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Dermal Fillers - A Mini Review

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Abstract: Aging is a continuous, complex, and dynamic process hampering the facial aesthetics of an individual. People's approach to various means of enhancing their aesthetics has changed. New generation of cosmetic consumers are demanding than ever. They want safe, minimally invasive, long-lasting techniques and natural results with less downtime. This resulted to an increasing demand for non-surgical facial rejuvenation and augmentation techniques world-wide among which dermal fillers is on the promising edge as the results are almost immediate. A thorough knowledge of the various dermal fillers used and the injection techniques is necessary for the best results.

Keywords: Calcium Hydroxylapatite, Poly-L-Lactic Acid, Hyaluronic Acid, Collagen, Polymethyl Methacrylate

INTRODUCTION

Dermal fillers are substances which are injected under your skin to enhance or replace volume that is lost in any part of the skin or subcutaneous fat. The first injectable filling agent was paraffin. However because of its complications, its use was abandoned.[1] In the 1940s and 1950s, silicone was used extensively and was banned by US-Food and Drug Administration (USFDA) because of similar complications. In 1981, bovine collagen was introduced and approved by FDI.[2] Later on, many dermal fillers have come into light of which some of them are being used extensively in the recent past. This article reviews the various materials used in soft tissue augmentation, injection techniques, advantages and complications associated with them.

They are primarily used for alleviation of wrinkles and folds, lip augmentation, treatment of postsurgical and traumatic scars, nasal depressions, AIDS lipodystrophy and to enhance facial contour. However, they are contraindicated in patients with hypersensitivity to the filler material, history of severe allergy or anaphylaxis, bleeding disorders and keloidal tendency. The dermal filling agent used should be effective, easily administerable, storable, inexpensive, inert and long-lasting. Ideally, it should be non-toxic, non-inflammatory, non-carcinogenic and natural looking with minimal side effects.[3]

TYPES OF DERMAL FILLERS

Dermal fillers can be classified in various ways based on the longevity in tissues or nature of filling material.

(1). Based on longevity, dermal fillers are classified as temporary, semipermanent, or permanent. Temporary fillers stay in the tissue for less than a year, semipermanent fillers stay for up to 1.2 years, whereas permanent fillers remain in the tissue for more than two years. However, there is some ambiguity in the classification of semipermanent and permanent status of some fillers, with some sources classifying permanent filler as any filler that lasts more than one year.[4]

(2). Based on the nature of filling material, dermal fillers are classified as absorbable and non-absorbable. Absorbable type of fillers may be derived from the natural sources or synthesized from biocompatible synthetic materials.[5]

1. **Absorbable:**
    - ***a. Synthetic:***
        - i. Calcium hydroxylapatite
        - ii. Poly(L-Lactic acid)
    - ***b. Natural:***
        - i. Hyaluronic acid
        - ii. Collagen
2. **Non-absorbable:**
    - a. Poly methyl methacrylate (PMMA)

Fillers: There are over hundreds of injectable fillers available in the global market. However, only a few of them have FDA approval. Commonly used FDA-approved dermal fillers are hereby discussed.

Absorbable Synthetic Fillers:

(i).Calcium Hydroxylapatite (CaHA): CaHA is the most abundant mineral component of bone. Radiesse is a biocompatible implant of calcium hydroxylapatite (CaHA) which is suspended in a cellulose gel. It is a FDA-approved filler used for facial soft tissue augmentation and specifically for correction of nasolabial folds, marionette lines and folds, soft tissue loss from HIV lipoatrophy[6]. When injected subcutaneously, CaHA microspheres are formed on which fibroblasts accumulate and cause neocollagenesis. In some patients, a layer of fibrin develops around the microspheres until the beads are broken down enzymatically into calcium and phosphate. Advantages of these fillers include biocompatibility and no skin allergy tests are required. However they may cause post treatment erythema, edema and ecchymosis.[7]

(ii) Poly-L-Lactic Acid (PLA)*:* PLA microspheres have been used to ameliorate wrinkles and to correct folds, volume losses and scars[8]. It is biocompatible, biodegradable, and immunologically inert synthetic polymer from the alpha-hydroxy-acid family[9]. Local anesthesia is recommended to reduce pain during treatment. Sculptra is injectable in the form of a sterile lyophilized cake. It is provided in a vial that must be reconstituted with 5 ml sterile water and incubated for at least two hours before use[10].

Absorbable Natural Fillers:

***(i).Hyaluronic Acid (HA) Fillers*:** HA is a mucopolysaccharide which was discovered in the vitreous of cow's eyes[11]. It forms the fluid matrix of the connective tissue. In its natural form, HA has a half-life of only one day in dermis and must therefore be chemically stabilized through cross-linking to function as dermal filler. Balazs and co-workers produced bis-ethyl-sulfonyl cross-linking process that links every hyaluronic acid molecule into a continuous cross-linked polymer network such that the individual molecules are no longer freely soluble[12]. HA is injected into the dermal tissue to provide a space-occupying viscoelastic supplement for the intercellular matrix of the connective tissue. This viscosupplementation or augmentation of the dermal tissue can result in the correction of skin contour deficiencies caused by wrinkles and depressed scars. Hylaform is a hyaluronic acid filler derived from rooster combs and remains in tissue for six to nine months. The advantage of HA is that it does not require any allergy tests. Persistent, bothersome hyaluronic acid derivative nodules formed after injection can be treated with hyaluronidase.[13]

(ii).Collagen: Bovine collagen (Zyderm 1 & 2, Zyplast) is the most commonly used injectable material for soft tissue augmentation in the world. However, the telopeptides in bovine collagen can elicit an immune response when implanted in a foreign host. To reduce the risk of an immune response, the telopeptides are removed from the bovine collagen using a protease enzyme, pepsin.[14] Bioengineered Human collagens are derived from cadaveric skin (Alloderm, Cymetra) or laboratory culture of human fibroblasts Cosmoderm 1 & 2, Cosmoplast) to reduce the allergic risk[15].

