

REVIEW ARTICLES

Efficacy of botulinum toxin in masseter muscle hypertrophy for lower face contouring

Nisha Kundu BDS, MSc (CosMed), MSc (IHM)¹ | Rohit Kothari MD²  |
 Nimish Shah MBBCh, MRCGP, DRCOG^{3,4} | Sunmeet Sandhu MD, DNB⁵ |
 Durga Madhab Tripathy MD, DNB⁶ | Hassan Galadari MD⁷  | Michael H. Gold MD⁸  |
 Mitchel P. Goldman MD^{9,10} | Martin Kassir MD¹¹ | Hadrian Schepler MD¹² |
 Stephan Grabbe MD¹² | Mohamad Goldust MD¹² 

¹Imperial College, London, UK

²Dermatology, Command Hospital Air Force, Bengaluru, India

³Cardiff University, Cardiff, UK

⁴University of South Wales, Pontypridd, UK

⁵Dermatology, 7 Air Force Hospital, Kanpur, India

⁶Dermatology, Military Hospital, Agra, India

⁷College of Medicine and Health Sciences, United Arab Emirates University, Al Ain, UAE

⁸Gold Skin Care Center, Tennessee Clinical Research Center, Nashville, Tennessee, USA

⁹Cosmetic Laser Dermatology: A West Dermatology Company, San Diego, California, USA

¹⁰Department of Dermatology, University of California, San Diego, California, USA

¹¹Worldwide laser institute, Dallas, Texas, USA

¹²Department of Dermatology, University Medical Center of the Johannes Gutenberg University, Mainz, Germany

Correspondence

Mohamad Goldust, Department of Dermatology, University Medical Center Mainz, Mainz, Germany.
 Email: mgoldust@uni-mainz.de

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Abstract

Background: Masseter muscle hypertrophy (MMH) usually presents with cosmetic concerns as it may lead to widening of the lower face. Apart from the traditional surgical approaches, botulinum toxin type A (BTA) injection is a non-invasive treatment option available. There are no standard guidelines for this procedure.

Objectives: To study the efficacy of botulinumtoxin A in MMH for lower face contouring.

Methodology: The Cochrane Library, PubMed/MEDLINE, Google-scholar, Science-Direct database, and ResearchGate from inception until September 2021 were searched using the keywords “botulinumtoxin type A,” “masseter muscle hypertrophy,” “lower face contouring,” and “masseter botox.” All available retrospective and prospective studies, case-series, case-reports, and expert reviews were included with an emphasis on efficacy of BTA in MMH and units injected into the muscle, points of placement, adverse events, and the duration of its effect. Reference lists of the resultant articles, as well as relevant reviews, were also searched.

Result: 40 articles were shortlisted for the review, of which 14 studies with sample-size ≥ 10 in accordance with the study requirements were summarized in a tabular form for analysis and easy comparison and reference.

Conclusion: BTA injection is a non-invasive, safe, and effective treatment for MMH. The optimum number of BTA units could not be ascertained due to wide variability in the studies as well as ethnicity of patients and extent or some measurement of MMH. The points of placement of injection should be well within the boundaries of the masseter muscle. The maximum effect of BTA after a single injection session is usually seen in ~3 months, and the duration may last for 6–12 months. Multiple injection

We confirm that the manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met and that each author believes that the manuscript represents honest work.

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sessions may be required to maintain a long-term effect. Injection technique and total number of injection units of neuromodulator must be individualized for each patient.

