

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. Farris, 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.

Arch Facial Plast Surg. 2001;3:245-250

From the Division of Facial Plastic and Reconstructive Surgery, Department of Otolaryngology, The Ohio State University, Columbus (Dr Powell), and the Farris Facial Plastic and Reconstructive Surgery Center, Tampa, Fla (Drs Farris and Chang). The authors have no financial relationship to Blood Recovery Systems Inc and received no financial compensation for using its services in the performance of this investigation.

PLATELET-DERIVED growth factors—released from the platelet's α granules when the platelets are activated—have been recognized as crucially important regulatory elements in wound repair.¹ 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.¹⁻⁴ The best understood of these factors are platelet-derived growth factor and transforming growth factor 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.³

Because these 2 growth factors are naturally concentrated in platelets at levels up to 100 times those found in most other body tissues,⁵ 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

*For commentary
see page 251*

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.⁶⁻⁸ Further-

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 face-lift under general anesthesia. The surgical technique is outlined in detail elsewhere.¹² 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



Figure 1. A dual-speed centrifuge is used to spin down the platelet-rich plasma ("buffy coat")—the thin, clear layer between the red outer layer (red blood cells) and the inner platelet-poor plasma layer.

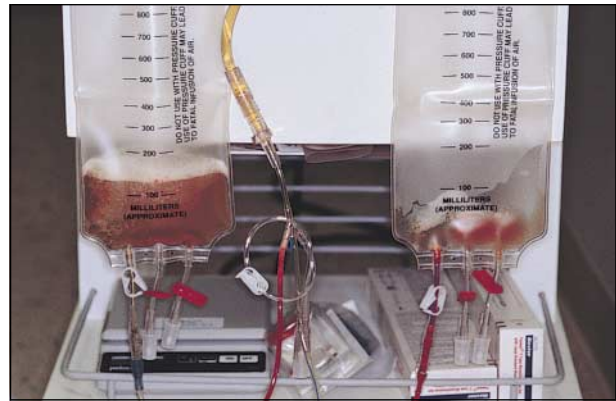


Figure 2. The platelet-rich plasma is starting to collect in the right pouch; platelet-poor plasma has already been temporarily siphoned off in the left pouch.

more, investigators have commented on the adhesive properties of APG that may be exploited as a tissue sealant in some instances.⁹

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,⁸ 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

allowed to sit undisturbed on the exposed surface for at least 5 minutes for maximum solidification. A thin layer is deposited because a very thick layer results in excess dead space and is not recommended by those experienced with PRP technique. In this protocol, 10 mL of APG was deposited under the deep-plane flap of buccal fat and superficial musculoapneurotic system; another 10 mL was deposited under the skin flap. See **Figures 1, 2, 3, and 4** for more detail on PRP harvest and APG deposition.

Wounds were also treated with pressure dressings and low-pressure suction drains. Drains were not attached to suction until after the wounds were completely closed, at least 20 minutes after maximum gel solidification. Drains were removed the following morning; dressings were continued for 2 to 3 days postoperatively.

Patients were evaluated postoperatively on a regular basis. Standard frontal and right and left oblique facial photographs were taken under uniform conditions with identical technique and equipment at each visit. Photographs were typically taken at regular intervals in the 4 weeks following surgery.

After all patients were enrolled and photographs documenting postoperative recovery were completed, photographs were reviewed in a blinded fashion by 3 judges experienced with facial plastic surgery. Patients were randomized, then individual patient photograph series were presented in chronological order from the immediate to late postoperative periods. Judges were asked to evaluate the buccal, preauricular, and cervical regions on both sides of

the patient's face at each stage of recovery, then to record the side of the patient's face that had greater edema and ecchymosis (these outcomes were recorded separately). Specifically, judges were asked to carefully inspect the frontal and right and left oblique photographs to identify if there was any detectable difference in the amount of edema or ecchymosis. If any difference was detected, the side with the greater amount of swelling or bruising was recorded; otherwise, the patient received a score of *equal* for that particular postoperative visit. Some patients had concurrent blepharoplasties through separate incisions, so judges were specifically requested to ignore this region.

Data were then tabulated for descriptive statistics. We defined a *positive* observation as one in which 2 or 3 judges identified more edema or ecchymosis on the untreated side of the patient's face than on the treated side. Greater edema or ecchymosis on the side treated with APG, if noted by 2 or 3 judges, was defined as a *negative* observation. When 2 or 3 judges recorded equal edema or ecchymosis on both sides of the face we recorded an equal observation. If conflicting data were entered (ie, each judge recorded a different observation), the final observation was recorded as equal for that particular photograph set.

