Facial Fillers and Their Complications

A number of facial filler materials that have not yet been approved by the Food and Drug Administration for use in the United States have been employed by physicians in Europe for several years. Although these products have proved efficacious, some complications events have been associated with their injection or inappropriate application. Moreover, the long-term effects of injecting into the face materials that often cannot be removed without surgical intervention is an issue that deserves serious consideration by both physicians and patients. (Aesthetic Surg J 2003;23:221-224.)

Several facial-filler materials not yet approved by the Food and Drug Administration for use in the United States have been marketed in Europe for several years. Their introduction has resulted in a dramatic decrease in the use of fat injections for facial filling in Europe. The new products include: Hyaluronic acid (Restylane, Juvederm, Fineline: Q-Med AB, Uppsala, Sweden; Juvederm: Corneal, Hallbergmoos, Germany; Hylaform: Inamed, Düsseldorf, Germany); Hyaluronic acid and collagen combined with polymethylmethacrylate (PMMA) or hydroxyethylmethacrylate (HEMA) (Artecoll: Rofil Medro, Düsseldorf, Germany; DermaLive and DermaDeep: Dermatech SARL, Paris, France); Polylactic acid (PLA: New Fill, European Aesthetics GmbH, Ismaning, Germany); and others (polyacryl injections: Amazingel, Fuhua Medical Co. Ltd., Shenzhen, China; Aqua-Mid, Bexbach, Germany). I do not use these latter 2 substances because the material injected has not been completely evaluated for possible toxicity.

Hyaluronic Acid

There are three different thicknesses of hyaluronic acid. Low-density hyaluronic acid products (Fineline, Juvederm18, and Hylaform Fineline) are designed to fill “smoker lines” of the upper lips, as well as crow’s feet; they dissolve after 2 to 3 months. Medium-density hyaluronic acid products (Restylane, Juvederm24, and Hylaform) are applied to the lips and generally last 4 to 6 months.

High-density hyaluronic acid products (Perlane, Juvederm 30, and Hylaform Plus) are applied in the nasolabial folds and may last up to 12 months if injected properly. A new version of hyaluronic acid with even larger molecules, called Macrolane (Q-Med) has been announced by the manufacturer but, as of January 2003, is not yet on the market. Macrolane is intended for deep implantations such as correction of breast surgery complications (filling rippling and dents) and the direct augmentation of the cheek and chin.

We have treated 500 patients with hyaluronic acid facial injections and found that it provided longer-lasting results than bovine collagen products for volume augmentation of the lips, wrinkles, and folds. In contrast to collagen, hyaluronic acid contains no products of animal origin. Consequently, no skin pretesting is necessary. We prefer to work with the thicker hyaluronic acid fillers because we have obtained more satisfactory results with them.

Hyaluronic acid must be injected properly into the lower levels of the dermis and upper levels of subcutaneous tissue. Intradermal injection will cause irritation and adverse reactions. Intramuscular or periosteal injections should be avoided because the material will be absorbed as result of the rich blood circulation in these areas. Also, areas subject to significant muscle movement, such as the perioral and mouth angle folds, are not well suited for hyaluronic acid injections because motion will cause rapid dissolution of the filler and reappearance of the folds.

Our clinical experience has revealed a 0.4% incidence of inflammatory local reactions to all hyaluronic acid fillers, appearing 1 to 14 days after treatment (Figure 1). In comparison, there is a reported 4% incidence of allergic reactions among patients injected with bovine collagen. The adverse reactions that occurred in our series resolved after a few days of corticoid and antihistamine treatment.
Granulomas occurred in 2% of patients but resolved after the injection of corticoids and topical application of antihistamine creams. Molding the granulomas and applying digital pressure also helped dissolve them. Patients can do this for themselves at home with good results.

**Artecoll**

Artecoll is a mixture of collagen and acryl particles (PMMA) that was developed by Dr. Gottfried Lemperle and introduced in Europe in 1992. It is designed to achieve augmentation by provoking fibrotic granulation under the skin through foreign-body reactions. The collagen in the material expedites the transportation of the acryl particles but does not act directly as a filler. Because Artecoll contains collagen, a skin pretest is always required.

Artecoll injection requires careful technique. It must be injected into the upper levels of the subdermis. Intradermal placement can result in beading or ridging caused by the foreign-body reaction; injection into muscle may lead to nodule formation. In several reports, it has been noted that complications correctable only by surgical excision can result from incorrect technique. Pollack has warned that Artecoll treatment involves a learning curve extending over the first few dozen treatments and recommends a highly conservative approach with respect to the amount used and the interval between treatments. (I have found that an interval of at least 1 month between injections is necessary to allow encapsulation and to assess results; Pollack recommends 6 to 8 weeks.)

