International Journal of Pharmaceutical Science and Research
ISSN: 2455-4685, Impact Factor: RJIF 5.28
www.pharmacyjournal.net
Volume 1; Issue 7; November 2016; Page No. 17-23

Facial rejuvenation and correction of facial deformities using dermal fillers and botulinum toxins

[1] Deepika Sondh, [2] Amrita Parle

[1] M. Pharm, Department of Quality Assurance, Delhi Pharmaceutical Sciences and Research University, New Delhi, India
[2] Associate Professor, Department of Quality Assurance, Delhi Pharmaceutical Sciences and Research University, New Delhi, India

Abstract
Injection of dermal fillers is the second most frequent nonsurgical cosmetic procedure performed in the world. Dermal fillers are an option in the treatment of volume deficiency, scars, and rhytides; facial sculpting; facial contouring; and augmentation of specific anatomical sites such as the lips. The number of injectable dermal fillers available on the market increases yearly. This paper extensively reviews the properties of the available fillers, such as their longevity, available combinations, clinical indications and adverse effects, and how these properties affect the choice of filler agent for a particular patient or a particular site. Also, future trends in the advancement of dermatological aesthetics been discussed.

Keywords: dermal fillers, rejuvenation, hyaluronic acid, collagen, poly-l-lactic acid, calcium hydroxyapatite

1. Introduction
Many types of dermal fillers are currently used in routine clinical practice for cosmetic and medical purposes. The main indication for these products in dermatology is facial rejuvenation. On the basis of longetivity the can be classified as temporary fillers and permanent fillers. The differences between these types of fillers are in their diverse modes of action and the length of time the filler material remains in tissue before it is absorbed. According to data published by the American Society of Aesthetic Plastic Surgery, more than 85% of dermal filler procedures are performed with hyaluronic acid derivatives. The widespread use of this type of filler is due to its excellent safety profile, ease of application, and the good results achieved.
Dermal fillers are an option for treatment of volume deficiency, scars, and hydrides, as well as for facial sculpting. Fillers are also used for facial contouring and augmentation of specific anatomical sites such as the lips. The perfect dermal filler should be safe, inexpensive, hypoallergenic, easy to distribute, easy to store, injectable with little time, and painless to inject; should require no allergy testing; exert no downtime on the patient; and have no risk of complications. Also, its results should feel natural under the skin and should be long lasting, consistent, predictable, and easy to remove if necessary. Although the perfect dermal filler does not exist, the number of injectable skin fillers available on the market increases yearly with advances in technology. Combinations of dermal fillers and botulinum toxins are extensively used for the treatment of facial aging and wrinkles. Since, botulinum toxin act as a paralyzing agent which reduces the muscular traction and avoid the problem of the withdrawal of fillers it can be considered to enhance the performance of the filler.

Dermal Fillers
Dermal fillers are used for treatment of volume deficiency, scars, wrinkles as well as for facial sculpting. Fillers are also used for facial contouring and augmentation of specific anatomical sites such as the lips. The ideal filler should be painless on injection, non-allergenic, non-carcinogenic, non teratogenic and non-migratory. The ideal filler should be stable at room temperature, should have a long shelf-life and be free from all transmittable diseases. There should not be any sort of local adverse reaction on the skin. Dermal fillers can be categorized into two types:-

2. Permanent Fillers
The permanent dermal fillers may be defined as the dermal fillers which are used to obtain a long lasting and permanent effect on the skin and/or other parts of body. On the basis of chemical constituent used, they can be further classified into following classes-

a) **Polymethyl methacrylate (PMMA)-** The injectable filler, that contains polymethyl methacrylate (PMMA) beads, is the only permanent filler approved by the FDA. The first, FDA approved, marketed product bella fill containing PMMA is manufactured in 2006, by artefill (suneva medical, inc.). Bella fill is the permanent filler used for correcting the nasolabial fold (NLF). It is a suspension of PMMA beads in a bovine collagen delivery vehicle containing 0.3 % lidocaine. The beads are tiny round plastic particles, which are not absorbed by the body but induce fibroplasia and become encapsulated by endogenous collagen. The product should be injected into the immediate subdermis or at the deepest dermal level and thus targets deeper folds and rhytides. A skin test is necessary before treatment to determine possible sensitivity to bovine collagen as it may cause hypersensitivity reactions. A significant number of nodules have been reported after injection of the lips; therefore, injection of Bellafill for lip augmentation is not recommended. The main concern about the use of permanent filler, is the possibility of late-onset adverse events or displacement of the material when facial structures change with the aging process.
b) **Hydroxyethyl Methacrylate in Hyaluronic acid-** The products based on a combination of hydroxyethyl methacrylate and HA (Hyaluronic acid) are Dermalive and Dermadeep. Dermalive is a mixture of 60% crosslinked HA fluid produced by fermentation in bacterial culture and 20%

hydroxyethyl methacrylate and 20% ethyl methacrylate particles. This filler must be implanted in the deep dermis and is not indicated for the treatment of superficial rhytides. Dermadeep must be implanted even more deeply, in the hypodermis or periosteum.