KEYWORDS

Botulinum toxin type A, lower face contouring, masseter botox, masseter muscle, masseter muscle hypertrophy

1 | INTRODUCTION

Sculpted high cheekbones with hollowness under them, giving a triangular or heart shaped female face is considered the most aesthetic ideal one. Usually, Asians have wider face with high malar prominence and a squared jawline. Smaller and slimmer faces with a triangular shape are considered more beautiful and attractive by many and are more desirable amongst women as compared with men. In males, wide and square shape jawline is considered more attractive and masculine.¹

The masseter muscle is one of the of mastication muscles which helps mainly in biting and chewing of food. Hence, the volume and width of this muscle is determined especially by the biting force, chewing habits, the type of food, diet, or habits such as teeth clenching, bruxism, or any other temporo-mandibular joint (TMJ) disorder. Any of these can lead to masseter muscle hypertrophy (MMH), which gives a squarish appearance to the face or jawline.¹

Surgical resection of the mandibular bone or masseter muscle or liposuction of the subcutaneous fat was performed historically as a treatment.² A more recent non-surgical treatment option includes botulinum toxin injections into the muscle to reduce its size.³ Type A Botulinum toxin (BTA) was first used to correct masseter hypertrophy in 1994.⁴ When the toxin is injected into the muscle, it inhibits the release of acetylcholine at the neuromuscular junction, causing a temporary flaccid paralysis of the muscle. However, the nerve terminals start to regenerate in ~3 months, and hence, it requires repeated sessions to maintain complete paralysis.⁵ Temporary atrophy of the muscle due to its chemo-denervation effect is noted and persists for 3–6 months.^{6,7} Various side-effects associated with the procedure have been reported and are most likely secondary to excessive infiltration or inaccurate placement of the neuromodulator. These consist of smile limitation or asymmetry, reduced chewing force, problem in wide mouth opening, bruising, incipient jowl and skin sagging, local pain at the site of injection, mild headache, awkward facial expressions, speech disturbances, uneven bulging of muscles, sunken cheeks, and herniation of the parotid gland through the attenuated overlying muscle.⁸

There are no available standard guidelines for this procedure. This review aims to provide an overview of efficacy of BTA in MMH and the optimum units injected into each side of masseter muscle, points of placement of injection, adverse events, and the duration of its effects.

2 | METHODOLOGY

The Cochrane Library, PubMed/MEDLINE, Google scholar, Science Direct database and ResearchGate from inception until September 2021 were searched using the keywords “botulinum toxin type A,” “masseter muscle hypertrophy,” “lower face contouring,” and “masseter botox.” All available retrospective and prospective studies, case-series, case-reports, and expert reviews were included with an emphasis on efficacy of BTA in MMH and units injected into the muscle, points of placement, adverse events, and the duration of its effect. The observations were analyzed to find the best possible dose of BTA and the location of points of injections to achieve the most desirable esthetic contouring of lower face. 40 articles were shortlisted for the review, of which 14 studies with sample-size ≥ 10 in accordance with the study requirements were summarized in a tabular form for analysis and easy comparison and reference.

3 | LOWER FACE AESTHETICS

Triangular shaped lower face with a perfect jawline is the most desirable shape among females as compared to a broad squarish lower face, which is considered more attractive in males for many people. In many Asian cultures small, slim and oval faces are known to bring good fortune, and hence, there is more interest to achieve this.² The aesthetics of lower face are determined by three main factors:

- Size of the bony mandible
- Mass of the masseter muscle
- Volume of subcutaneous fat tissue

The size and shape of the mandible is predetermined at the time of birth and is fixed by the time of adulthood. It also varies between different ethnicities and races. The volume of subcutaneous fat varies from person to person depending on the individual body mass index. In addition, it is found that different ethnicities have variations in thickness of facial fat pads.⁹

4 | MASSETER MUSCLE HYPERTROPHY

Masseter is one of the four muscles of mastication in the maxillo-facial region. It is a quadrangular muscle, which is divided into superficial and deep portion. The superficial portion arises from thick

aponeurosis on the zygomatic bone and the anterior two third of zygomatic arch and the deep portion arises from zygomatic arch and is covered anteriorly by the deep fibers and posteriorly by the parotid gland. Masseter muscle contractions help in elevation and protrusion of the mandible.¹⁰

The first known case report of MMH dates back to 1880 in a 10-year-old girl reported by Legg JW.¹¹ Benign or idiopathic MMH is a relatively uncommon condition, with unilateral or bilateral enlargement of the muscle. Patients are usually asymptomatic and seek advice only when they notice aesthetic concerns due to asymmetry of lower face.¹² The most common reasons leading to masseter hypertrophy can be dietary habits, chewing gums, bruxism, and TMJ disorders, which may be stress induced. As per Teixeira, masseter hypertrophy can be classified as congenital and acquired, that is, functional hypertrophy.¹² Masseter hypertrophy should be accurately diagnosed and differentiated from similar looking conditions such as parotid or masseter tumor, inflammatory parotid disease, salivary gland disease, and masseter intrinsic myopathy.

