Clinical Experience With Polymethylmethacrylate Microspheres (Artecoll) for Soft-Tissue Augmentation

A Retrospective Review

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Objective: To evaluate patient satisfaction and clinical outcomes with soft-tissue augmentation using an injectable alloplast composed of polymethylmethacrylate microspheres 30 to 40 µm in diameter suspended in atelocollagen (3.5% collagen solution) (Artecoll; Artes Medical Inc, San Diego, California).

Design: A retrospective review of the literature and an evaluation of our clinical experience with Artecoll implantation for facial soft-tissue augmentation were performed. In a large private metropolitan clinical facial plastic surgery practice, 72 patients (62 females and 10 males) underwent Artecoll implantation between January 1, 1997, and June 30, 2002. Artecoll was implanted into different facial sites, including the philtrum, acne scars, corners of the mouth, upper and lower lips, melolabial folds (also known as nasolabial folds), and other facial creases to attain permanent soft-tissue augmentation. Via completion of an anonymous survey, patients performed subjective evaluation of the aesthetic results. Subjective evaluation of aesthetic results by the surgeon was based on review of photographic documentation. Objective variables, including complications, sites most often treated, total number of treatments, and volume of implant material injected, were obtained by reviewing patient medical records.

Results: Among 72 patients, 40 returned a completed patient satisfaction survey (56% response rate). The most common reason cited by patients (35 of 40) for selecting Artecoll implantation was that the implantation offered permanent correction. Five of 40 patients reported persistent problems with Artecoll (firmness of the lip in 1 patient, increased sensitivity of the lip for 6 months in 1 patient, and lumps in their lips in 3 patients). Eighty-five percent of patients (34 of 40) reported that the treatment met or exceeded their expectations, 13% (5 of 40) reported that the treatment was less satisfying than expected, and 3% (1 of 40) reported that the treatment was much less satisfying than expected. Ninety-five percent (38 of 40) reported that they would recommend Artecoll implantation to a friend or relative, and 90% (36 of 40) reported that they would undergo Artecoll implantation again. The retrospective medical record review revealed that the most commonly requested facial areas for augmentation were (in order of frequency) upper lip, lower lip, melolabial folds, corners of the mouth, and other facial creases. Seventy-two patients underwent 177 Artecoll implantation procedures. The mean number of treatments required to obtain favorable soft-tissue augmentation was 2.4. The medical record review confirmed that 5 of 72 patients had complications after Artecoll implantation (nodule formation in 4 patients and persistent lip pain in 1 patient). Sixty-two of 72 patients (86%) achieved favorable soft-tissue augmentation with a total Artecoll implant volume of 3.0 mL or less.

Conclusions: Artecoll is a satisfying treatment for lip augmentation or for treatment of facial creases and furrows among patients seeking permanent correction. However, implantation success is technique sensitive. Conservative gradual implantation provides favorable results and few complications. Implantation in the subdermal plane is critical to obtain favorable outcomes using this injectable alloplast.

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PMMA (PMMA) is an alloplast that has been used by reconstruction surgeons for soft-tissue augmentation for years. Artecoll (Artes Medical Inc, San Diego, California) is an injectable implant material composed of PMMA microspheres 30 to 40 µm in diameter suspended in atelocollagen (3.5% collagen solution). Artecoll has been used successfully in Europe and in Canada for the past 10 years. ArteFill (Artes Medical Inc) (the American equivalent of Artecoll) gained Food and Drug Administration approval on October 27, 2006, for use in the United States. The objective of this study was to review clinical applications and outcomes in patients after Artecoll implantation for soft-tissue augmentation.