c) **Polyacrylamide Gel-** Presently used permanent dermal fillers of polyacrylamide gel include Interfall (Interfall Ltd., Kiev, Ukraine), Formacryl and Argiforn, and Amazing Gel. They have replaced the 2 most widely known polyacrylamide gel products Bio-Alcamid and Aquamid. Aquamid is a hydrogel, composed of 2.5% polyacrylamide and 97.5% water. This product is used to correct deep defects, it has a high complication rate and its use is often associated with the formation of granulomas, therefore its use is increasingly rare.

d) **Silicone-** Injectable liquid silicone was one of the permanent fillers mostly used in the past, but now they are replaced with permanent fillers like polyacrylamide gel and PMMA. Still there are various liquid silicone products available in the market, including Adato SIL-OL 5000 (Bausch & Lomb, Rochester, NY, USA), Silikon 1000, and SilSkin 1000. There is also a product, marketed under the brand name Bioplastique (Uroplasty BV, Netherlands), that consists of solid silicone particles suspended in a polyvinyl pyrrolidone carrier. All these materials must be implanted in the deep dermis or on the dermis-panniculus adipose plane.

3. Nonpermanent Dermal Fillers

Most dermal fillers used today are temporary or re-absorbable products which last between six to nine months. These types of fillers are considered to be very safe as the product is absorbed by our body over a period of time so any unwanted side effects are not long lasting. They can be used to address a variety of concerns from fine lines and wrinkles to volume loss. Non – permanent fillers are made from various kinds of man-made and synthetic materials including collagen, hyaluronic acid and calcium hydroxylapatite. The FDA has approved a number of nonpermanent dermal fillers, which can be classified into following classes-

a) **Poly-L-Lactic Acid-** The first filler which was approved by FDA to restore and/or correct the signs of facial fat loss (lipoatrophy), was poly-L-lactic acid (PLLA; Sculptra (Galderma), in 2004. It was approved by FDA in 2009 for shallow to deep NLF (naso labial fold) deficiencies and other facial wrinkles in immune competent individuals. The area most frequently and successfully treated is the hollow of the cheek, the NLF and pre-jowl folds, the malar area, and the temporal areas. The injected area should be vigorously massaged for 5 min to assure proper dispersion in order to optimize results and avoid nodule formation. PLLA is considered to be a deep tissue regenerator, providing soft-tissue augmentation through stimulation of fibroblast production.

b) **Calcium Hydroxylapatite (CaHA)-** It is a synthetic, non-animal, inorganic compound with a chemical structure identical to components like Hydroxyapatite – Ca5(PO4)3OH + Ca CO3 and Carbonate apatite – Ca10(PO4)6CO3, found in bone and teeth. Hence, CaHA injectables are considered non-immunogenic, minimizing any risk of an allergic reaction to the product. Over time, the CaHA microspheres are degraded into calcium and phosphate, and are excreted by the body. Within several weeks after injection, the gel carrier is absorbed. It consists primarily of carboxymethyl cellulose, water, and glycerin. CaHA is an injectable product approved by the FDA in 2006 to restore and/or correct the signs of facial fat loss (lipoatrophy) in patients, as well as for sub-dermal implantation for correction of moderate to severe facial wrinkles and folds, such as the NLF. Injections should be placed deeply rather than superficially to avoid visible material. CaHA, should be avoided in areas such as the lips because of the increased risk of nodule formation. There have been reports regarding nodule development after injection of fillers into the dorsum of the hands.

c) **Hyaluronic acid**

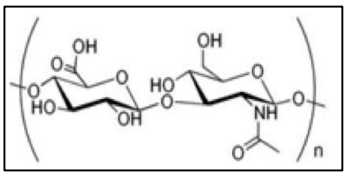

Fig 1: structure of hyaluronic acid

Hyaluronic acid is the most abundant glycosaminoglycan found in the human dermis. It is found in the extracellular matrix of the skin, the vitreous body of the eye, and the articular cartilage. It is an extremely hygroscopic molecule, binding up to 1000 times its weight in water. This property allows it to contribute to the hydration and volume of tissues, as well as providing structural support. Naturally occurring HA is a viscous liquid in its non-cross-linked or free form. It is completely metabolized in a few days, after an injection into the skin, by free radicals and enzymes such as hyaluronidase, which are naturally present in the skin. Hyaluronic acid dermal fillers play an integral part in the correction of changes associated with aging; especially those associated in the lower one-half of the face, from the nasolabial folds to the vertical lip lines of the lips, the marionette lines around the mouth, and in the thinning of the lip itself. They also can be used for volume enhancement of the cheeks.