Most patients usually present with increase width or dimensions of the lower face also termed as "square face." The associated symptoms can be pain in the TMJ, headache, muscular stress, or trismus. The diagnosis of MMH is established by clinical examination and palpation of the muscle. The palpation of the muscle carried out in both contracted as well as relaxed state helps in pin pointing the location of hypertrophy. Ultrasonography (USG), magnetic resonance (MR) images help to detect the enlarged muscle. Computed tomography (CT) scans and panoramic radiographs may be used to observe any reactive bone formation in the mandible.¹³

5 | TREATMENT MODALITIES FOR MMH

The treatment of MMH largely depends on the underlying cause. If its stress induced, then psychological endorsement is essential. Mouth guard, antispasmodics, and/or analgesics can be used as well. Surgical resection of the masseter muscle through a submandibular incision was first proposed by Gurney¹⁴ in 1947 and later by Beckers who used an intraoral approach to avoid facial nerve injury and facial scarring.¹⁵

The commonly used surgical technique for MMH is an extraoral approach, following a submandibular incision, avoiding the mandibular nerve.¹² With bony hyperplasia, reduction osteoplasty is preferred. The possibility of post-operative complications such as facial nerve paralysis, hematoma formation, trismus, infection, and other general anesthesia-related complications is rare. The use of radiofrequency energy to reduce the size of muscle is claimed to be long lasting with less side effects as compared with surgical procedures.¹⁶ The least invasive and most widely used modality is BTA. It was first used by Smyth, Moore, and Wood in 1994.^{17,18} BTA treatment helps in decreasing the muscle bulk, which also reshapes the lower face along with improving pain, grinding, and clenching symptoms. Adverse effects are minimal and short lasting.¹⁹

6 | PATIENT SELECTION

Contouring of the lower face is a cosmetic procedure, and hence, patient selection is important. Patients over 40 years with sagging face and jowls are not ideal candidates, as loss of muscle volume will enhance incipient jowl. Patients with very high cheekbones also need to be counselled as the results may further accentuate the appearance of cheekbones.¹ Those with excess fatty tissue on the face may not appreciate the difference after the reduction of masseter muscle; therefore, other means of fat reduction such as liposuction or injection with deoxycholate should be considered.² Patients with other medical or psychological conditions like bruxism or stress may need other therapies as previously described.²⁰ Ideal patients for this procedure are between 16 and 50 years with broad or square shaped lower face due to overdeveloped masseter with realistic expectations.²

7 | INJECTION TECHNIQUES

Various techniques for injecting BTA into the masseter muscle are demonstrated in Figure 1 and summarized in Table 1. Moore, Woode, and Smyth first published on this procedure.^{17,18} Kim HJ et al uses two injection points marked on a line from tragus to corner of mouth 1 cm apart. Another two injection points are given 1cm above and below this reference line.²¹ The 3-point injection technique involves one point inferior to tragus-mouth line at the thickest point of muscle and two points 1cm away from the anterior and posterior borders of masseter. This helps to reduce the chances of affecting the risorius muscle or causing a herniation of the parotid gland.²² 5-point injection technique involving the most bulging points is another method.²³ Two points of injections, one at angle of mandible, and other one in the region of zygomatic arch was used by Lindern et al.²⁴ A 2-point injection technique in the lower one third of muscle 1 cm apart may also be used.^{25,26} Some authors prefer lower outer quarter of muscle for injecting after marking the anterior and posterior margin of masseter, earlobe to mouth corner line, and border of mandible and dividing the muscle into four equal parts.²⁷ A more recent technique uses ultrasound guided injections at 2–4 points, 1.5cms apart within the borders of the muscle and tragus-mouth line.²⁸ The most important concept while injecting masseter with BTX is to remain well within the boundaries of the muscle to avoid complications most commonly asymmetry.