The search for an ideal implant material for soft-tissue augmentation continues to challenge facial plastic surgeons. The ideal implant substance would contour readily and would be simple to use, cost-effective,
biocompatible, and readily available in large quantities. The injectable options available for soft-tissue augmentation include collagen, autologous fat, hyaluronic acid derivatives, and micronized acellular human dermis. Collagen from bovine and human sources is available for clinical use. Examples include Zygderm I and Zygderm II (Isolagen Technologies, Inc, Paramus, New Jersey), which contain 3.5% and 6.5% purified bovine collagen, respectively. When collagen from a bovine source is used as a soft-tissue filler, a potential disadvantage is that patients must undergo skin testing for 1 month to screen for a possible hypersensitivity reaction. Recently, collagen from a human source has been developed and eliminates the need for hypersensitivity screening (NAMED Aesthetics, Santa Barbara, California). Hyaluronic acid derivatives have been popular in Europe and Canada, and most recently Restylane (Medicis, Scottsdale, Arizona) was approved by the Food and Drug Administration for use in the United States. Cymetra (LifeCell Corp, Branchburg, New Jersey) is an injectable form of micronized human dermis with elastins, proteoglycans, and collagens that has been used for soft-tissue augmentation. Autologous fat may also be used for soft-tissue augmentation; however, it is disadvantageous because of its potential to create irregularities as it degrades. Unfortunately, the primary disadvantage with the available soft-tissue fillers is that they provide temporary correction and augmentation of soft tissues.

Alloplastic implants such as expanded polytetrafluoroethylene (Gortex [WL Gore and Associates Inc, Flagstaff, Arizona] and SoftForm and UltraSoft [Collagen Corporation, Palo Alto, California]) have been used for permanent augmentation of soft tissues but may shorten or shift and become visible with time. Radiance (BioForm, Franksville, Wisconsin) is an injectable alloplast composed of synthetic calcium hydroxylapatite in an aqueous gel suspension and provides 2 to 5 years of augmentation. Polymethylmethacrylate has an established biocompatibility profile and has been used clinically in joint replacement, cataract surgery, and dental and neurosurgical procedures with success. Polymethylmethacrylate microspheres ranging from 30 to 40 µm in diameter are produced by a suspension-polymerization process and are dispersed in a heated 3.5% solution of bovine collagen at a ratio of 1:3. As the solution cools, the suspension forms a gel. The collagen solution functions as the vehicle to implant the PMMA microspheres. After implantation in soft tissues, atelocollagen dissipates, and permanent correction is achieved from the PMMA microspheres.
microspheres. Animal studies using PMMA microspheres have yielded conflicting reports. The findings from one study\(^2\) suggest that the particles are resistant to phagocytosis and degradation and do not have carcinogenic potential. This study attributes the resistance to phagocytosis to the smooth surface of the PMMA particles and reports that by 4 months a delicate fibrous capsule forms around each particle that prevents dislocation of the implanted material. However, findings from another study\(^3\) suggest that PMMA microspheres in atelocollagen have the potential to evoke an immune response in the guinea pig model and that the microspheres are susceptible to phagocytosis and elimination.

A large sample European clinical study\(^4\) investigating soft-tissue augmentation using Artecoll revealed a patient satisfaction rate of 89\%. Disadvantages of using PMMA microspheres for soft-tissue augmentation reported in this clinical investigation were possible nodule formation, potential allergic reaction, need for multiple treatments, and a 1:10 000 chance of granuloma formation. The indications for PMMA microsphere implantation established by this European study include acne scars, deep glabellar creases, lip and philtral augmentation, melolabial (also known as nasolabial) fold effacement, and treatment of depressed corners of the mouth. Contraindications to PMMA microsphere implantation include superficial creases, allergic reaction to bovine collagen, and excessively thin atrophic skin.

A recent randomized controlled trial in the United States compared results among patients undergoing PMMA microsphere implantation with those of a control group receiving collagen only.\(^5\) There was no significant difference in adverse events between the 2 groups. During a follow-up of 12 months, 16.4\% of patients had adverse events mostly involving increased sensitivity, persistent redness or swelling, and lumpiness at injection sites.

The objective of the present study was to evaluate and report our clinical experience with patients who electively underwent Artecoll implantation for soft-tissue augmentation. This retrospective patient study reports subjective outcomes among patients as determined through an anonymous patient survey and subjective outcomes reported by the surgeon based on evaluation of photographic documentation and medical record review. Advantages and complications of PMMA microsphere implantation are also discussed.

**METHODS**

The implantation technique used in the present study is a linear technique. The tissue to be implanted is gently grasped between the forefinger and thumb of the nondominant hand. The syringe containing the implant material is inserted into the tissue in a subdermal plane. Gradual even pressure is applied to the syringe as the needle is withdrawn from the tissue, allowing the implant substance to be deposited into the subdermal plane. At the conclusion of the injection, the needle is brought perpendicular to the tissue before exiting. This last maneuver minimizes the likelihood of the implant material being deposited too superficially as the needle is withdrawn from the tissue. The drop technique is not used because of the potential for uneven distribution and gaps where the implant substance may not be deposited. The implant material is deposited in a strictly subdermal plane using a 25-gauge 1.27 cm needle.