Table 1: Characteristics of the branded hyaluronic acid (HA) dermal fillers approved by the US Food and Drug Administration (FDA)

S. No.	Characteristics	Restylane	Perlane	Juve derm ultra	Juve derm ultra plus	Belotero	Juve derm voulma	Restylane silk
1.	Indications	NLFLip augmentation	NLF	NLF	NLF	NLF	Cheek augment-ation	Lip augmenta-tion
2.	HA concentration	20 mg/ml	20 mg/ml	24 mg/ml	24 mg/ml	22.5 mg/ml	20 mg/ml	20 mg/ml
3.	Form	Particle 125-10,000/ml	Particle 325-10,000/ml	Homogeneous	Homogeneous	Homogeneous	Homogeneous	Particle 50-220/ml
4,	Cross-linker	BDDE	BDDE	BDDE (6%)	BDDE (8%)	BDDE	BDDE	BDDE (1%)

Table 2: Some of the Indian brands of Hylauronic acid dermal fillers

S. no	Brand name	Manufacturing company	Indication
1	Emerve	GALDERMA	NLF, Marionette lines
2	Juvederm	ALLERGAN	NLF, cheek augmentation
3	Yvoire	LG life sciences	NLF, jowl lines, fine lines.
4	Restylane	ALLERGAN	NLF, lip augmentation

d) Collagen Fillers- Collagen makes up 70% to 80% of the dermis. With age, dermal collagen is lost and becomes fragmented, as the transformation from new and complete collagen (type I) to fibrotic collagen (type III) gives rise to the appearance of rhytides and folds. One of the advantages of collagen fillers over HA is that they are less viscous and can be more useful for the correction of fine lines and wrinkles because they are less likely to produce irregularities when injected superficialy. Depending upon the origin, they can be classified into following categories-

1) Bovine Collagen- The two bovine collagen products most used are Zyderm and Zyplast (Allergan Inc, Santa Barbara, California, USA). Bovine collagen is a temporary and biodegradable filler. It was the first collagen to be sold as a filler. Pretreatment skin testing is necessary. The incidence of local hypersensitivity reactions in patients tested prior to treatment is estimated to be between 3% and 5%.
2) Human Collagen:- Human collagen is produced from human dermal fibroblast cell lines using bioengineering techniques. No pretreatment skin test is required. The two most frequently used dermal filling products are Cosmoderm and Cosmoplast (Allergan Inc, Santa Barbara, USA). Both products are biodegradable and therefore temporary and have duration of effect from 3 to 7 months.
3) Porcine Collagen-Porcine collagen is also temporary and biodegradable and has about around 12 months duration in the tissue. A number of products on the market contain porcine collagen like Evolence and Evolence Breeze (ColBar Life Science, Herzliya, Israel).

e) Autologous cell therapy- The product consists of cultured autologous fibroblast cells. Fibroblasts are obtained from the patient by performing biopsy and the fat is extracted from areas such as the thighs or abdomen using special cannulas. The harvested fat is then purified by centrifugation. The processed fat is then injected into the treatment areas depending on the needs of the patient (forehead, brow, cheeks, suborbital region, perioral areas, jaw line, etc). Fat is injected at different depths (subdermal, intramuscular, and subperiosteal) and in different quantities depending on the patient and the anatomical area being treated. The current treatment regimen is three administration sessions 5 weeks apart, with a dose of 0.1 ml of a suspension. The use of the patient's own fat as a filler is a safe and natural method. One drawback of this technique is that it must be performed in an operating theater environment with local anesthesia and sedation. The longevity of injected autologous fat ranges from 8 months to several years.

4. Botulinum neurotoxins used as an adjunct

Botulinum neurotoxin is the exotoxin produced by Clostridium botulinum. Seven distinct serotypes of the neurotoxin, designated type A to G, have been identified. Type A is the most commonly used toxin for cosmetic purposes, although there are some reports about the use of type B toxin in aesthetics. The toxin is a protein molecule consisting of a 50-kd light chain and a 100-kd heavy chain, linked by a disulfide bonding.

All BoNTA (Botulinum neurotoxin –A) molecules consist of 1 heavy chain and 1 light chain polypeptide linked by a disulfide bond. They all share the same 3-step mechanism of action, which inhibits release of acetylcholine from peripheral cholinergic nerve endings at the neuromuscular junction.