Non-absorbable Fillers:

(i).Polymethyl Methacrylate (PMMA) Microspheres: It is used widely in fabrication of dentures and in prosthetic devices. The filler is suspended in 3.5% bovine collagen and 0.3% Lidocaine Hydrochloride. Most commonly used to fill in nasolabial area, glabella, radial lip lines, and corners-of-the-mouth[16].

Artecoll is an FDA approved soft tissue filler composed of PMMA microspheres in bovine collagen. PMMA microspheres act as a matrix to stimulate collagen deposition over a long period of time. Skin test should be optimally carried out 14 to 21 days prior to the procedure[17].

INJECTION TECHNIQUES

The dermal fillers are injected into the subcutaneous tissues using different injection techniques[18,19]. The most common injection techniques used for facial augmentation are serial puncture, retrograde linear threading or tunneling, fanning and cross-hatching. Different dermal fillers have different site of deposition of the material and the injection technique used also varies. Some of them do require an anesthetic for the procedure[20] (Table-1):

1. **Serial Puncture:** The skin is pulled taught to stabilize the defect and multiple boluses of filler are delivered along the defect line. The injection sites should be close enough to form a continuous smooth bead.
2. **Retrograde Linear Threading Or Tunneling**: When the linear threading or tunneling technique is used, the needle enters the skin, bevel up, at a 30° to 45° angle and is fully inserted to create a tunnel for filler placement. The filler is then uniformly distributed, in a retrograde fashion.
3. **Fanning**: With fanning, the needle is inserted, bevel up, through a single entry point and then pivoted to create a series of linear tunnels in a fanlike pattern by radially changing the needle direction.
4. **Cross-Hatching:** Cross-hatching delivers linear threads in a predetermined grid by multiple punctures.

Table 1: Injection techniques and Site of placement for various dermal fillers

Dermal Filler	Brand	Site Of Placement	Injection Technique	Mechanism Of Action	Allergy Test	Anesthetic
Hydroxyl Apatite	Radiesse	Deep dermis	Threading	Stimulator	No	None
Poly-Lactic Acid	Sculptra	Deep dermis	Threading	Stimulator	No	None
Hyaluronic Acid	Hylaform	Mid-dermis	Serial puncture and threading	Stimulator	No	None
Collagen	Zyderm 1&2, Zyplast Alloderm, Cymetra Cosmoderm 1&2, Cosmoplast	Dermis	Serial puncture, threading	Volumizer	No	None
Polymethyl Methacrylate	ArtecolI	Reticular dermis	Layered, tunneling technique	Stimulator	Yes	Lidocaine

COMPLICATIONS

Complications with the use of dermal fillers are infrequent and are usually minor. These complications can be categorized as immediate-, early-, or late-onset events (Table-2) Thorough knowledge of the technology and potential adverse effects is essential to maximize patient benefit and to avoid serious complications. Sometimes even with the best technique, complications can occur. Gentle massage and warm compresses can be beneficial in vascular complications. In cases of impending massive skin necrosis, hyperbaric oxygen can be used. Symptomatic and visible nodules, which may appear white, tan, skin-colored, or red when acutely inflamed, require treatment. Physician should go for corticosteroid treatment in non-inflammatory nodules and antibiotics in case of inflammatory nodules. Persistent, bothersome hyaluronic acid derivative nodules can be treated with hyaluronidase.[4,21]

Table-2: Complications of dermal fillers

Immediate-onset complications (0–2 Days)	• Hypersensitivity reactions • Haematomas and ecchymoses • Nonhypersensitivity-related swelling • Acneiform eruptions • Erythema (transient or permanent) • Skin necrosis • Arterial occlusion • Venous occlusion
Early-Onset Complications (3–14 Days)	• Inflammatory or non-inflammatory nodules • Angioedema
Delayed-Onset Complications(4-14 Days)	• Implant migration • Telangiectasia • Granulomas • Lipoatrophy • Hypertrophic scarring • Sterile abscess

PRECAUTIONS TO BE FOLLOWED

Certain precautions are to be taken before any procedure to avoid complications. Skin testing may be required before injection of dermal fillers derived from nonhuman sources such as bovine collagen, but is generally not required for fillers derived from synthetic sources. A proper injection technique with recommended depths is mandatory to avoid the reactions associated with injections placed too superficially. As a general rule, non-permanent, absorbable fillers can be injected more superficially and the more permanent fillers need to be injected more deeply. Avoid injection into blood vessels as vascular occlusion (and possible subsequent tissue necrosis) may occur. Anatomical locations that are more susceptible to unwanted reactions should be identified and care should be taken be avoid injecting dermal

fillers into those areas. The patient should avoid touching the area, doing strenuous exercises, and consuming alcohol at least for 6 hours post treatment. The patient is advised to stop taking aspirin and other anti- platelet drugs, as they will increase bruising and swelling. All complications should be taken seriously and patients followed closely. With regular follow-up and appropriate treatment, complications of dermal fillers can be limited [22].

CONCLUSION

Dermal fillers have become versatile tools for facial rejuvenation. By understanding the properties of each filler material, proper injection techniques and prevention of complications, dermal fillers will provide excellent cosmesis.

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