Included in the retrospective medical record review were 72 ethnically diverse patients who underwent Artecoll implantation performed by one of us (P.A.A.) in a private facial plastic surgery practice. Of these patients, 62 were women and 10 were men. Written informed consent was obtained from all patients. Patients underwent implantation between January 1, 1997, and June 30, 2002. Artecoll implantation was performed in an office setting in all except 2 individuals who underwent implantation under general anesthesia while undergoing other surgical procedures. All patients were mailed a detailed 4-page patient satisfaction survey. Surveys were reviewed, and data were obtained in a blinded fashion. Surveys included questions about discomfort associated with implantation. Pain scores were reported by application of a visual analog pain scale (with 1 indicating minimal pain and 10, worst pain). The medical records of all 72 patients were reviewed to collect additional data about the surgeon’s documentation of results. Aesthetic results were assessed by analysis of photographic documentation by one of us (P.A.A.). Other variables investigated included complications, volume of implant material injected, and total number of treatments required to achieve aesthetically favorable correction of the patient’s problem.

**RESULTS**

Results of patients who underwent Artecoll implantation are shown in Figures 1, 2, 3, 4, and 5. The minimum follow-up for clinical evaluation and patient satis-
faction survey data was 23 months, and the mean follow-up time was 34 months. Figure 1 shows results in a woman who underwent upper and lower lip augmentation with Artecoll. Figure 2 shows pretreatment and posttreatment results in a man with bilateral melolabial fold augmentation with Artecoll. Figure 4 shows a woman before and after treatment with Artecoll to camouflage vertical rhytids of the glabella and left brow. Figure 5 shows pretreatment views of a woman who was dissatisfied with her melolabial and melomental folds, as well as results of melolabial and melomental fold augmentation 3 years after treatment with Artecoll.

PATIENT SATISFACTION SURVEY

Of 72 surveys mailed, 40 (56%) were returned for review. The single most common reason, reported by 35 patients (88%), for treatment with Artecoll was the potential for permanent correction of their aesthetic problem. Eight patients (20%) secondarily selected the treatment because it was a minimally invasive injectable treatment. Shorter recovery time was reported as a reason for their treatment choice by 13 patients (33%). Three patients reported a history of prior Artecoll implantation by a physician other than a study physician. Patients reported a range of overall subjective improvement from 20% to 100% correction. Based on 37 responses, the mean overall subjective correction was 70.1%. More than half of the patients reported the ability to return to work or to normal activities immediately or within a couple of hours. Of those who reported delayed return to normal activities, bruising and swelling were the 2 most common reasons cited for the delay. The overall mean pain score, reflecting the degree of discomfort experienced during the implantation, was 3.18. The Table gives the mean pain scores according to the type of anesthetic used. The mean pain score for 22 patients who received trigeminal nerve (V2 or V3) local anesthetic blocks was 3.09. The mean pain score for 10 patients who received no anesthetic was 3.20. The mean pain score for 3 patients who received topical EMLA (eutectic mixture of local anesthetics) cream was 4.67. The mean pain score for 3 patients who received topical EMLA cream followed by local anesthetic blocks was 2.67. The 2 patients who underwent procedures under general anesthesia were excluded. Five of 40 patients (13%) reported persistent problems; 3 reported lumps and bumps, 1 reported increased sensitivity of the lip for 6 months, and 1 reported firmness of...
the lip. The lips were the site where problems were most frequently reported.

Among the patients participating in the survey, 85% (34 of 40) reported that treatment with Artecoll met or exceeded their expectations, 13% (5 of 40) reported that the treatment was less satisfying than expected, and 3% (1 of 40) reported that the treatment was much less satisfying than expected. Among 40 patients, 95% (38 patients) reported that they would recommend treatment with Artecoll to a friend or relative. When reflecting on their experience retrospectively, 90% (36 patients) reported that they would undergo Artecoll implantation again.

