

A Review on the Combined Use of Soft Tissue Filler, Suspension Threads, and Botulinum Toxin for Facial Rejuvenation

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Abstract

The aim of combining different minimally invasive techniques is to achieve the most harmonious and most natural-looking facial rejuvenation as effectively and as safely as possible. Due to their safety and versatility, botulinum toxin and soft tissue fillers have become the most sought-after modalities for correcting the signs of facial aging. Recently, bioabsorbable threads used for repositioning ptotic facial tissue have been added into the picture. More practitioners are also combining threads with fillers and botulinum toxin to achieve longer-lasting and natural-looking results. Our aim is to provide guidance on basic anatomical landmarks and areas where botulinum toxin injections, subcutaneous filler injections, and bioabsorbable suspension threads are placed on the face. We would also like to share our best practices on the best combination, spacing the appropriate time intervals in between each procedure to allow for the shortest possible recovery time, as well as periprocedural advice for an integrated treatment approach.

Keywords: Barbed bioabsorbable threads, botulinum toxin, combination, consensus, soft tissue fillers

INTRODUCTION

This article is the first consensus publication to discuss facial rejuvenation as well as provide recommendations on the combination of botulinum toxin, HA fillers, and double-needle barbed bioabsorbable threads. The importance of morphological differences between Asian and Caucasian patients has been considered when providing specific treatment recommendations.

The Board of Aesthetic Leaders and Investigators (BALI) is an international panel of dermatologists and surgeons who convened in July 2018 in Bali, Indonesia to address the need for clinical guidance on combination therapy incorporating thread lifting. Specific management recommendations were described based on prevailing practices while keeping published guidelines in mind.

RATIONALE FOR COMBINING TREATMENT MODALITIES

There is currently a paucity of evidence-based recommendations intended to guide clinicians who manage three-dimensional facial aging, especially with

bioabsorbable barbed suspension threads, one of which is the poly-L-lactic acid-*co*- ϵ -caprolactone based Definisce™ Threads (RELIFE S.r.l., Florence, Italy). In light of years of their extensive experience in choosing and combining various modalities, the members of BALI had convened for the first time in a focus group discussion to identify common challenges when managing patients in a multicultural setting and subsequently held consensus-building sessions via a few rounds of teleconferencing and online voting. A concurrent literature search of the Medline®, Embase®, and Google Scholar database was conducted by using search terms “Asian,” “Caucasian,” “eastern,” “western,” “global,” “management,” “combination,” “review,” “meta-analysis,” “systematic review,” “evidence-based,” and “aesthetics.” The material

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reviewed included recent meta-analyses, clinical practice guidelines, reviews, and clinical trials relevant to the use of combination treatment and suspension threads. Literature searches included journal articles published before 31 August 2018. Lastly, written informed consent to publish anonymized pretreatment and posttreatment photos was obtained from the patients featured in this article.

Facial aging comes as a result of the normal wear of facial skin, adipose tissue, muscles, ligaments, and bones. Therefore, to address age-related aesthetic concerns, there is a need for a multifaceted treatment strategy targeting all of these tissue types.^[1,2] It is not uncommon to employ different approaches with the following mechanisms: lifestyle modification and daily skin care, including photoprotection, topical pharmacological agents, systemic agents, and integrating invasive strategies to correct visible signs of aging.^[3]

Because no single modality can be used to address all areas effectively and safely, consensus guidelines on facial rejuvenation have been developed that discuss combined techniques for different parts of the face, namely, the upper, mid- and lower facial thirds. Most guidelines have also provided specific approaches for subjects of various ethnicities.^[2,4,5] It is common to see the use of different combinations of injections (e.g., fillers, toxins) or energy devices (e.g., ultrasound) along with other modalities. The aim of using these techniques is to relax, resurface, and volumize facial tissue, and ultimately, to achieve the most harmonious and most natural-looking facial rejuvenation possible.^[2] Hyaluronic acid (HA) fillers have now become the most common filler of choice due to their versatility, ease of use, and because they are well tolerated by most patients.^[6]

Clinicians are often required to address the two major physical factors that contribute to aging, namely volume loss and muscular hyperactivity.^[7] Botulinum toxin continues to be the treatment of choice to relax visible lines caused by muscle hyperactivity.^[7] For dynamic lines or wrinkles or rhytids such as those on the forehead at the glabellar area and the lateral canthi (i.e., crow's feet), a number of botulinum toxin preparations have been developed and approved for aesthetic use.^[8] It can also be used in younger patients for correction of masseter hypertrophy and platysma or mentalis hyperactivity.^[4] Typically, the effect of the toxin lasts from about two to six months.^[7] Augmentation using soft tissue fillers can correct volume loss associated with bone resorption and fatty hypotrophy, and it can lift superficial soft tissue and subcutaneous and skin tissue through tightening of the relaxed facial ligaments.^[9] Nonsurgical treatments such as laser skin tightening devices and intradermal injection of low G prime HA can be used to address sagging skin and superficial fine lines.^[10] Most aesthetic practitioners employ a combination of two or more of these modalities to achieve optimal results.

