Recovery From Deep-Plane Rhytidectomy Following Unilateral Wound Treatment With Autologous Platelet Gel

A Pilot Study

David M. Powell, MD; Edward Chang, MD; Edward H. Farrior, MD

Objective: To determine the effects of treatment with autologous platelet-rich plasma mixed with thrombin and calcium chloride to form an autologous platelet gel (APG) on postoperative recovery from deep-plane rhytidectomy.

Study Design: A prospective, randomized, controlled pilot study.

Setting: An accredited ambulatory facial plastic surgery center.

Patients: Healthy volunteer women (N=8) undergoing rhytidectomy.

Intervention: Unilateral autologous platelet-rich plasma wound treatment during standard deep-plane rhytidectomy.

Main Outcome Measures: Staged postoperative facial photographs were graded in a blinded fashion by 3 facial plastic surgeon reviewers for postoperative ecchymosis and edema. Each facial side treated with APG that demonstrated less edema or ecchymosis than the non-APG-treated side was designated a positive response; otherwise, the response was equal (no difference) or negative (untreated side had less edema or ecchymosis).

Results: Twenty-one positive and 21 equal responses were observed compared with 8 negative ones. Of 20 unanimous observations, 15 were positive, only 3 equal, and 1 negative.

Conclusions: Treatment with APG may prevent or improve edema or ecchymosis after deep-plane rhytidectomy. This trend is more apparent for ecchymosis than for edema, and is chiefly demonstrable in the early phases of recovery. These observations are consistent with previous reports of cell tissue culture and wound response to concentrated platelet product.

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PLATELET-DERIVED growth factors—released from the platelet's or granules when the platelets are activated—have been recognized as crucially important regulatory elements in wound repair. A substantial amount of work has demonstrated the efficacy of these angiogenic peptides both in vitro with cell tissue culture and in vivo in bony and soft tissue wound-healing models. The best understood of these factors are platelet-derived growth factor and transforming growth factor (TGF-β), 2 families of growth factors that modulate healing through a variety of mechanisms. In general, both platelet-derived growth factor and transforming growth factor β exert most of their effects on wound healing through their stimulation of macrophages, which in turn release a variety of other directly acting angiogenic growth factors.

Because these 2 growth factors are naturally concentrated in platelets at levels up to 100 times those found in most other body tissues, platelets may be an accessible, inexpensive source for such agents. Generation of the so-called autologous platelet gel (APG) from the platelet-rich plasma (PRP) layer of centrifuged blood requires the technically simple steps of platelet harvest and mixture with commercially available thrombin and calcium chloride. Clinical trials have been reported detailing improvement of wound healing after treatment with APG in such clinical endeavors as dental rehabilitation, treatment of macular degeneration, and management of chronic lower extremity ulcers caused by systemic illnesses such as diabetes or venous stasis.

For commentary see page 251
PATIENTS, MATERIALS, AND METHODS

This study was a randomized, prospective, controlled clinical trial. Study participants were a volunteer sample of healthy women undergoing rhytidectomy in an accredited facial plastic and reconstructive surgery center. During a preoperative informed consent process, it was emphasized to the patient that during the procedure a randomly selected side of the patient’s face would be treated with APG. Although this study was executed in a private-practice setting, an informed consent protocol was followed using as a model the elements of informed consent required by the institutional review board of The Ohio State University Medical Center, Columbus.

A total of 8 patients volunteered to participate in this study. Participants underwent standard deep-plane facelift under general anesthesia. The surgical technique is outlined in detail elsewhere.4 All rhytidectomies were performed by the senior author (E.H.F.), using identical technique on each side of the face and on every patient. Before the surgical procedure, one side of the patient’s face was randomly selected to be treated with the APG. Furthermore, the side of the patient’s face to be operated on first was randomly selected as well. This generated 4 patient groups (left first/left APG, right first/left APG, left first/right APG, and right first/right APG).

Platelet-rich plasma was harvested intraoperatively. After the patient was placed under general anesthesia and intubated, an antecubital venotomy was performed and approximately 450 mL of blood was collected using standard sterile technique. Blood was centrifuged, first at 5600 rpm then at 2400 rpm, to isolate and harvest the PRP. Thirty to 50 mL of PRP was harvested from the initial volume of 480 mL of blood, and platelets were concentrated at a level 3 to 6 times that found in blood (500,000/mL to 1 million/mL).

The remaining platelet-poor plasma and red blood cells may be discarded or retransfused (since the autologous material has no potential for infection). Patients who have a latex allergy, or who express anxiety about receiving processed blood, may forgo autotransfusion without significant effects because the overall volume is hemodynamically insignificant.