1. First, the heavy chain binds to specific surface receptors on nerve endings.
2. The BoNTA molecule then undergoes internalization via receptor-mediated endocytosis and the disulfide bond is cleaved.
3. The light chain undergoes translocation to the cytosol, where it cleaves polypeptides essential for docking, fusion which inhibit the release of acetylcholine vesicles through the cell membrane and further resulting in chemical denervation of the muscle. Recovery of neurotransmission occurs as the neuromuscular junction recovers from SNAP25 (synapsomal associated protein) cleavage and as new nerve endings are formed. The mechanism of Botox is to prevent the release of acetylcholine at the motor end plate. Without this release, the electrical impulse is not transmitted; hence, the muscle does not move.
4. Role of acetylcholine in skin aging - Healthy ageing is associated with mild endothelial dysfunction (Singh *et al*. 2002), and a decreased vasodilatory response to ACh. Aged human skin exhibits altered contributions of COX products to both tonic cutaneous blood flow and exogenous ACh-mediated vasodilation. In the older subjects COX isoenzymes produces both vasoconstrictor (PGE2, thromboxane A2) and vasodilator (PGI2) substances, and with growing age there is a shift in the balance between COX vasoconstrictor and vasodilator products. So to favor vasoconstriction COX is inhibited. Specifically, there may be alterations in the expression of the COX isoenzymes. This age-related shift toward increased vasoconstriction through alteration in COX products as well as COX isoenzyme expression leads to increase in vasoconstrictor of COX products that contribute to tonic cutaneous vascular tone in aged skin responses.

   Currently, there are four commonly used preparations of botulinum toxin-

   - Onabotulinumtoxin A (Botox; Botox Cosmetic, Allergan, Irvine, CA),
   - Abo-botulinumtoxin A (Dysport; Ipsen, Ltd, Berkshire, UK),
   - Incobotulinumtoxin A (Xeomin; Merz Pharma-ceuticals, Frankfurt, Germany),
   - Rimabotuli-numtoxin B (Myobloc; Solstice Neurosciences, San Francisco, CA).

Although the clinical effect of each is similar, they differ in their chemical structure, associated proteins, manufacturing and purification processes and clinical efficacy.

Treatment using botulinum neurotoxin as an adjunct- The concomitant use of botulinum toxin and dermal fillers is well suited for associated wrinkles. This combined approach appears to promote longer-lasting results than their isolated use. Biodegradable fillers are influenced by the movement of the muscles that act in the area into which they are injected.

Mechanical forces resulting from mimetic action might break the polymers of fillers.

Botulinum toxin act as a paralyzing agent which reduces the muscular traction and avoid the problem of the withdrawal of fillers it can be considered to enhance the performance of the filler. Fillers can also improve the result of botulinum toxin. Because fillers are considered tissue micro-expanders, the dermis becomes thicker and fewer wrinkles are produced with mimetic movements. So, the chemical denervation using botulinum toxins would have the following purposes-

1. It eliminates or reduces the dynamic/muscular component of rhytides formation;
2. It may increase the longevity of dermal fillers by reducing the supposed mechanical inflammatory influence on atrophy on the implant
3. It may simply reduce the immediate micro-extrusion at the injection sites by repetitive muscular action.

Dosage, Duration and Storage

The average dose of the botox injection depends on the severity, brand name, duration as well as frequency of the treatment.

Table 3: below contains few examples of the different BoNT formulations.

BoNT-A formulations	Dose	Duration
Myoblac	50:1U, 100:1U	16 weeks
Dysport	25U,50U,75U	6 months
Botox cosmetic	50U	90 days

The dosage is based on the biologic potency of the toxin and is expressed in units (1 U is the median lethal dose of the toxin when injected intraperitoneally in the rat). A 100-U vial of the preparation contains 5 mg of toxin as lyophilized powder. Because the preparation is in powder form, it needs to be reconstituted before the injection. The recommended diluents is 0.9% saline without preservatives. It is usually recommended to gently inject the diluents into the vial, avoiding the formation of foam in the complex, which could result in toxin denaturation. Once reconstituted, the solution must be stored at a temperature of 2 °C to 8 °C. After reconstitution, the solution should be used within 4 hours.

Common indications of botulinum neurotoxin includes- indicated for the temporary improvement in the appearance of moderate to severe glabellar lines, the treatment of forehead lines, crow's feet, bunny lines, upper and lower perioral lip lines, gingival smile, marionette lines, dimpled chin, vertical neck lines.