Recently, there has been focus on minimally invasive techniques to reposition and realign ptotic facial tissue by using bioabsorbable suspension threads. Repositioning of facial tissue by using bioabsorbable suspension threads profoundly reduces procedural and recovery time, eliminates the need for general anesthesia, and is more preferred by patients than conventional face lifts.^[11,12] It works by safely repositioning facial tissue, instantly anchoring under the dermis into the subcutaneous layer. When the tissue heals, the surrounding thread is absorbed with resulting fibrosis, giving a lasting, holding effect.^[12,13] Several threads that are derived from synthetic sources and specific techniques have been introduced over the years.^[14] Since then, instructions for placement in specific areas of the face, such as the mid-face, lower face, or neck area, have been introduced.^[12]

Treatments may be scheduled or administered in separate visits to achieve optimal outcomes; although in some instances patients are unable to return for a subsequent visit and so procedures have to be accomplished on different areas and/or planes of the face in a specific sequence.^[8] In general, the goal of combination treatment is to achieve results that are long lasting and natural looking through techniques that allow the shortest recovery time. Note that areas that are not in the same region or those without overlapping planes may influence each other aesthetically.

It is important to note that patients from different age groups and of varied ethnic backgrounds have diverse aesthetic needs. As a result of the growing demand for aesthetic services in international hubs around the world where migration has become the norm, more clinics encounter a mix of different ethnicities with varied aesthetic indications. For instance, the aging process may be delayed in some ethnicities (i.e. wrinkles appear one to two decades later in Asians than in Caucasians). Because of this, younger Asians tend to seek less wrinkle treatment than their Caucasian counterparts; however, when mature Asians (older than 55 years) who have not been previously treated seek correction, they will tend to have more cumulative age-related changes of underlying facial structures (although there may be variations and exceptions).^[4,15,16] In addition, younger patients are known to request for correction of proportion and structural deficiencies whereas more mature individuals seek maintenance treatment and corrective reversal of the signs of aging.^[4]

OVERVIEW OF THE ANATOMY OF THE FACE

It is fundamental for all clinicians who delve into aesthetic medicine to understand the basic anatomy of the face and its structures. This article reviews common areas of the face with the most usual of aesthetic concerns; however, specific details on blood supply, innervation, and danger zones are the topic of other publications by the authors. The following text provides an overview of the basic anatomical landmarks and areas where botulinum

toxin injections, subcutaneous filler injections, and bioabsorbable suspension threads are placed on the face.

Asians, in general, possess a rounder face as accentuated by a wider bitemporal, bizygomatic, and bigonial width. They typically have a retruded forehead, orbital rims and medial maxillary/pyriform areas, a low nasal bridge, and a characteristic mandibular contour.^[15,17] Conversely, the Caucasian face is observed to be narrower and longer, has

greater anterior projection of the orbital rims with deeper set eyes, higher nasal bridge, and a more protruded maxilla and mandible.^[15] As a result of these fundamental anatomical differences, their requested procedures vary slightly.

BOTULINUM TOXIN

A wrinkle, or rhytid, is categorized as either dynamic or static. Static wrinkles are either more superficial fine lines or deeper



Expression lines	Muscle	Action
Frown lines	Corrugator supercilii Procerus and depressor supercilii	Eyebrows drawn medially Eyebrow depressors
Horizontal forehead lines	Frontalis	Eyebrow levator
Crow's feet	Lateral orbicularis oculi	Lateral eyebrow depressor
Bunny lines	Nasalis	Nose drawn up and medially
Radial lip lines	Levator labii superioris alaeque nasi Orbicularis oris	Lip puckering
Marionette lines and downturned smile	Depressor anguli oris	Corner-of-mouth depressor
Masseter hypertrophy	Masseter muscle	Elevates the lower jaw
Gummy smile and nasolabial fold	Levator labii superioris alaeque nasi	Central lip levator
Chin line and pebbly chin	Mentalis	Chin texture and lower lip levator