Seven or 8 mL of harvested PRP was stored in 10-mL syringes at room temperature until elevation of flaps and excision of excess soft tissue had been completed. When wound closure was imminent, a small amount (1 mL) of mixed topical thrombin and 10% calcium chloride were drawn into the syringe with the PRP, and the syringe was inverted repeatedly until the liquid began to solidify, forming a gel of moderate viscosity, the APG. Gel formation began within a few seconds.

The APG was applied by injecting it into the wound on the flap undersurface through an 18- or 14-gauge angiocatheter or needle. The PRP and thrombin/calcium chloride might also be concurrently sprayed through an atomizer, mixing the solutions as they are deposited on the wound surface. Further solidification occurred after the gel was harvested.

The positive results observed in clinical trials such as these, as well as the ever-present search for improved outcomes in a highly competitive market, have led investigators to examine the applications of PRP and APG in the field of cosmetic surgery. Marketed as a simple technology with few risks and the potential to greatly reduce recovery from elective surgery, treatment with APG has recently been reported for cosmetic surgery procedures such as face-lift, brow lift, and laser skin resurfacing.10 Companies providing dual-speed centrifuge platelet-harvesting services have begun aggressive advertising campaigns in the field of facial plastic surgery, purporting dramatic benefits and guaranteeing more rapid patient recovery from cosmetic procedures in healthy patients. These claims have been supported chiefly by the clinical studies previously mentioned.5,11

Although crossover trials have demonstrated improved wound healing in patients with systemic illnesses after treatments with PRP,1 a MEDLINE review fails to reveal data from similarly well-designed studies investigating wound healing in healthy patients undergoing cosmetic surgery. This investigation was designed to determine the effects of APG on recovery from...
operative visits were photographically documented, and were observed in the patient group. A total of 25 post-trial. No intraoperative or postoperative complications were typically healthy patient population undergoing facial plastic surgery.

The goal of this investigation is to document whether there is detectable improvement in wound healing after treatment with APG in the typically healthy patient population undergoing facial plastic surgery.

RESULTS

A total of 8 patients were enrolled in this pilot clinical trial. No intraoperative or postoperative complications were observed in the patient group. A total of 25 postoperative visits were photographically documented, an average of 3 visits per patient (range, 2-4). The range of days patients were seen and photographed was postoperative day 1 to day 26 (mean, day 9). Three judges made 150 individual assessments for postoperative edema and ecchymosis (75 in each category).

The average day of the first assessment was day 3 (range, 1-7); 7 patients were successfully photographed during their first postoperative visit. The remaining patient was photographed, but the film was overexposed during development, and these photographs were not acceptable for evaluation by the judges. The average day of the second assessment was postoperative day 7 (range,

**Figure 3.** Platelet-rich plasma is stored in 10-mL syringes at room temperature after harvest. It is mixed with commercially available bovine topical thrombin and calcium chloride immediately before application; solidification starts within seconds.

**Figure 4.** Platelet-rich plasma is applied under the more superficial cutaneous flap during deep-plane face-lift and may be seen as a glossy, clear layer in the wound (the deep-tissue plane has already been closed).
Table 1. Pooled Observations by 3 Blinded Reviewers of Photographs Examined for Edema and Ecchymosis After Unilateral Autologous Platelet Gel (APG) Treatment During Deep-Plane Face-lift

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>APG-Treated Side</th>
<th>First Postoperative Visit (N = 25 Visits)</th>
<th>Postoperative Visit</th>
<th>Edema Score*</th>
<th>Ecchymosis Score*</th>
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*Numbers 2 and 3 indicate number of judges who agreed on the observation; R, right side of the face has more edema or ecchymosis; L, left side of the face has more edema or ecchymosis; 3, equal response; 1, unanimous positive (the untreated side of the face has more edema or ecchymosis); dagger, pictures for this visit were overexposed on development and were discarded; exclamation mark, unanimous observation; and question mark, the only unanimous negative observation.

Table 2. Condensed Data From Postoperative Photograph Review by Postoperative Visit* with respect to the side treated with APG or the side operated on first. None of the comparisons between groups were found statistically significant using the McNemar test.

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COMMENT

Although no statistically significant differences were identified in the data, trends suggest that APG may enhance recovery or reduce postoperative swelling or bruising in healthy women after deep-plane face-lift. This trend was most apparent early in the recovery period (postoperative days 3-12; visits 1-3), and disappeared by the fourth and final visit (day 18) among the examined cohort of volunteer patients. In general, this trend toward clinical improvement was more apparent with observations of ecchymosis than edema. Interestingly, the only predominantly negative cluster of observations occurred in the edema scores for the first postoperative visit (Table 2). The major data trends were revealed chiefly by the greater number of positive (21) and equal (21) observations than negative ones (8) among the pooled data, and by the vastly greater number of positive (15) than equal (3) and negative (1) unanimous observations.

