ELSEVIER SAUNDERS

FACIAL PLASTIC SURGERY CLINICS OF NORTH AMERICA

Facial Plast Surg Clin N Am 15 (2007) 55–61

Collagen Fillers

Elizabeth Rostan, MD

Over the last decade there has been increasing patient demand for minimally invasive cosmetic procedures. Many patients desire a more youthful look that is natural in appearance and achieved gradually and maintained over progressive years. This interest has fueled a boom in soft tissue fillers. Soft-tissue augmentation can achieve what no other procedure can—the replacement or restoration of facial volume. Collagen was one of the first fillers to hit the aesthetic market and has been in use for more than 20 years. In recent years there has been a surge of new injectable fillers, with more anticipated in the near future. Despite the large number of new products for augmentation and wrinkle filling, there still remains a role for injectable collagen—alone and in combination with other wrinkle fillers. This article reviews the collagen fillers currently available and their use in aesthetic practice.

History of injectable collagen

In 1958, researchers at Harvard University demonstrated that collagen in solution could be made into a solid gel by heating the solution to body temperature [1]. Antigenicity of collagen molecules was later shown to be greatly diminished by removing the amino and carboxy terminal peptides. The groundwork was laid for the development of a clinically useful collagen implant [2,3]. In a 1977 report, researchers at Stanford successfully implanted soluble, telopeptide-digested, purified collagen from human, rabbit, and rat into the subcutaneous tissue of rats [4]. These same investigators later injected 28 human subjects with human and bovine collagen and showed 50% to 85% improvement in acne scars, wrinkles, and other volume deficits that persisted for 3 to 18 months [5].

These early findings led to the development and, in July 1981, US Food and Drug Administration (FDA) approval of a bovine collagen implant for soft-tissue augmentation: Zyderm. Later the US FDA approved two other formulations of collagen implants: Zyderm II and Zyplast. In March 2003, the US FDA approved two new collagen implants that are derived from human-based collagen: CosmoDerm 1 and CosmoPlast [6]. Additional products have been introduced and approved by the US FDA since that time. Table 1 reviews the currently approved collagen products.

Bovine collagen implants

Currently three types of bovine-derived collagen implants are FDA approved for soft-tissue augmentation: Zyderm I, Zyderm II, and Zyplast. Zyderm I contains 3.5% bovine collagen, which is suspended in a phosphate-buffered sodium chloride solution

Private Practice, Dermatology and Cosmetic Surgery Center of Charlotte, 1918 Randolph Road, Suite 580, Charlotte, NC 28207, USA
E-mail address: er@dcsc-charlotte.com

1064-7406/07/$ – see front matter
doi:10.1016/j.fsc.2006.11.001
facialplastic.theclinics.com

Table 1: **Comparison of collagen fillers**

Product	Composition	Allergy test required	Storage	Duration of effect
Zyderm I	3.5% bovine collagen, 0.3% lidocaine	Yes	Refrigeration	3–4 mo
Zyderm II	6.5% bovine collagen, 0.3% lidocaine	Yes	Refrigeration	3–4 mo
Zyplast	3.5% bovine cross-linked collagen 0.3% lidocaine	Yes	Refrigeration	4–6 mo
CosmoDerm I	3.5% human-derived collagen 0.3% lidocaine	No	Refrigeration	3–6 mo
CosmoDerm II	6.5% human-derived collagen 0.3% lidocaine	No	Refrigeration	3–6 mo
CosmoPlast	3.5% human-derived, cross-linked collagen 0.3% lidocaine	No	Refrigeration	4–7 mo
Dermologen	Human cadaveric collagen and matrix material (elastin, GAGs)	No	Not currently manufactured	Not known
Cymetra	Human cadaveric dermal matrix	No	Refrigeration	4–18 mo
Isologen	Autologous collagen	No	Refrigeration, immediate use	Not known

and 0.3% lidocaine. Zyderm II has increased collagen composition, 6.5%, also suspended in the lidocaine and sodium chloride solution. Zyderm I and II are used for the correction of superficial skin lines in areas such as the forehead, around the eyes (crow's feet), and upper lip. Zyderm II may be used in deeper lines because it has greater concentration of collagen. Zyplast has the same collagen composition as Zyderm I, 3.5% bovine collagen, but it is cross-linked with 0.0075% glutaraldehyde. This glutaraldehyde cross-linking strengthens the collagen fibers and extends the duration of clinical effect by decreasing degradation by collagenase. Zyplast is helpful in treating deeper lines, such as the nasolabial fold, and is a good choice for the vermilion border of the lip. These products are composed of 95% type I collagen and 5% type II collagen. They are available in 0.5- to 1.5-mL syringes and must be refrigerated. Cosmetic correction with these bovine collagen products typically lasts 3 to 4 months.

Before injection of any of these bovine collagen products, allergy testing is necessary. Approximately 3% of the population is sensitive to bovine collagen. Prescreening with two separate skin tests helps detect sensitivity to bovine collagen before cosmetic correction with these fillers [7,8]. A commercially available skin test that consists of 0.3 mL of Zyderm I is injected into the volar aspect of the forearm. At 48 to 72 hours and then again at 2 weeks, the site is checked for erythema, swelling, induration, tenderness, or pruritus. If none of these signs of hypersensitivity is present, then a second skin test is placed and evaluated in another 2 to 4 weeks. A positive skin test result is a contraindication to treatment. Even with one negative skin test result, some patients develop a hypersensitivity reaction to treatment with bovine collagen. The second skin test helps detect the possibility of this delayed hypersensitivity reaction. The risk of allergy after one negative test result is still significant—estimated at 1.5% to 6.2%. This risk is reduced to 0.5% after two tests and may occur rarely after multiple treatments with bovine collagen. If there are no signs of hypersensitivity with either test injection, then the patient may proceed with treatment 4 weeks after the first skin test. For patients who have had a bovine collagen injection in the past without reaction but it has been longer than 1 year since the last injection, one test injection is recommended and a second skin test is not necessary.

Bioengineered human collagen

In March 2003, the US FDA approved two new human-derived bioengineered collagen implants: CosmoDerm I and CosmoPlast. CosmoDerm II was later granted US FDA approval and is currently available. The content of CosmoDerm I and II are the same as their bovine collagen counterparts,