Complications- Overcorrection, Under correction, Asymmetric result Upper eyelid ptosis, Dysphagia, neck weakness, Perioral droop, Bruising, Globe perforation, Diplopia (lateral rectus),Psychosomatic problems

5. Process of using Dermal Fillers

Pretreatment preparation is important to minimize risks and unwanted side effects of dermal fillers. A complete medical history is always necessary and should cover allergic or hypersensitivity reactions to any substance, including anesthetics. Dermal fillers are contraindicated during pregnancy and breastfeeding and are not recommended in immune compromised individuals, patients with autoimmune diseases or receiving certain drugs such as interferon. Patients should be instructed not to take any medication, 10 to 14 days prior to treatment, to minimize the increase risk of bleeding. Non-steroidal anti-inflammatory drugs and vitamin complexes containing vitamin E should be avoided prior to 1 week of the treatment to minimize bruising. Particular attention must be paid to avoiding overcorrection. Topical anesthetics or a nerve block will be used depending on the patient's pain threshold. Some dermal fillers contain lidocaine, which helps the patient to tolerate the injections. Some examples of dermal fillers containing lidocaine are Restylane-L, Restylane Silk, Perlane-L, Juve´derm Ultra XC, Juve´derm Ultra PlusXC, Juve´derm VolumeXC

6. Injection Techniques

A certain amount of practice and experience is required to inject dermal fillers. It is essential to choose the filling agent best suited to each patient, the anatomical site involved. It is also important to determine the appropriate amount of filler to be injected. Another crucial aspect in achieving a good outcome with dermal fillers is the depth at which the material to be implanted. Most dermal fillers are injected into the deep dermis or the fatty tissue. Following are the number of different injection techniques:-

a. Linear Threading or Tunneling - In the linear threading technique the needle is introduced along the length of the fold or line and a thread of filler is then gradually deposited as the needle is withdrawn. This technique is mainly used to correct isolated rhytides or folds, such as the nasolabial fold.
b. Serial Puncture:-Serial puncture involves multiple injections along the wrinkle or fold. These must be placed close enough together to prevent irregularities, and massaging the area will help to distribute the product evenly.
c. Radial Fanning:-In the radial fanning technique, threads of filler are deposited using the tunneling technique. However, before the needle is completely withdrawn, it is reinserted in a radial pattern and another thread is deposited along the new axis. This is repeated as necessary until the desired effect is achieved. This technique is used to augment volume in the malar region.
d. Cross hatching- Crosshatching is another variation on the tunneling technique. Several parallel lines of filler are created across the treatment area followed by a second set of parallel threads perpendicular to the first set forming a grid pattern. This technique is used to correct marionette lines and the prejowl sulcus.

7. Major indications for Dermal Fillers

a. Facial rejuvenation-The main indication for the use of dermal fillers is facial rejuvenation. Their use, often in combination with botulinum toxin injections, produces very satisfactory results with a very low incidence of side effects. Ideal subjects are patients with early signs of aging. The nasolabial fold becomes accentuated with age, forming an increasingly pronounced furrow. In this area, dermal fillers should be injected deeply. The techniques most often used are tunneling and serial puncture. The injection is usually made parallel and medial to the fold, with the initial insertion point at the lower end. The desired effect can usually be achieved with 0.5 to 2 ml of filler per side.
b. Correction of lower eyelids-The area of improvement is the tear trough located below the lower eyelid in the transition area between the eye and the malar region. The loss of natural convexity between the lower eyelid and the malar

region gives rise to a tired look and a more aged appearance, with the formation of a depression and an unsightly shadow. Tunneling and serial puncture are the preferred techniques for correcting tear trough deformity. Permanent fillers are not usually recommended for this purpose because poor technique can easily give rise to surface irregularities in this area.

c. Lip augmentation- In young patients, increased volume in the central part of the lips is all that is needed. The filler is injected into the lip mucosa along the transition line between mucosal tissue and skin. Temporary fillers are usually used for this purpose. The injection techniques used are tunneling and serial puncture. The filler should be injected into the sub mucosa above the orbicularis oris muscle. When the needle is correctly positioned, filler can be injected without resistance and elevation of the edge of the lip is immediately apparent. The overall appearance of the lips can be enhanced by shaping the philtral columns through injection of filler into the mid dermis starting from the base of the columns.
d. Treatment of marionette fine lines- Dermal fillers are used in the treatment of marionette lines, the folds that extend downwards from the corners of the mouth and give rise to an aged appearance and an unhappy expression. The injection techniques usually used in this case are tunneling and serial puncture. Dermal fillers can improve this defect and gives the patient a younger appearance by restoring the transition between the chin and the posterior jaw line.
e. Nose remodeling-Nose remodeling with dermal fillers is a very attractive alternative to conventional surgery. The tip, bridge and root of the nose can all be projected or raised. Temporary fillers are normally used for this purpose. To prevent lateral spread of filler, the skin should be pinched during the procedure. The injections should be deep, and small volumes (0.5 to 1 ml) are usually sufficient to achieve the desired effect.