The arrows represent the direction of motion of each muscle.
Purple = depressor muscles; pink = levator muscles; cyan = sphincteric muscles

Figure 1: Areas for botulinum toxin treatment

lines known as furrows. Most static wrinkles arise from dynamic wrinkles and come as a result of aging. Dynamic wrinkles are often seen at the glabellar region, the lateral canthal areas or around the periorbital regions as a result of overuse of the muscles of facial expression. The nasolabial folds and glabellar lines are examples of furrows.^[7,18,19]

Although botulinum toxin is often believed to be the mainstay of wrinkle correction, it is not recommended for all types of wrinkles. Specifically, it is only useful for the correction of dynamic wrinkles such as forehead lines, glabellar lines, periorbital lines (canthal), wrinkles seen on the dorsum of the nose, and fine lines around the lips. Because the effect of botulinum toxin is relatively poor for furrows, such as the deep nasolabial folds and marionette lines, fillers are mainly used to improve the appearance of these grooves. Botulinum toxin is also not recommended in some dynamic wrinkles such as the transverse infraorbital wrinkles and zygomatic wrinkles due to the risk of worsening the aesthetic appearance of the area [Figure 1].^[19]

Asians characteristically have a thicker dermis and a thicker facial adiposity above and below the superficial muscular aponeurotic system (SMAS), denser fat and fibrous connections between the SMAS and deep fascia of the parotid gland and the masseter. Asians may have facial muscles that tend to have less mass, are shorter, narrower, and less hyperdynamic than in Caucasians (e.g. corrugators). However, most Caucasians tend to have less developed masseter muscles than Asians. These differences account for the varying amounts of toxin applied on different parts of the face.^[20]

SOFT TISSUE FILLERS AND BIOABSORBABLE THREADS

The deeper subcutaneous planes of the midface can be imagined as having localized fat compartments that are separated by septal tissue. These can be classified as either

superficial or deep. The superficial fat compartments are located between the skin and the plane of the SMAS. The SMAS is a continuous and organized fibrous network connecting the facial muscles, the other fascia (e.g., parotid fascia) and the periosteum, with the dermis. It is made up of a three-dimensional structure of collagen fibers, elastic fibers, fat cells, and muscle fibers.^[21]

The fat tissue of the superficial compartments is found within this fibrotic network. Specifically, the deep fat compartments are seen under the SMAS plane and beneath the mimetic muscles [Figure 2].^[21] Soft tissue fillers may be used to correct deep furrows of the glabella, periocular lines, inferior orbital rim/tear trough, cheeks/zygomatic area, nasolabial folds, and perioral areas, as well as to augment the lips, jawline, and the crease of the chin.

The fat compartments are known to develop changes as one ages, such as when the medial and central group of fat compartments undergo hypertrophy, ptosis, and downward migration. The only fat compartment, a superficial pad, that undergoes hypotrophy without ptosis is the lateral temporal-cheek fat (LTCF). The medial and central group are often the areas that require lifting.^[21] In Asians, the chin and the Marionette or prejowl sulcus and jawline are the most predominantly corrected areas whereas Caucasians seek volume correction of the zygoma, lateral maxillary areas, and the lips.^[4,17]

For a more profound and longer-lasting effect, that is, in more mature patients, static lines may need to be corrected with the combination of botulinum toxin and low-density HA fillers.^[4]

The primary purpose of HA fillers is to correct age-related volume loss^[7] but these products have recently been used to lift and support sagging tissue, as well as to contour the face and rejuvenate the skin.^[18,22] Restoration

