Autologous Human Collagen and Dermal Fibroblasts for Soft Tissue Augmentation

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BACKGROUND. Augmentation of soft tissue defects can be achieved through intradermal injection of silicone, animal collagen, plasma-gelatin mixture, and fat. Due to their rapid degradation in vivo, however, clinical effects are typically transient. The use of autologous human collagen could conceivably result in sustained clinical improvement due to decreased collagen degradation.

OBJECTIVE. The purpose of this study was to determine whether prolonged dermal correction could be achieved through injection of autologous human fibroblasts.

RESULTS. Significant sustained clinical improvement was observed in two of the original 12 patients enrolled in the study. The nasolabial fold region was shown to be the most responsive facial area to treatment.

CONCLUSION. The use of injectable autologous human collagen for soft tissue correction remains an intriguing prospect. While the findings of this study indicate possible sustained clinical improvement using this autologous system, in some patients it remains difficult to predict the degree and duration of individual response in various areas. © 1998 by the American Society for Dermatologic Surgery, Inc. Dermatol Surg 1998;24:510–512.

For centuries physicians have attempted to augment soft tissue defects through intradermal injection of a variety of agents, including silicone, animal collagen, plasma-gelatin mixture, and fat. The bovine collagen products that have been popular for soft tissue augmentation are rapidly degraded by collagenase, resulting in the disappearance of their effects within 3–6 months following implantation. The use of autologous human fibroblast injections would be expected to result in a longer duration of correction based on local production of collagen as well as decreased collagen degradation. The purpose of this investigation was to determine whether prolonged correction could be achieved using a newly described autologous collagen system with cultured human fibroblasts.

Materials and Methods

Twelve patients (11 female, one male; age range, 32–54 years; mean, 44 years) with facial rhytides, atrophic facial scars, or lip atrophy were enrolled in this internal review board-approved study. Seventeen skin regions receiving treatment included the nasolabial folds (seven), glabella (two), lips (five), and cheeks (three). All scarred regions (cheeks) had been present for at least 5 years. Study exclusion criteria included autoimmune disease, systemic steroid use, concurrent chemotherapy, history of organ transplantation, prior collagen or other filler implantations, and dermabrasion, facelift, or laser resurfacing procedures within 12 months of study initiation.

At the initial study visit, a 3-mm punch biopsy was obtained from sun-protected postauricular skin of each subject. Dermal fibroblasts from these biopsies were then cultured in vitro using sterile technique (Isolagen Technologies, Paramus, NJ). Type I collagen and fibroblasts were harvested from each biopsy specimen after 4–6 weeks and a 0.1-ml intradermal test dose was injected in the volar aspect of each subject's forearm. Two weeks later, 1 ml of the cultivated autologous material was implanted into each study region. Implantation technique involved placement of the material within the superficial mid-dermis. Two additional injections (1 ml each) were delivered biweekly to the study areas as deemed necessary by clinical examination, for a total of three implantations per region.

Clinical photographs were obtained at baseline, immediately prior to each treatment, and 3 months following the final treatment session in all subjects. Six-month follow-up photos were obtained in six patients. Before and end-treatment photographs were graded by two blinded assessors as follows: 0 = no improvement, 1 = minimal correction, 2 = moderate correction, and 3 = total correction.

Results

Eleven subjects with 15 treatment sites completed the study. All patients received three collagen treatments. Only one of the original 12 patients discontinued her participation due to pain and burning experienced during the initial treatment session.

Two of the remaining 11 subjects demonstrated fa-
Figure 1. 41-year-old woman with prominent nasolabial folds A) before and B) 6 months after three consecutive autologous collagen injections (Isologen). Note: continued clinical improvement was observed between 3 and 6 months following the final (third) intradermal injection.

Figure 2. 45-year-old woman with prominent nasolabial folds A) before and B) 6 months after the third autologous collagen injection.

Discussion

Type I collagen accounts for 85% of the protein in human dermis, whereas type III collagen accounts for approximately 10%. Adult dermal collagen content decreases annually by 1% with more rapid decline following chronic sun exposure.

Bovine collagen implants consist of sterile, purified, reconstituted fibrillar bovine collagen (type I and type III collagen) that are injected into the dermis for the purpose of soft tissue augmentation. Following its injection, bovine collagen is detected as a foreign substance by human collagenases, which, along with inflammatory cells, slowly degrade it over the next several months. Human investigations have shown that the material cannot be detected after 3 months, however, up to 30% of patients treated with bovine collagen report correction lasting up to 18 months. The prolonged clinical improvement observed following injection of bovine collagen has been hypothesized to be due
to stimulation of fibroblasts that synthesize new collagen around the implant. As has been shown with silicone, deposition of newly formed collagen occurs within 1-3 months after implantation. However, there is no convincing evidence in humans that host collagen production contributes to the longevity of clinical correction. Loss of correction occurs as bovine collagen is displaced into the subcutaneous space from the overlying dermis. Frequent collagen injections must therefore be administered.

The largest drawback to the use of bovine collagen is the possibility for hypersensitivity. While the rate of an allergic reaction is low (3-5%), it remains a concern. The presence of erythema and induration correlate with the presence of circulating antibodies to bovine collagen. Granulomatous responses in the absence of positive skin tests have been shown to occur in 0.5% of patients in a large retrospective study. Lastly, systemic side effects have been documented. Unfortunately, other implantation techniques including Fibrel and silicone have also been wrought with technical, systemic, and/or regulatory (FDA) difficulties. Because of the hypersensitivity and inflammatory reactions in particular, the development of an autologous collagen system is most intriguing.

The use of autologous human collagen and fibroblasts for soft tissue augmentation represents a potentially exciting natural alternative to the use of bovine collagen. While clinical results are difficult to predict, the use of autologous collagen is indicated in those patients unwilling to accept injections of foreign material as well as in those who are known to be allergic to bovine collagen. The nasolabial fold region was shown in this study to be the most responsive facial area to treatment. The observation of sustained soft tissue augmentation at 3 months with continuing clinical improvement at 6 months in two study patients strongly suggests that the autologous material may provide more prolonged results than that achieved with the use of bovine collagen.

Several drawbacks associated with the use of this autologous human collagen system, however, were clearly demonstrated in this study. Clinical enhancement is often low or subtle compared with other forms of augmentation such as bovine collagen. While the absence of complete correction may be related to the low viscosity of the vehicle used, patients expecting immediate clinical results may be dissatisfied with the lack of noticeable improvement in the early stages following implantation. In addition, logistical problems are commonly encountered with transport of the material, making it difficult to ensure the required implantation of cells within 48 hours of harvestment from the culture medium. Lastly, there is greater expense associated with the use of autologous collagen and fibroblasts due to the labor-intensive process of harvesting and culturing cells from each individual as well as the costs incurred with material storage and transport.

Conclusion

In summary, clinical results remain difficult to predict following the use of autologous human collagen and fibroblasts for soft tissue augmentation using the above-described system. Based on this limited study, the nasolabial folds appear to be the anatomic area most responsive to treatment. Further studies are indicated to investigate the nature of cellular interactions following implantation of autologous collagen and fibroblasts, including confirmation of fibroblast viability following implantation. A better understanding of the number and timing of injections necessary to achieve optimal clinical results is warranted before patients can reasonably be expected to accept the financial costs and delayed improvement associated with treatment.

References