8. Minor indications of Dermal Fillers

a. Scarring- The injection of HA can improve the patient's appearance, especially in the case of atrophic acne scars. Small amounts of filler should be injected over a number of sessions. Good long-term results have also been reported with poly-L-lactic acid and porcine collagen.
b. Chin Shaping in patients with Implants- In patients with chin implants, contouring with HA can improve the transition between the implant and the adjacent soft tissue. To obtain the best results, these treatments are usually combined with botulinum toxin treatment.
c. Earlobe Treatment- growing age leads to sagging of ear lobes. Treatment injection of fillers such as HA can improve their appearance. The effects of treatment last longer in the earlobes than elsewhere, probably because it is metabolically inactive tissue that moves very little.
d. Hand Rejuvenation- Hands can also be improved with dermal fillers, although this application is not very widespread. Stabilized HA fillers are a good choice. Other fillers that have been used in the hand include calcium hydroxylapatite and bovine collagen.

9. Complications Associated with Dermal Fillers

Temporary dermal fillers are associated with a very low incidence of complications in comparison to permanent dermal fillers. For temporary dermal fillers most complications are mild and of limited duration.

Complications Associated with Temporary Fillers

- Complications that may appear immediately are local redness, inflammation, and bruising. Bruising is caused when a vessel is accidentally punctured by the needle or when pressure is exerted on the vessel by the filler. Both erythema and edema are due to inflammation after trauma caused by the injections but may also be related to the hygroscopic properties of the injected material. While erythema usually resolves within a few hours, edema may persist for 2 to 3 days. The risk of edema can be minimized by limiting the number of percutaneous punctures, by using anesthetics containing epinephrine, by applying ice or cold compresses after the procedure.

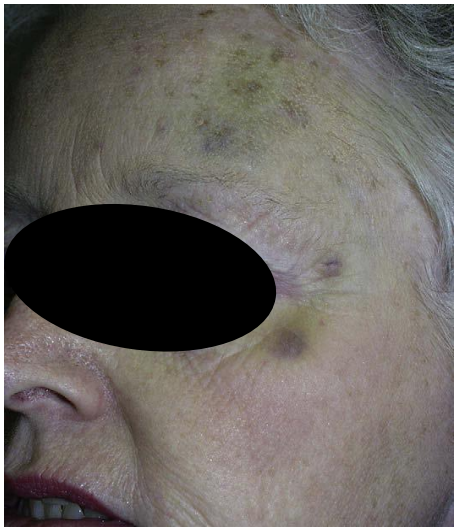

Fig 2: Bruising effect

- The presence of visible filler material in the form of whitish papules or palpable or visible nodules is also observed. This complication is usually caused by poor technique, when the filler material is injected very superficially. All types of nodules can be treated by firmly massaging the tissue. If the problem does not resolve, nodules can be pricked with a needle and drained or they can be injected with corticosteroids. If they persist despite these measures, systemic treatment with corticosteroids can be considered.
- Necrosis at the injection site is a rare but severe complication. It may occur when the material is injected into the angular artery of the nasolabial fold or the supratrochlear artery in the glabellar region.
- Headache, sinusitis and respiratory symptoms are other short term complications related to the use dermal filler.

10. Complications Associated With Permanent Dermal Fillers

Asymmetry-Asymmetric treatment results are not uncommon and can be a result of injector placement or patient anatomic variation. One of the most common asymmetries is the Spock eyebrow. This is a demonic curvature of the lateral brow that occurs when the central frontalis is deactivated but the lateral frontalis is active and only lifts the brow tail (Fig.3). This is easily corrected by placing some additional Botox at the active area on the frontalis.

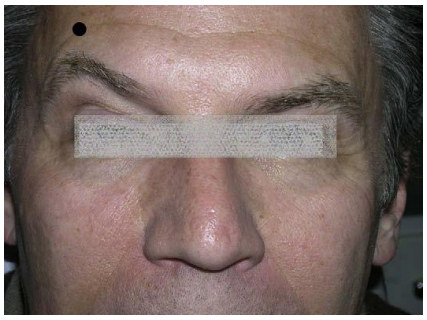

Fig 3: this patient exhibits the Spock eyebrow from under treatment of the lateral frontalis. The black circle illustrates the area to retreat to correct the problem.

Perioral Droop- Injecting Botox in combination of other dermal fillers in the lips to address vertical rhytids, injecting the depressor anguli oris (DAO) to upturn the corners of the mouth, and injecting the mentalis to address skin puckering of the chin have become commonly requested treatments. Injecting the lower face is more tenuous in terms of complications that the upper face. Lip, DAO, and mentalis injections all can cause or contribute to dysfunctional animation of the perioral region (Fig.4). The best treatment for this is prevention.

