In one autor's twenty years of masseter toxin injection experience, there were no cases of this side effect [41]. There is only one case report where the patient experienced temporary paralysis of the marginal mandibular nerve, which resolved in two weeks [42]. Moreover, toxin impact on the marginal mandibular nerve may also affect facial expressions [6].

2.11 Lack of effect

Resistance or lack of response to treatment is extremely rare [5] and may be caused by the presence of toxin antibodies which results from individual differences in the immune system [21].

2.12 Osteopenic changes

Studies have shown that injecting botulinum toxin into the masseter muscle can lead to various effects on the mandibular condylar cartilage (MCC) and surrounding structures. For example, reduced proteoglycan and glycosaminoglycan distribution, decreased expression of certain proteins like pSMAD 1/5/8 and VEGF, as well as decreased mineralization and matrix deposition in the MCC after botulinum toxin injection was observed [43]. This indicates a negative impact on the cellular and matrix response in the mandibular condylar cartilage. Additionally, a significant decrease in bone quality and quantity in the condylar head was reported [44]. It was shown that repeated botulinum toxin injections in the masseter muscle of adults induced significant bony changes over time [45]. These studies collectively underscore the potential for botulinum toxin to impact bone density and structure in the jaw, necessitating careful consideration of injection frequency and dosage to mitigate adverse skeletal effects.

3. Risk Mitigation Strategies

3.1 Precision in Injection Technique

Proper injection technique is paramount in achieving optimal results and minimizing risks. When seeking to find the appropriate injection points for botulinum toxin administration in the masseter muscle, it is crucial to consider a multi-point injection approach, accurate localization of the motor point, and the dosage of the toxin. A consensus recommendation suggests a 6-point injection technique into the masseter muscle, with 3 points per side, to effectively target masseter hypertrophy [11]. First injection should be performed at the most prominent point in the masseter muscle while clenching the teeth [46]. The needle tip should be positioned well below the subcutaneous fat, at a depth of around 1 cm in the skin [47]. Keeping injections inside the safe zone, at least 1 cm from any border, is crucial for the prevention of complications [5]. Guidelines suggest that when injecting into the anterior part of

the masseter muscle, superficial injection should be avoided to prevent diffusion to surrounding muscles and potential asymmetry in smiling [29]. It is essential to palpate the ramus of the mandible and withdraw the needle slightly before injecting to avoid facial muscle involvement [48]. Moreover, studies have indicated that the efficacy of botulinum toxin injections in the masseter muscle can be influenced by the dosage and distribution of the toxin. For instance, injecting 80 UI of botulinum toxin A at three points in both masseter muscles has been compared to saline solution applications, highlighting the impact of dosage and injection sites on treatment outcomes [49]. This underscores the need for careful consideration of dosage and injection points based on the specific condition being treated. Additionally, research has shown that injecting botulinum toxin into multiple points within the masseter muscle can be beneficial. For instance, a study mentioned injecting 30 MU of Botox type A at three places in the masseter muscles, along with 20 MU at two points in the anterior temporalis muscles, for the treatment of nocturnal bruxism [35].

3.2 USG as a useful tool

Ultrasound guidance can aid in precise localization of the injection points within the masseter muscle, ensuring accurate delivery of the toxin. This technique enhances the safety and efficacy of the procedure by allowing for real-time visualization during the injection process.

By visualizing the internal architecture of the masseter muscle, ultrasonography assists in identifying optimal injection points and ensuring accurate delivery of the toxin [50]. This technique has been particularly beneficial in cases where repeated Botox injections may lead to muscle fibrosis, as ultrasonography can detect changes in muscle volume and composition, guiding treatment decisions [51]. Additionally, ultrasonography has played a crucial role in monitoring the effects of Botox injections on the masseter muscle post-treatment. Studies have utilized ultrasonography to observe changes in muscle thickness, volume, and structure following injections, offering valuable insights into the treatment outcomes [52,53]. By evaluating muscle atrophy and other structural changes through ultrasonography, healthcare providers can customize treatment plans and dosage adjustments for optimal results [52].