The retrospective medical record review revealed that the most commonly requested facial areas for augmentation were (in order of frequency) upper lip, lower lip, melolabial folds, corners of the mouth, and other facial

<table>
<thead>
<tr>
<th>Anesthetic Type</th>
<th>Mean Pain Score</th>
<th>No. (%) of Patients</th>
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<tbody>
<tr>
<td>Local block</td>
<td>3.09</td>
<td>22 (58)</td>
</tr>
<tr>
<td>No anesthetic</td>
<td>3.20</td>
<td>10 (26)</td>
</tr>
<tr>
<td>EMLA only</td>
<td>4.67</td>
<td>3 (8)</td>
</tr>
<tr>
<td>EMLA and local block</td>
<td>2.67</td>
<td>3 (8)</td>
</tr>
</tbody>
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Table. Distribution of Patients According to Anesthetic Type and Mean Pain Score

Abbreviation: EMLA, eutectic mixture of local anesthetics.

MEDICAL RECORD REVIEW

Figure 5. Woman who underwent implantation of an injectable alloplast composed of polymethylmethacrylate microspheres 30 to 40 µm in diameter suspended in atelocollagen (3.5% collagen solution) (Artecoll; Artes Medical Inc, San Diego, California) for melolabial (also known as nasolabial) and melomental folds. A and C, Pretreatment views. B and D, Melolabial and melomental fold augmentation at 3 years after treatment with Artecoll.
creases. Seventy-two patients underwent 177 Artecoll implantation procedures. The mean number of treatments required to obtain favorable soft-tissue augmentation was 2.4. Variables that were analyzed in the medical record review included site of treatment, number of treatments required to obtain favorable aesthetic results, total volume of implant material used to achieve aesthetic results, previous alternative treatments that patients had undergone before implantation, and complications that occurred after implantation. Of 72 medical records reviewed, 35 patients (49%) had attempted alternative treatment modalities before Artecoll implantation. Of the alternative treatments tried by patients before Artecoll implantation, temporary fillers were the most commonly attempted. These included collagen (Zyderm and Zyplast [Isolagen Technologies, Inc]), hyaluronic acid fillers (Restylene [Medics] and Perlane [Q-Med Esthetics, Uppsala, Sweden]), and treatment with botulinum toxin (Botox; Allergan, Irvine, California). Among 35 alternative treatments, 7 patients had previously undergone rhytidectomy, and 8 patients had previously received expanded polytetrafluoroethylene implants (SoftForm). Two patients had undergone previous Artecoll implantation at another center. Volumes injected ranged from 0.5 to 7.7 mL. Sixty-two of 72 patients (86%) were able to achieve correction with a total Artecoll implant volume of 3.0 mL or less. Medical record review and patient satisfaction survey data indicated that 5 of 72 patients (7%) experienced complications after Artecoll implantation. Four of these 5 patients had nodule formation, and the fifth patient experienced persistent lip pain. All complications occurred in patients in whom the lip was the site of treatment.

Overall, Artecoll implantation was reported by most patients to be a satisfying treatment. Findings from our study suggest that Artecoll implantation should be a treatment option for individuals seeking permanent correction of a particular aesthetic problem. It is critical that patients be informed of the potential problems with PMMA microspheres and of the need for prolonged follow-up. Patients who have not previously tried a temporary filler should be encouraged to try one before treatment with PMMA microspheres. The potential challenge to attaining successful results using PMMA microspheres for soft-tissue augmentation is that the results obtained are technique sensitive. Implantation with PMMA microspheres must occur precisely in the subdermal plane to minimize the risk of complications. Furthermore, patients should be advised that more than 1 treatment may be required. Our low rate of complications may be attributed to the gradual rate of implantation and to the precise technique we prefer to use. The literature reports the risk of granuloma formation to be 1 case per 10 000 procedures.4 With a mean follow-up of 34 months, nodule formation was the most common complication in this series of patients and occurred at a rate of 6% (4 of 72) exclusively in patients in whom the lip was the primary treatment site. Our follow-up of 34 months is substantial, as it has been suggested by Lemperle et al that most granulomas occur 1 to 2 years after placement, and a study by Cohen and Holmes5 had a follow-up of only 12 months. The challenge for surgeon and patient if granulomas occur is to attempt to surgically excise the PMMA microspheres from the site of implantation. However, our results suggest that Artecoll implantation is an excellent option for permanent correction of deep melolabial folds, depressed corners of the mouth, and deep glabellar furrows unresponsive to treatment with Botox.

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REFERENCES