8 | DOSAGE, FREQUENCY, AND EFFICACY

Various dosage regimens and frequency of injecting BTA are summarized in Table 2. The first case report of treating MMH by Moore and Woode (1994) utilized 300 units of BTA in a 30-year-old Caucasian male with stress-related TMJ dysfunction arthropathy, myofascial pain syndrome, and masseter hypertrophy. 2-weeks after injection, slight reduction in volume of muscle was noted

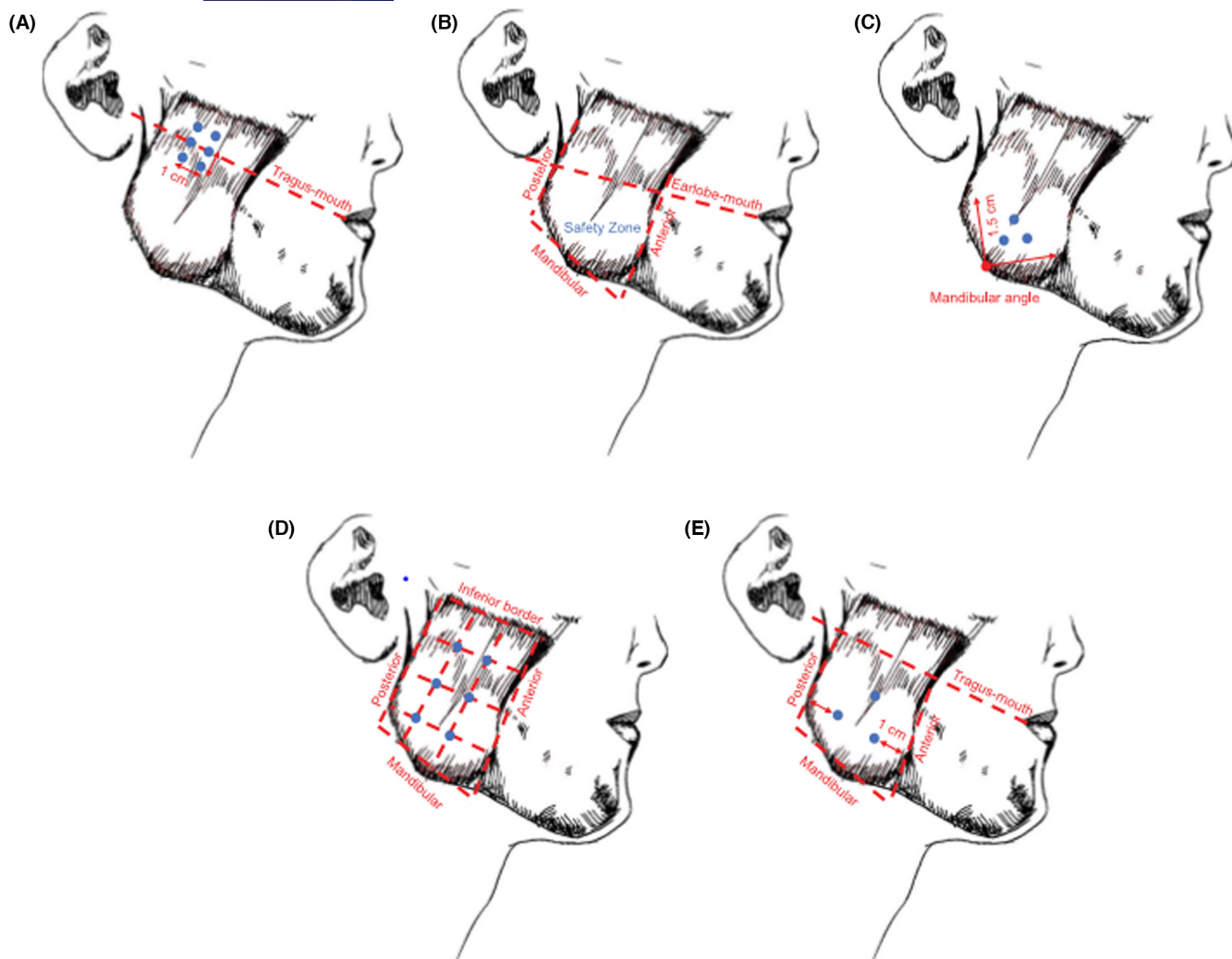


FIGURE 1 Injection points for masseter botox

which lasted for ~6 months without any side-effects.¹⁸ Multiple studies using much lower dosages have since been reported with a variable success rate. One of the largest studies by Kim NH et al involved 1021 patients treated with 100–140 units of abobotulinumtoxin A (ABO) for lower face contouring (383 patients could be followed up for >3 months). Thickness reduced by 31% and maximum reduction in muscle strength was seen after 10–12 weeks and 50% required a second injection after 4–7 months. Biopsy of muscle tissue four months after the procedure revealed atrophy, necrosis, and hyaline degeneration.² Xie et al.²⁹ (2014) used a lower dose (20–40 units) onabotulinumtoxin A (ONA) in 220 patients with MMH. Maximum effect was observed at 3 months, with reduction in muscle thickness from 12.9 ± 2.9 to 8.7 ± 1.7 mm in 40 patients who could be followed-up till four months. They observed 60% of complications in those who had received higher dosage of BTA. Maximized masticatory movement for more than 2 h/day post masseter-BTA may result in longer lasting results may be up to 1 year even with lower dosage of BTX.²⁷ Frequent BTA or Xeomin [incobotulinumtoxin A (INCO)] injections given at intervals of 3–6 months may be effective in long term

management of masseter hypertrophy and contouring of lower face.^{30,31} Prabotulinumtoxin A (PRA) in a dosage of 48–72 units followed by reinjection after 12-weeks is also effective in a dose-dependent manner; however, higher doses may lead to discomfort during jaw movement.³² It is important to note that studies which reported on the use of higher doses of BTA are almost always from Asian countries, especially Korea. Our experience is that Caucasian patients achieve acceptable results using 15–30 units per side (Figures 2, 3).

USG can observe the deep inferior tendon of masseter muscle which may reduce the side-effects of masseteric bulging when applying dual-plane or retrograde injection methods.³³ In the quest of searching for a safer and more efficient injecting technique, Bae H et al. concluded that USG-guided method is better than a blind procedure due to direct visualization of the muscle and may prevent paradoxical masseteric bulging that may occur during the blind injection.³⁴

Botulinum toxin type A may even be combined with other therapies such as autologous fat grafting for masseter hypertrophy and wide faces with very few complications and rapid recovery.³⁵