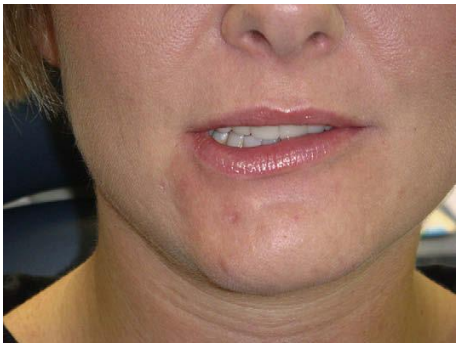

Fig 4: this patient was treated for the lip depressors (likely the depressor labii) were affected. The patient's left side is affected in this image.

Bruising/Hematoma- they are a harmless but disconcerting problem for patients and surgeons. The lips and perioral areas are vascular and even the best injectors on occasion experience bruising and, less frequently, hematoma. Making sure that patients are not taking any substances that effect platelet aggregation is a primary consideration. Also, icing the lips before and immediately after injection is helpful. Fig.5 shows bruising or hematoma that can occur with facial fillers. These areas are treated initially with ice, then with heat.

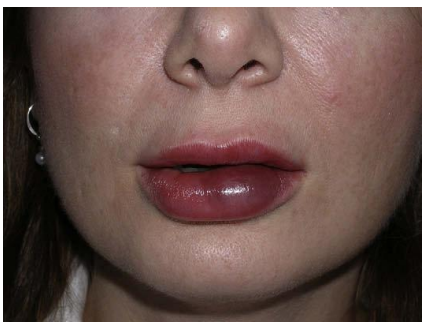

Fig 5: This patient developed swelling, bruising and minor hematoma immediately after filler injection.

11. Lumping

One of the most common novice problems is an in homogeneous placement of the filler material. Massage is just as important as filler placement. The filler is placed in small spheres or strands and is fluid in the tissues. By massaging the injected areas, the filler compacted and blended to form a more contiguous and smooth texture. Failure to do this can lead to palpable and visible irregularities (Fig.6)

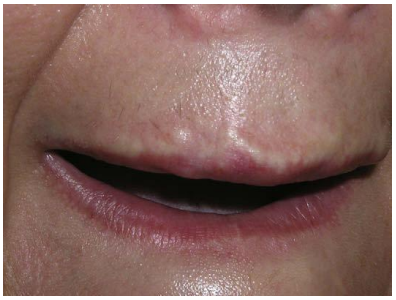

Fig 6: this patient was injected with particulate filler that not only was improperly placed as interrupted boluses but also was not blended by massaging

Tyndall Effect- it is a common complication of facial filler injections. The characteristic blue hue occurs because of superficial placement of hyaluronic acid (HA) filler. Superficial injection of HA in the upper dermis or higher region can result in Tyndall effect. Low concentration HA products (Prevelle® Silk) can be employed to treat fine lines and avoid Tyndall effect. Tyndall effect is easily treated with hyaluronidase, a natural enzyme that catalyzes the hydrolysis of HA. Hyaluronidase (Vitrase®) can be injected subcutaneously into the affected area and carefully massaged. Resolution of Tyndall effect should occur within a day or two.

Fig 7: right-sided nasolabial fold Tyndall effect

Skin Necrosis-it is due to intravascular injection of filler and is perhaps the most dreaded complication of dermal fillers. Prevention and early recognition are absolutely key because treatment of subsequent skin necrosis can be difficult and unsightly to manage. If during injection one encounters immediate pain, skin blanching, or color changes in the distribution of the regional blood vessel the treatment should be immediately stopped. Warm compresses should be applied to the affected area, topical vasodilator can also be applied, and preparation of hyaluronidase can also be injected if an HA is used.

12. Conclusion

There are number of dermal fillers which are used for the treatment but according to the studies it was concluded that hyaluronic acid have least number of side effects as compared

to the other temporary dermal fillers, whereas permanent dermal fillers may cause long lasting adverse complications when injected imperfectly, so to evade the complications it's better to avoid treatment using permanent dermal fillers.

Botulinum neurotoxins used as an adjunct with the dermal fillers helps in attaining the desirable and long lasting effects. The most accepted dermal filler used for treatment of wrinkles is combination of hyaluronic acid with botulinum neurotoxins. A combination of product characteristics contribute to filler selection, such as the appropriate depth of the product placement, the necessity or not of performing an allergy test before the treatment, the number of treatments usually necessary to achieve the desired result, the most frequent adverse effects, whether the product is reversible or not, and the longevity of the product. Also, the anatomical area to be injected is very important in determining the best filler option. For example, for the lips, this review shows that HA dermal fillers are the best option.