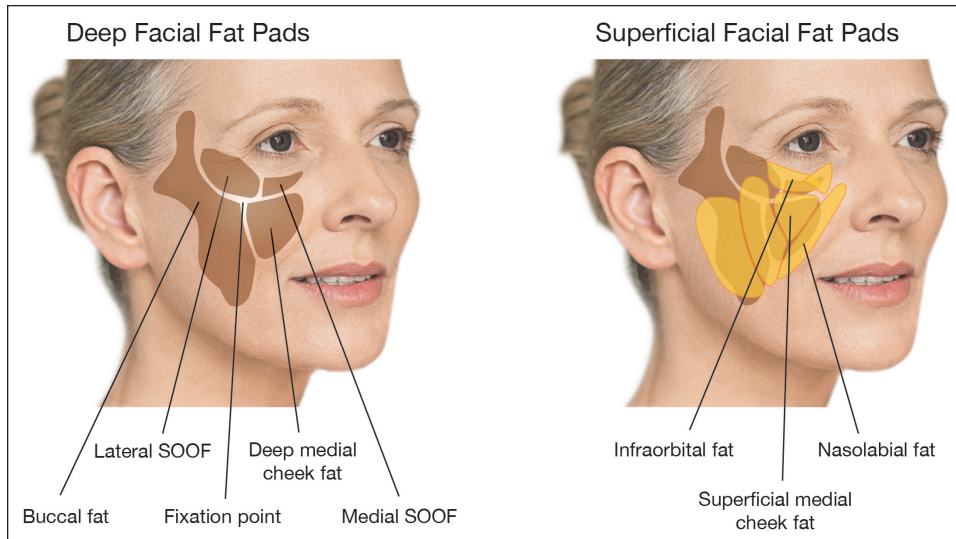


Figure 2: Superficial and deep facial fat compartments. SOOF = suborbicularis oculi fat

of tissue volume loss is commonly done in the area of the midface (i.e., malar areas, periorbital and perioral regions); however, HA fillers have also been used to correct structural deficiencies of the jawline, and for reshaping the chin and the nose.^[4] In this article, the basis of choosing suitable soft tissue fillers is underpinned by the current understanding of the physical properties of HA fillers (i.e., rheology); for example, the recent introduction of the novel HA range with proprietary eXcellent Three-dimensional Reticulation (XTR™) Technology, resulting in three different levels of rheological characteristics (touch, restore, core) to cater to different clinical needs in volumizing and reshaping.^[23]

The effects of the combination of botulinum toxin and fillers have been documented widely in several clinical studies. On the upper face, the combination has been shown to provide better cumulative benefit when used for treating the forehead/glabella rhytide complex and was nominally more preferred by patients than toxin treatment alone.^[24] Patients who have previously been treated with toxin alone for correction of periorbital, temporal, glabellar lines, and crow's feet have rated the combination as "superior" and had only mild and transient reactions.^[25] In the large prospective, multicenter study HARMONY, the investigators evaluated the impact of a global approach to facial rejuvenation by using a staged therapy of several minimally invasive modalities, namely botulinum toxins, subcutaneous fillers, and bimatoprost (indicated for eyelash hypotrichosis). There was a significant increase in baseline satisfaction ratings and perceived younger facial appearance in those treated with the combination.^[26]

Bioabsorbable threads are useful for lifting, mobilizing, and contouring facial tissue. These effects are brought about by the physical effect of traction on the surrounding tissue and biostimulation.^[21] As a result, threads not only address the mild to moderate tissue ptosis that is characteristically seen in the midface and lower face, but they also stimulate the formation of a supportive collagen matrix in the soft tissue.^[12,14,21] Evidence from early, small

nonblinded studies suggests that threads in combination with other aesthetic modalities provide temporary improvement in facial rejuvenation.^[27] However, newer-generation bioabsorbable threads were developed (e.g., anchoring/lifting and stimulating threads) to address the limitations of earlier thread technologies and these have been shown to generate high patient satisfaction.^[28] More studies on the effects of these novel threads in combination with conventional aesthetic techniques to address aesthetic concerns of the midface and lower face are expected to be published in the near future.

Bioabsorbable suspension threads are used in Caucasians to treat ptosis of hypertrophic fat compartments that are often repositioned upward and laterally. For Asians, insertion techniques that reposition soft tissues laterally are desired less because these will further widen the face. A more vertical repositioning of soft tissue using vertical vector techniques and reducing the volume along the jawline and redistributing it in midface is preferred.^[21]

When used altogether, a synergistic effect has been described to occur between botulinum toxin, HA filler, and bioabsorbable threads. Because these modalities have effects that may overlap, pairing or combining these modalities may also lead to improved aesthetic outcomes [Table 1].^[24,29,30] Lastly, the use of multiple modalities avoids use of excessive products.

TECHNICAL CONSIDERATIONS OF COMBINATION TREATMENTS

Every patient must be considered as an individual with unique needs. The fundamental step for each aesthetic procedure is a thorough anatomical–aesthetic–clinical assessment followed by an open discussion with the patient regarding possible outcomes of the procedure.