TABLE 1 Various injection techniques of masseter botox

S. No.	Study	Injection technique
1	Moore & Wood et al ¹⁸ (1994)	Injected at the most prominent point in the masseter muscle
2	Smyth AG et al ¹⁷ (1994)	Marked two points for the injection; first point was at the most prominent point upon clenching the teeth and second point, 1-2cm above the first one
3	Mandel & Tharakan et al ²³ (1999)	5 points of injection at most bulging points of the masseter muscle
4	Lindern J.J et al ²⁴ (2001)	Gave another technique for injecting BTA into the masseter muscle. Two points of injections, one at the angle of mandible and other one in the region of zygomatic arch was used
5	Kim H. J, Yum KW et al ²¹ (2003)	A line is drawn from tragus to the corner of mouth and two injection points are marked on this line 1cm apart. Another two injection points are given 1cm above and below this reference line (Figure 1A)
6	Kim N.H et al ² (2005)	Multiple injections given at 3-4 points, 1.5cm above the mandibular angle (Figure 1C)
7	Chang CS et al ⁶ (2007)	Establishing the area of injection by marking the anterior and posterior margins of masseter, inferior margin of zygomatic arch and border of mandible and then dividing the area into six equal sized grids to inject BTA 1cm apart (Figure 1D)
8	Kim NH, Park RH et al ²⁰ (2010)	A safety zone can be established by marking the boundaries of the masseter muscle, anteriorly and posteriorly by borders of the muscle, superiorly by earlobe-mouth corner line, inferiorly by mandibular border. 50% of BTA is injected into the centre of the safety zone and 25% is given at two other points within the safety zone (Figure 1B)
9	Shim et al ²⁵ (2010)	2-point injection technique in lower one third of the masseter muscle 1 cm apart
10	Cha YR et al ²⁵ (2013)	2 points of injection 1cm apart in lower third of the muscle at the points of maximum prominence
11	Bae J.H et al ²² (2014)	Three point injection technique: One point inferior to the tragus-mouth line at the thickest point of the muscle, and two points 1 cm away from the anterior and posterior borders of the masseter muscle are marked for injection. This helps to reduce the chances of affecting the risorius muscle (Figure 1E)
12	Wei J et al ²⁷ (2015)	Marked anterior and posterior margin of masseter, earlobe to mouth corner line, border of mandible and divided the muscle into four equal parts. The injection of BTA was given in the lower outer quarter of the muscle
13	Quezada-Gaon et al ²⁸ (2016)	Suggested an ultrasound guided injection technique at 2-4 points, 1.5 cm apart within the borders of the muscle and tragus-mouth line
14	Hong JY et al ³² (2021)	An imaginary line linking the tragus and mouth corner was used to mark a safe injection zone. Needle tip was inserted until it reached the mandible and then retracted 1-2 mm to avoid injection into superficial facial musculature. 0.72 ml of the test solution at each side using the 3-point injection technique below the drawn line

9 | SIDE EFFECTS

As with any other treatment modality, BTA injection also carries a risk of various side-effects albeit mild and manageable in most cases. ~50% patients may experience these effects with muscle weakness, reduced crunching power, or reduced bite force being the most commonly reported, especially in Asian patients treated with dosages >30 units/side. Kim & colleagues² observed these side effects in 192/383 participants. These were temporary and usually resolved within a period of 1-2 months. Another study by Wei et al reported bite weakness and muscle fatigue in 44/98 patients. Diffusion of BTA into the surrounding musculature such as the zygomaticus or buccinator can cause changes in facial expressions or facial asymmetry. To avoid this, BTA should be injected well within the boundaries of masseter muscle and superiorly a line joining the tragus to

oral commissure should be considered as the upper margin.²⁰ MMH treatment may at times lead to temporal fossa volume increase, which may be secondary to masseter paralysis or a transient bulge in the muscle, which may be secondary to minor bleeding.^{36,37}

10 | CONCLUSION

BTA injection is a non-invasive, safe, and effective treatment for MMH. The optimum number of BTA units could not be ascertained due to wide variability in the studies as well as ethnicity of patients and extent or some measurement of MMH. The points of placement of injection should be well within the boundaries of the masseter muscle. The maximum effect of BTA after a single injection session is usually seen in ~3 months and the duration may last for

TABLE 2 Summary of studies on masseter botox ($n \geq 10$)

Study No.	Study	Sample Size	Type of BTA	Units injected	Methods of assessment
1.	Park, Ahn et al ⁴ (2003)	45	ONA	25–30	USG, CT, Patient satisfaction
2.	Kim et al ²¹ (2003)	11	ONA	30	CT, clinical photographs
3.	Kim, Chung et al ² (2005)	383	ABO	100–140	USG, Clinical photographs
4.	Choe SW et al ³⁸ (2005)	22	ONA	10–30	USG, clinical photographs, Patient satisfaction scores
5.	Kim JH et al ³⁹ (2007)	32	ONA	25–35	CT, EMG
6.	Liew & Dart et al ³⁷ (2008)	34 48	ONA	25–30 40–45	Clinical photographs, Patient feedback
7.	Shim et al ²⁶ (2010)	15	ONA	25	3D Laser Scan
8.	Cha YR et al ²⁵ (2013)	10	ONA	25	3D Laser scan
9.	Klein et al ³ (2014)	10	ABO	90	Clinical photographs
10.	Xie Y et al ²⁹ (2014)	40	ONA	20–40	USG, Clinical photographs
11.	Wei et al ²⁷ (2015)	98	ONA	35	USG, CT
12.	Shome, D, Khare S et al ³⁰ (2019)	50	ONA	30	USG, Clinical photographs
13.	Shome D, Vadera S, et al ³¹ (2020)	30	INCO	30	USG, Clinical photographs
14.	Hong JY et al ³² (2021)	90	PRA	24–96	USG, Clinical photographs, 3D imaging

