The Case for Synthetic Injectables

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KEYWORDS

• Synthetic fillers • Dermal fillers • Permanent fillers • Liquid injectable silicone
• Polymethyl methacrylate • Acne scarring • Nasolabial folds

KEY POINTS

- Bellafill (previously known as Artefill) has been marketed and sold in the United States as a permanent dermal filler for the correction of nasolabial folds since 2007 and received FDA approval for acne scarring in December 2014.
- Bellafill is currently the only "on-label" dermal filler approved by the FDA for the treatment of moderate to severe, atrophic, distensible facial acne scars on the cheeks of patients over the age of 21.
- The number of subjects affected by granuloma in the 5-year Bellafill postmarketing study was small (1.7%), with most events being mild to moderate in severity.
- Liquid injectable silicone was the first highly popularized injectable filler and is one of the oldest and longest lasting.
- Medical-grade silicone oil used off label for soft tissue augmentation with the correct indications and with the microdroplet technique is safe and economic permanent dermal filler.

INTRODUCTION

With the wide acceptance of temporary fillers, such as hyaluronic acid (HA), it is easy to see why permanent fillers with longer-lasting effects are quickly gaining popularity.[1] According to the American Society for Plastic Surgery Procedural Statistics, there were 2.2 million soft tissue filler procedures performed in 2013, representing an increase of 13% over prior year.[2] It is not uncommon for patients who experience superior results with temporary fillers to request more permanent enhancements.[1] Their tolerance for the inconvenience and repeat cost of short-term, temporary fillers is waning as newer-generation fillers with longer durations are coming on the market (Joseph J, Eaton L, Cohen S. Current concepts in the use of Bellafill. Submitted for publication).

Before the modern era of injectable collagen and HA as dermal fillers, several unapproved materials were used. The first permanent facial filler in the twentieth century was paraffin oil.[1] This was followed by a variety of other synthetic fillers, such as mineral oil, linseed oil, beeswax, and lanolin.[1] Medical-grade silicone was approved in 1959 by the US Food and Drug Administration (FDA). Liquid injectable silicone (LIS) oil has been used as permanent soft tissue filler in aesthetics for more than half a century under the auspices of "off-label use of an approved medical device."[1]

There are currently more than 200 dermal fillers and volume enhancers available internationally.[3] In the United States, the Center for Devices and Radiologic Health division of the FDA regulates injectable dermal fillers as medical devices. To receive a premarketing approval in the United States, a medical device manufacturer must demonstrate safety and effectiveness supported by human clinical studies for specific indications, such as "moderate to severe wrinkles and folds."

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Approval typically requires clinical evidence supported by a US, multicenter, randomized pivotal study using the approved standard of care, which historically was collagen, as a comparator. With more new fillers coming on the US market, head-to-head clinical trials between products of the same or similar type are now the gold standard. Only first-in-class fillers tend to gain approval with a single-arm study, or by using a no-treatment control as a comparator.

Currently there is no universally accepted classification system for injectable fillers; however, the source of the filler may be categorized as natural/animal, synthetic, or natural synthetic.[1] Fillers are further classified by the duration of effect, such as temporary, semipermanent, or permanent.[1] Permanent fillers are basically nonresorbable.[1] This article addresses two products that are currently being used as permanent soft tissue fillers in the United States: polymethyl methacrylate (PMMA) (eg, Bellafill) and LIS oil used in an off-label capacity.

LIQUID INJECTABLE SILICONE

Overview

LIS was the first highly popularized injectable filler and is one of the oldest and longest lasting.[4] LIS is not FDA approved as dermal filler; however, highly purified liquid silicone oil is frequently used "off-label" as a medical device for soft tissue augmentation, such as facial volumizing of lips and cheeks, or as filler for correction of facial wrinkles and folds, such as glabellar lines and nasolabial folds (NLFs). LIS is highly purified long-chain polydimethylsiloxane trimethylsiloxy terminated silicone oil, which is a sterile, generally inert, nonpyrogenic, clear, colorless oil with a viscosity of 1000 centistokes.[5,6] Silicone oil is well accepted because of its natural feel and ease of injection,[1] and is well tolerated in small volumes.[1,7–10] The mechanism of action of silicone oil is the stimulation of a fibrotic reaction within the dermis, which is followed by low-grade inflammation and subsequent capsule formation.[1]

Legal Status of Liquid Injectable Silicone

FDA guidance on "off-label" use of marketed drug and devices allows for physicians to use legally available products for an indication that is not in the approved labeling, providing that the physician uses good medical practice in the best interest of the patient, is well informed about the product, bases its use on firm scientific rationale and on sound medical evidence, and maintains records of the product's use and effects.[11]

Product Information

Two forms of LIS are FDA approved as medical devices in the United State, both for use in ophthalmology as retinal stabilizing agents. Silikon 1000 (Alcon, Ft. Worth, TX) is available in 10-mL glass vials filled with 8.5 mL of sterile silicone oil,[5] and ADATO Sil-OI-5000 silicone oil (Bausch + Lomb, Rochester, NY) is available in prefilled syringes. Silicone oil is found in abundance from manufacturers in Mexico and South America; however, these formulations may contain impurities that can results in undesirable complications.[1] Therefore, their use should be strictly avoided.

Patient Selection

Any facial defect can be examined for filling with silicone, including thin lips, nasal defects, smoker's lines, glabellar frown lines, NLFs, poorly defined cheekbones or chins, or postsurgical deformities. Broad-based facial scars from trauma or surgery (**Figs. 1** and **2**), and acne scars that disappear with manual stretching, are good candidates for treatment with silicone. Patients who are pregnant, are nursing, or who have active skin infections or uncontrolled systemic diseases are not candidates.

Silicone Injection: Microdroplet Technique

The ideal injection technique of silicone oil as a facial filler, after the treatment area has been cleaned and prepared, consists of microdroplet application with a 27-gauge by 0.5-inch needle, or with a 25- or 27-gauge microcannula into the dermal-subcutaneous junction.[7–9,12] After entering the skin at a 30° angle, fluid silicone is injected in a retrograde fashion at 2- to 4-mm intervals,[4,13] starting outside of the perimeter of the depressed area. For larger areas, multiple passes with a fanning injection technique may be required. Serial puncture technique of 0.05- to 0.1-mL aliquots of LIS is also a commonly used way to administrator the microdroplets of LIS in the area to be treated. Multiple treatment sessions are usually required to obtain the desired outcome. The microdroplet injection technique requires spacing the injections by at least a month or longer to allow adequate fibroplasia to occur.[13] The injected microdroplets of silicone become surrounded by a capsule of collagenous fibrous tissue, which holds them in place and minimizes migration.[13] In addition, this gradual fibroplasia ensures the injected area has the same texture as the adjacent tissue and that the product is not palpable.[13]