BEFORE THE PROCEDURE

- Patients often approach us with a specific goal in mind. However, it is up to us to educate the patient so they

Table 1: Synergistic effects of botulinum toxin, HA fillers, and bioabsorbable threads^[24,29]

Region	Combination	Key areas and recommendations
Forehead	Botulinum toxin HA filler	• Dynamic rhytides of the forehead, glabella, temple, and lateral canthi
Medial and lateral cheek	Barbed absorbable threads (MR, LR) STR-2 STR-3 HA filler	• Ptotic and hypertrophic facial shape • Infraorbital area appears flat or slightly concave, convex lower cheek
Jaw line	Barbed absorbable threads (JR) HA filler Botulinum toxin	• Reshaping of the frame of the jawline and prejowl folds, and repositioning ptotic tissues of the lower face • Restoring a smooth contour and reshaping the masseter in order and relaxation of the mentalis muscle to create a smoother and more oval or V-shaped jawline
Nasolabial folds	Barbed absorbable threads (OR-V, OR-H) HA filler	• Hollowing of the cheek and malar areas, convex nasolabial region, and prominent nasolabial folds ^[7]

HA = hyaluronic acid; OR-V = oval reshaping – Vertical technique; OR-H = oval reshaping – H technique; JR = jawline reshaping MR = malar reshaping; LR = lateral reshaping; STR soft tissue reshaping

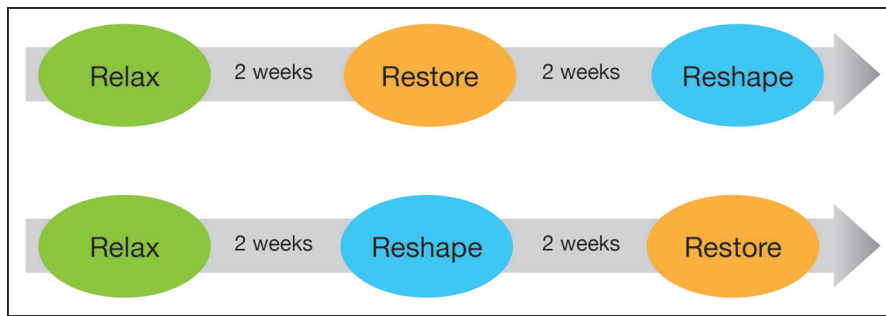


Figure 3: Recommended time intervals in between procedures

know that we should address an anatomic problem rather than focus only on one problem to achieve the endpoint. For example, clients may show pictures of celebrities and may want correction of specific features but are unaware of the appropriate procedures. Hence, the patient should be educated regarding the outcomes of the requested procedures and to undergo only the recommended treatment options. They should also be aware of the risks and benefits of the procedures.^[31]

- A pretreatment photograph may be useful in showing the patients improvements. Ensure adequate lighting and the availability of high-quality cameras in your clinics.
- One must be aware of modern standards of attractiveness to ensure that patient expectations of achieving ethnicity-specific enhancements are met. For instance, it is no longer true that Asians would want to achieve a Western look.
- Proper product selection should be made based on patient needs. For instance, physicians may want to “clean the house” by performing skin resurfacing procedure one to two weeks earlier, using chemical peel or other modalities.
- To treat sagging skin (i.e. marionette lines, jowls), a micro-focused ultrasound (MFUS) and radiofrequency may be used.^[31]
- These resurfacing and rejuvenating procedures are held first to avoid unnecessary manipulation of the face when products, such as fillers or threads, are placed (i.e. bruising or displacement of the injected materials may occur when the sequence is incorrect).
- Mapping of the injection sites by using dermal pencils may be very helpful, particularly for more invasive procedures (i.e. thread procedures).
- Observance of the aseptic technique is a must.^[21] Local anesthesia and/ or icing may be the pain management technique of choice for deeper procedures—ensure that the patient experiences minimal pain during the visit.

DURING THE PROCEDURE

- Injection of botulinum toxin on the face and neck can be done by using a fine needle with the appropriately adjusted dose based on the patient’s muscle mass and hyperdynamic muscle activity (i.e. Asians tend to require lower doses of toxin).^[22]

A



B



Figure 4: (A) Before treatment. (B) A defined, sharper and more masculine jawline can be seen after fillers and threads in a middle-aged male

- As a rule, botulinum toxin should be administered during the first treatment session. The toxin targets dynamic wrinkles related to the expressions; hence, treatment effects can be best shown before other procedures.
- Two weeks later, this can be followed by either HA fillers or threads. Though some practitioners tend to do combination injections at one go, BALI does not recommend performing filler injections, threads with toxins on the same day together to prevent



Figure 5: (A) Before treatment. (B) A slimmer and younger-looking appearance can be observed in this female in her 50s after fillers and threads



Figure 6: (A) Before treatment. (B) Concerns of premature signs of aging were addressed in this patient in her early 40s by using toxins and threads

overcorrection and managing untoward events from multiple procedures.