The most serious complication associated with Artecoll is granuloma (Figures 2 and 3). Lemperle reported that an early form of Artecoll and its predecessor, Arteplast, were associated with a 3% to 5% incidence of granuloma because the microspheres of which the product was composed did not have absolutely smooth surfaces. Consequently, electrostatic charging caused the adherence of very small particles to the surfaces of some microspheres. This problem was resolved after multiple
washings were implemented in 1994.\textsuperscript{6-8} A 1998 study reported a low (1:1000) incidence of granuloma after 2 years' follow-up, although the rare occurrence of granuloma as a late side effect of unknown cause was noted.\textsuperscript{4} In addition, granuloma can result from overly aggressive treatment in which too much material is injected.\textsuperscript{3}

I have encountered granuloma as a late side effect of Artecoll injection in my own practice. In my cases, the incidence of nodule formation was higher than that reported above and led to complaints from patients 3 to 4 years after treatment.

**DermaLive and DermaDeep**

DermaLive and DermaDeep have been available in Europe and South America for the past 5 years. Their mechanism of action is similar to that of Artecoll, except that instead of collagen, a hyaluronic acid/hydrogel solution is mixed with acryl particles (HEMA) and acts as a carrier to transport the acryl-hydrogel particles into the treated tissue. This solution is absorbed after a few months. DermaDeep contains more acryl particles than DermaLive and is designed to be implanted only in deeper layers, close to the bones (periosteum). No skin pretesting is required for these products.

We use DermaDeep to augment the bony structures of the face, implanting it only sub- or epiperiosteally. It must be injected over a solid base. It is effective in filling the fossa canine of the nasolabial region and for the augmentation of the chin and cheek. However, when used to fill defects not located over a bony or otherwise solid base (e.g., the chin and the cheekbones), the particles and their capsules form a compact unit that can be detected on palpation and is sometimes visible (Figure 4). Bergeret-Galley et al\textsuperscript{9} reported a low rate (1.2:1000) of long-term side effects associated with these products. The main complication they noted was the appearance of palpable nodules approximately 6 months after treatment; these were treated successfully with corticoid injections.

In our clinical experience, both DermaLive and DermaDeep can cause dramatic hardening if injected into the muscle or deep mucosa of the lips, or intradermally. In our series of 200 patients, 22 (11\%) complained of hardening at 1-year follow-up. At 2-year follow-up, 51 patients (25.5\%) complained of hardening. We also encountered 11 cases of granuloma (5.5\%) in long-term (more than 2 years) follow-up, some of which required surgical excision.

In our experience, the results of injection with Artecoll, DermaLive, and DermaDeep did not stabilize after 3 months, as claimed by these products’ manufacturers. We observed further macroscopic enlargement as long as 24 months after treatment.

**PLA Injections**

New Fill is a PLA described as a biocompatible, bioabsorbable synthetic polymer belonging to the family of aliphatic polyesters. The L-PLA is in the form of microspheres, ranging in diameter from 40 to 60 m, held in suspension in a gel. The microspheres are more than 10 m in diameter, to avoid immediate phagocytosis by macrophages, and more than 30 m, to avoid intracapillary dispersal; however, they measure less than 100 m,
guaranteeing ease of injection through fine intradermal needles.

In our experience, particles of this size may cause a granulated appearance and can also result in granulomas. We have injected PLA in 100 cases and have observed 5 cases of infection and 12 cases of granuloma formation (Figure 5). In addition, 3 cases of long-term allergic reaction have occurred; these are still under investigation.

The development of facial-filler material designed for permanent implantation offers obvious benefits to patients and physicians in terms of convenience and cost. However, I believe that a prudent approach to their use is called for; my own clinical experience and reports in the literature indicate the possibility of long-term complications after injection of these materials.

In addition, the long-term aesthetic consequences of using permanent or long-lasting facial-filling material merit careful consideration. Facial contours change over time; in particular, the soft tissues can shrink as the patient grows older. Permanent fillers that provide satisfactory results at first may become more visible or create an unnatural appearance as aging progresses. Precisely because these products are so long-lasting, such untoward consequences would be difficult or impossible to correct without surgical intervention. Given these problems, in my opinion, it is legitimate to question the necessity for such permanent fillers.

References


Reprint requests: Ziya Saylan, MD, Konigsallee 22, Düsseldorf 40212, Germany; e-mail: saylan@aol.com. Copyright © 2003 by The American Society for Aesthetic Plastic Surgery, Inc. 1090-820X/2003/$30.00 + 0 doi:10.1067/maj.2003.45