13. References

1. Journal of cutaneous and aesthetic surgery managing complication of fillers: rare and not so rare complications by Eckart Haneke, Department of dermatology, Inselepital university of Bern, Bern Switzerland. 2015; 8(4):198-210.
2. Clinics in Dermatology, Advanced botulinum toxin techniques against wrinkles in the upper face by Giovanni Salti, MD, Ilaria Ghersetich.
3. Journal of Dermatology, Hyaluronic acid gel filers in the management of facial aging by Fredric S. Brandt, private practice in Coral Gables Florida USA and Manhattan, Dermatology Research Institute, USA, Alex Cazzainga, Dermatology Research Institute, Florida USA.
4. Current Concepts in Filler Injection- Amir Moradi, MDa,*, Jeffrey Watson, MDb.
5. Dermal Fillers: An Update-Annelyse Cristine Ballin1 • Fredric S. Brandt2,3,4 • Alex Cazzaniga2.
6. Dermal Fillers: Types, Indications, and Complications I. Sánchez-Carpintero,* D. Candelas, and R. Ruiz-Rodríguez Unidad de Dermatología, Clínica Rúber, Madrid, Spain.
7. Long-term complications associated with permanent dermal fillers Jayanth Kunjur a,∗, a.Helen Witherow b,1ST4 in Oral and Maxillofacial Surgery, St George's Healthcare NHS Trust, Blackshaw Road, Tooting, London SW17 0QT, UK b St George's Healthcare NHS Trust, Blackshaw Road, Tooting, London SW17 0QT, UK.
8. Synthetic Fillers for Facial Rejuvenation Johnson C. Lee, MDa,*, Z. Paul Lorenc, MDb.
9. Injectable Filler Techniques for Facial Rejuvenation, Volumization, and A ugmentation Lawrence S. Bass, MD, FACS.
10. Use of Fillers in Rhinoplasty Hyoung Jin Moon, MD.
11. A mechanistic model for the aging of human skin Paolo U. Giacomoni*, Glen Rein Clinique Laboratories, Inc and Estee Lauder Research Park, 125 Pinelawn Road, Melville, NY 11747, USA.
12. Introduction to SKIN aging- Desmond J. Tobin, BSc., PhD.
13. Over-the-counter anti-ageing topical agents and their ability to protect and repair photoaged skin- Eleanor J. Bradley c,∗, Christopher E.M. Griffiths a, Michael J. Sherratt b, Mike Bell c, Rachel E.B. Watson a a Centre for Dermatology Research, Institute of Inflammation & Repair, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK b Centre for Tissue Injury & Repair, Institute of Inflammation & Repair, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK c Alliance Boots Ltd., Thane Road, Nottingham, UK.
14. Complications from Toxins and Fillers in the Dermatology -Clinic Recognition, Prevention, and Treatment Steven H. Dayan, MD.
15. Complications in Fillers and Botox-Joseph Niamtu III, DMD.
16. Overview of Botulinum Toxins for Aesthetic Uses-Michael S. Gart, MDa, Karol A. Gutowski, MD.
17. Complications of hyaluronic acid fillers and their managements-Mohammed H. Abduljabbar a,1, Mohammad A. Basendwh b,a Department of Dermatology, King Abdulaziz University Hospital, Jeddah, Saudi Arabiab Department of Dermatology, College of Medicine, Umm Al-Qura University, P.O. Box 1109, 21912 Al-Qunfudah, Makkah Region, Saudi Arabia.
18. Combination of chemical peelings with botulinum toxin injections and dermal fillers Marina Landau, MD Dermatology Unit, Wolfson Medical Center and Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.
19. Review of the literature on combined treatments with lasers, intense pulsed light, radiofrequency, botulinum toxin, and fillers for rejuvenation- ESTHER CUERDA-GALINDO, MARÍA ANGUSTIAS PALOMAR-GALLEGO & RAFAEL LINARES-GARCÍAVALDECASAS Department of Human Anatomy and Embriology, Universidad Rey Juan Carlos, Madrid, Spain.
20. Botulinum Toxin Examining Duration of Effect in Facial Aesthetic Applications-Timothy Corcoran Flynn1,2 Cary Skin Center, Cary, North Carolina, USA, University of North Carolina, Chapel Hill, North Carolina, USA.
21. Botulinum toxin in association with other rejuvenation methods-Maurı´cio de Maio.
22. Advances in Facial Rejuvenation: Botulinum Toxin Type A, Hyaluronic Acid Dermal Fillers and Combination Therapies–-Consensus Recommendations Jean D. A. Carruthers, M.D. Richard G. Glogau, M.D. Andrew Blitzer, M.D., D.D.S. and the Facial Aesthetics, Consensus Group Faculty Vancouver, Canada; San Francisco, Calif.; and New York, N.Y.
23. Facial Filler and Neurotoxin Complications Kartik Nettar, M.D. Corey Maas, M.D. The Maas Clinic for Aesthetic and Facial Plastic Surgery, University of California, San Francisco e-mail: Drnettar@maasclinic.com.
24. Journal of Dermatological science, 2009; 53(2):96-102, Won-serk *et al*, Byungsoon perk *et al.* 1