- It is preferable to have HA filler injections progressively applied on several visits from the deeper planes going outward to avoid abrupt facial changes as well as bruising and swelling [Figure 3].^[9]
- The application and timing of thread insertion, on the other hand, requires extensive knowledge of dissection and fixation planes as well as technical knowhow.^[14] Guidance on technical approaches and practical approaches relevant to HA filler injections and the placement of bioabsorbable threads are the subject of other publications by BALI.

AFTER THE PROCEDURE

- After filler injections and/ or thread placement, advise the patient to avoid massaging the areas for about 6 h

and to avoid exposure to extremes in temperature to prevent bruising. There should be no strenuous activity for the same period to avoid raising blood pressure caused by the vasomotor effects of epinephrine and/ or lidocaine.^[32]

- Sleeping with the head elevated for one night may be necessary to prevent short-term post-traumatic edema,^[32] and over-the-counter pain medications may be used only if appropriate.
- Use of skin care products can only be resumed after a day of the procedure, again to prevent bruising.
- Another skin resurfacing procedure using chemical peel, may be a useful combination to optimize aesthetic treatment outcome during follow-up (2–4 weeks after).^[33] Touch ups may be done also during the same visit.

CASES WITH POSTPROCEDURAL OUTCOMES

A male patient sought treatment for deep grooves in the nasolabial folds and moderate sagging facial tissue around the jawline and the neck area. After filler injections at the nasolabial area and the chin, and suspension thread placement to lift the sagging tissue, there is noticeable improved definition of the facial lower thirds [Figure 4A and B]. Similar outcomes can be observed in this female patient [Figure 5A and B] who underwent filler and thread injections to correct signs of aging in the lower third of the face. She also went radiofrequency therapy to target wrinkles. There is a noticeable lift, which provides her a slimmer and younger-looking appearance. A younger female patient sought treatment for concerns of premature signs of aging [Figure 6A and B]. With botulinum toxin injected at the forehead and at the masseter, her frown lines are less visible whereas the mandibular angle looks softer. Followed up by threads inserted directed up and laterally, she now appears to have a youthful, less tired-looking appearance.

MANAGEMENT OF ADVERSE EVENTS

Compared with single procedures, adverse events can be more frequent and, therefore, it is important to have adequate knowledge and proper patient assessment, as well as ensure correct technique and postoperative care [Table 2].^[34]

Adverse events may be classified according to the onset (i.e. immediate onset or delayed). It is advised to educate the patient about seeking prompt medical attention when encountering adverse events and most especially to report reactions distal to the injection site (i.e. tissue necrosis or blurred vision), as these may signify vascular compromise.^[34-36]

Existing consensus guidelines on facial rejuvenation have focused on the optimal use of combined injectable modalities (e.g. fillers, toxins) with the aim of relaxing facial muscle and restoring volume loss. In recent years, more practitioners have expanded their practice and

Table 2: Overview of adverse events associated with combination treatment

Adverse event	Signs	Symptoms	Prophylaxis and treatment
Injection site reactions	Prolonged erythema, tenderness	Pain, itching, edema	Hot compress, ice therapy, surgical correction, or removal of threads
Hypersensitivity	Erythema, nonfluctuant nodules	Itching, redness	Antihistamine or steroids
Infections	Warmth and tenderness	Discharge, edema, pain	Antibiotics, surgical intervention, debridement, drainage, and meticulous dressing
Errors in placement	Nodules, tenderness, asymmetry	Compromised movement, dysesthesia, paresthesia, anesthesia	Surgical correction, hyaluronidase dissolution of the filler materials, and manual adjustment of the thread track; for toxins, usually the effect will improve after four to eight weeks
Vascular compromise	Blanching, tissue necrosis	Blurred vision, loss of vision, pain	Emergency treatment by specialists in vascular surgery/ophthalmology

armamentarium to include not only botulinum toxin and HA filler injections but also bioabsorbable suspension threads to reshape facial contour and redefinition. Finally, chemical, physical, and mechanical peels for a skin resurfacing can complete the panel of treatments for an integrated treatment approach.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/ have given his/ her/ their consent for his/ her/ their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

The authors of the article have received honoraria from A. Menarini Asia Pacific, Pte Ltd for their participation in the meeting.

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