These trends for improved healing are similar to results of other clinical trials evaluating wounds treated with APG. Knighton et al observed that 17 of 21 chronic lower extremity ulcers reepithelialized during an 8-week course of twice-daily wound treatment with an autologous platelet concentrate, vs 2 of 13 similar wounds treated with placebo. Crossover treatment resulted in reepithelialization among all of the previously unresponsive control pa-
tients. An earlier study by the same group demonstrated a 93% reepithelialization rate among 71 chronic wounds in 41 patients after daily treatments with autologous platelet concentrate.11 A similar clinical protocol was reported in a case series of 171 patients with 355 wounds present an average of 75 weeks; results included a 78% rate of limb salvage after daily 12-hour treatments with APG for an average of 10 weeks.1 Marx et al6 reported enhanced bone formation in mandibular bone grafts treated with PRP, an effect lasting up to 6 months postoperatively that was documented by biopsy-proven enhanced bone deposition among PRP-treated grafts. In the field of facial plastic surgery, one nonrandomized case series documented a single postoperative hematoma among a cohort of 100 consecutive patients undergoing face-lifts treated with bilateral APG, an outcome reported as a significant reduction in postoperative complication incidence by the clinical investigator.10 One attribute of APG that was not examined during this investigation was its reported efficacy as a tissue sealant. In this study, drains were placed bilaterally in all cases (the usual practice of the senior author) to isolate the effect of APG on postoperative recovery. In contrast, Welsh10 placed no drains in his series of 100 consecutive face-lifts treated with APG, and encountered only the single hematoma mentioned above. These results are comparable to those described by advocates of fibrin glue in face-lift surgery.13 Hood et al9 reported a case series detailing the use of APG to seal multiple dural tears, a renal incision, and an aorta graft. Whitman et al14 report

Figure 5. Oblique photographs of patient 3 at the first postoperative visit. Note the greater submandibular swelling and ecchymosis on the left side of her face and neck (patient was treated with autologous platelet gel on the left and received largely negative scores; see Tables 1 and 2). Patient received concurrent blepharoplasties, and judges were instructed to ignore the periorbital region when making their observations.

Figure 6. Patient 5 at her third postoperative visit. Autologous platelet gel was applied to the left side. Judges observed equal edema but greater ecchymosis on the right side (compare buccal and cervical regions; see Tables 1 and 2 for recorded observations).
the use of APG for various applications in oral and maxillofacial surgery, such as achieving hemostasis in iliac crest bone graft donor sites, repair of oral-antral and oral-nasal fistulas, and adhesion of particulate bone matter when reconstructing mandibular defects. Although these reports are anecdotal, the knowledge that platelets contain thrombin and other factors participating in the clotting cascade, and the supraphysiologic concentration of platelets generated in APG, suggest the likely mechanisms responsible for these observations.

Significant wound-healing and tissue-sealant properties of APG have been suggested by multiple investigators. Two other characteristics of APG have also generated comment. One is the autologous source for APG, which eliminates the potential for infection previously observed with pooled, donated blood products. Another is the relative affordability of the procedure. Cardioperfusionists typically charge $400 to $500 for this service in Florida, a small expense compared with the typically larger ones associated with rhytidectomy surgery such as the surgeon and operating room fees. These 2 features are of particular importance because they bring the cost and ease of use of wound-modulating agents into the realm of clinical applicability. Local delivery systems for wound-modulating agents such as APG have previously had limited clinical application in the field of cosmetic surgery owing to the expense of such agents when harvested or bioengineered using conventional techniques.

The observations from this pilot study are consistent with reports from multiple other investigators, and suggest possibly beneficial effects of APG for healthy patients undergoing cosmetic surgery. Further data are needed, ideally in the form of results from a large, multi-institutional trial. Although this study was conceived chiefly to determine if a difference in wound healing could be detected after unilateral wound treatment with APG, a more comprehensive study design would assign scores or grades to denote degrees of edema, ecchymosis, and other indicators of surgical injury. Tissue sealant properties influencing the requirement for or avoidance of drain placement should also be investigated. A clinical comparison between fibrin glue and APG would help characterize this anecdotally reported quality. Such an investigation has the greatest potential to define and quantify the true wound-modulating properties of APG.

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REFERENCES