4. Patient Selection and Counseling

4.1 Patient Selection

Selecting appropriate candidates for botulinum toxin injections in the treatment of masseter hypertrophy and bruxism is crucial to ensure optimal outcomes and minimize adverse effects. The following factors should be considered:

Medical History: Evaluate the patient's history of bruxism, including the frequency, severity, and impact on daily life. Consider other underlying conditions such as temporomandibular joint disorders (TMJD) or stress-related factors. Determine if the hypertrophy is idiopathic or secondary to other conditions, such as TMJD or bruxism. A thorough history of muscle overuse or habits that may contribute to hypertrophy is essential.

Physical Examination: Assess the size and symmetry of the masseter muscles. Palpate the muscles to determine the extent of hypertrophy and check for tenderness or trigger points. Examine the patient's bite and occlusion to identify any dental issues that may contribute to bruxism or hypertrophy.

Imaging: Utilize imaging modalities like ultrasound or MRI to visualize the masseter muscle's size and structure. This can aid in confirming the diagnosis and ruling out other potential causes of hypertrophy.

Contraindications: Identify any known allergies to botulinum toxin or its components. Patients with neuromuscular disorders such as myasthenia gravis or Lambert-Eaton syndrome may not be suitable candidates due to the increased risk of adverse effects. Avoid injections in pregnant or breastfeeding women due to the lack of sufficient safety data.

4.2 Counseling

Effective patient counseling is essential to ensure that patients have realistic expectations and understand the potential risks and benefits of BoNT injections. Key points to address during counseling include:

Treatment Goals and Expectations: Explain the primary goals of the procedure, such as reducing muscle size, alleviating pain, and decreasing the frequency of bruxism episodes. Set

realistic expectations regarding the onset of effects (typically within 1-2 weeks) and the duration of results (usually 3-4 months).

Procedure Details: Describe the injection process, including the number of injections, the sites of administration, and the approximate duration of the procedure. Inform patients about the sensation during injections, such as mild discomfort or a pinching feeling.

Potential Risks and Adverse Effects: Discuss common side effects, including localized pain, bruising, temporary muscle weakness, and asymmetry. Address less common but potential risks, such as difficulty chewing, changes in facial expression, or systemic reactions.

Post-Treatment Care: Provide guidelines for post-injection care, such as avoiding strenuous activities, massaging the treated area, or applying heat for a specified period after the procedure. Advise patients on signs and symptoms of complications that require immediate medical attention.

Follow-Up and Maintenance: Emphasize the importance of follow-up appointments to monitor the effects and make any necessary adjustments to the treatment plan. Discuss the potential need for repeated injections to maintain results and manage symptoms effectively.

Post-Injection Follow-Up: Scheduling follow-up visits to monitor for adverse effects. Providing clear instructions on when to seek immediate medical attention.

CONCLUSION

Botulinum toxin injection in the masseter muscle is generally a safe and effective procedure with a predictable safety profile. While adverse effects are typically minor and transient, awareness and prompt management of these effects are essential for optimal patient care. Common side effects include pain, swelling, bruising, dizziness, muscle weakness, and changes in facial expression, among others. Rare but notable complications such as osteopenic changes and neurapraxia highlight the need for careful consideration and technique during treatment. To minimize the risk of complications, clinicians must adopt precise injection techniques, consider the use of ultrasound guidance, and carefully select and counsel patients. Understanding the underlying mechanisms of adverse effects and implementing appropriate

risk mitigation strategies are crucial for optimizing treatment outcomes and maintaining patient safety. Further research is needed to refine techniques and improve safety, ensuring the best possible outcomes for patients. Continuous monitoring and follow-up care are essential to manage and address any complications promptly.

Author's contribution

Conceptualization, KR; methodology, KR, AK, JK; software, MK, OB, AN, OK, MS; check, ZS, KP; formal analysis, JK, OB, MK; investigation, AK, AN, OK; resources, MS, ZS, KP; data curation, AK, AN; writing – rough preparation, KR, JK, OB; writing-review and editing, KR, MK; visualization, OK; supervision, ZS, KP; project administration, MS

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