Note: Conversion factor for various botulinumtoxin A is ONA: INCO: ABO: PRA=1:1:2.5:1.

Abbreviations: ABO, Abobotulinumtoxin A; INCO, Incobotulinumtoxin A; ONA, Onabotulinumtoxin A; PRA, Prabotulinumtoxin A.



FIGURE 2 Masseter botox with 30 units of BTA on each side at baseline and at 10-weeks follow-up



FIGURE 3 Masseter botox with 30 units of BTA on each side at baseline and at 12-weeks follow-up

Results	Side effects	Follow-UP	Maximum effect	Duration of effect
Reduced muscle thickness by 19.5%, improved satisfaction	Masticatory difficulty, Muscle ache	10 months	3 months	10 months
Reduced muscle volume by 35.4%	Masticatory difficulty, Altered Facial expressions, Sunken cheeks	6 months	3 months	6 months (50%)
Reduced muscle thickness by 31%	Reduced crunching power, Bulging of muscle, Facial asymmetry	24 months	3 months	7 months (50%)
25% reduced muscle thickness, improved scored	Pain at injection site, Headache	9 months	4 months	9 months
27.5% reduced muscle thickness and cross-section, Reduced EMG values	Muscle weakness, pain at injection site, headache	3 months	3 months	-
Aesthetic & functional improvement, 30% volume reduction	Muscle bulge, asymmetry	10–24 months	2–3 months	9–12 months
Reduced volume & width of lower face	No side effects	6 months	3 months	6 months
Decreased volume and thickness of lower face	Not side effects	3 months	3 months	-
Reduction in lower face width	Smile limitation, Smile asymmetry, Masticatory fatigue	6 months	3 months	-
Reduction in muscle thickness by 33%	Dizziness, headache, smile limitation, disappearance of dimple	4 months	3 months	-
Reduced muscle volume by 30.5%	Bite weakness, Headache, bruise	15 months	3 months	6–12 months
Reduced volume by 12%	Pain at injection site, Headache	4 Years	3 months	-
Reduced volume by 26.85% (02 injection) & 43.42% (03 injection)	Mild pain at injection site	2 Years	6 Months	12–24 months
11.51±1.13% mm to 20.53± 8.37% at 12 weeks with 96 units	Transient masseter muscle pain	4 months	3 months	3–4 months

6–12 months. Multiple injection sessions may be required to maintain a long-term effect. Injection technique and total number of injection units of neuromodulator must be individualized for each patient.

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CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Nisha Kundu contributed in writing and revising the manuscript. Rohit Kothari, Nimish Shah, Sunmeet Sandhu, Durga Madhab Tripathy, Hassan Galadari, Michael H. Gold, Stephan Grabbe, Hadrian Schepler, Martin Kassir, Mitchel P Goldman involved in review and revising the manuscript. Mohamad Goldust involved in conception, writing, review, and revising the manuscript.

ETHICAL APPROVAL

This was a review article and needs no ethical approval, Written consent was obtained from the patients regarding their pictures.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Rohit Kothari  <https://orcid.org/0000-0002-9875-2563>

Hassan Galadari  <https://orcid.org/0000-0001-8223-2769>

Michael H. Gold  <https://orcid.org/0000-0002-5183-5433>

Mohamad Goldust  <https://orcid.org/0000-0002-8646-1179>

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