McNemar's test of equality of paired proportions was used for statistical analysis to determine whether there was a statistically significant difference between the scores received for the treated vs the untreated sides of the patients' faces, with a *P* value of .05 or lower designated as statistically significant.

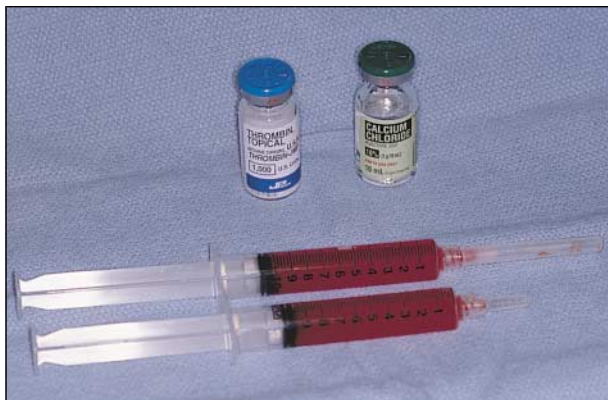


Figure 3. Platelet-rich plasma is stored in 10-mL syringes at room temperature after harvest. It is mixed with commercially available bovine topical thrombin and calcium chloride immediately before application; solidification starts within seconds.

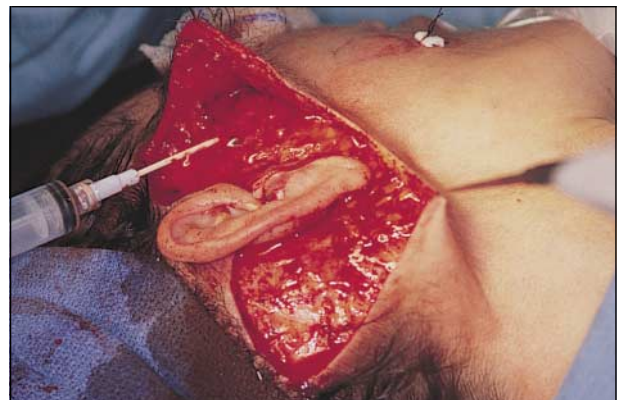


Figure 4. Platelet-rich plasma is applied under the more superficial cutaneous flap during deep-plane face-lift and may be seen as a glossy, clear layer in the wound (the deep-tissue plane has already been closed).

deep-plane face-lift in a randomized, controlled study. 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,

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

Patient No.	APG-Treated Side	First Side Treated	Postoperative Visit (N = 25 Visits)	Edema	Ecchymosis
				Score*	Score*
1	Right	Right	1	2=	3L!
			2	2=	3L!
			3	2=	3L!
			4	3=!	3=!
2	Right	Left	1	<i>2R</i>	<i>3R!?</i>
			2	2=	<i>2R</i>
3	Left	Left	1	<i>2L</i>	2=
			2	<i>2L</i>	<i>2L</i>
			3	<i>2L</i>	2=
4	Left	Left	1	2=	2=
			2	2R	3R!
			3	2R	3R!
			4	2=	3R!
5	Left	Left	1	2=	<i>2R</i>
			2	2R	3R!
			3	2=	3R!
6	Left	Right	1	3R!	3R!
			2	3R!	3R!
			3	3R!	2=
			4	2R	2=
7	Left	Right	1	†	†
			2	3R!	3R!
			3	2=	2=
8	Left	Right	1	<i>2L</i>	2R
			2	2=	3R!

*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; equal sign, both sides of the face have an equal amount of edema or ecchymosis; boldface, observation is positive (the untreated side of the face has more edema or ecchymosis); italics, observation is negative (the APG-treated 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.

2-13); all 8 patients were photographically documented at this visit. The average day of the third assessment was postoperative day 12 (range, 6-22); 6 patients were photographed; 2 refused photographs secondary to time constraints. The average day of the fourth assessment was postoperative day 18 (range, 9-26); 4 patients were photographed; 4 were not photographed because recovery was thought to be complete by the performing surgeon and senior author (E.H.F.).

Scores for postoperative edema and ecchymosis were recorded by postoperative visit. Data points defined as identical observations by 2 or more judges are presented in comprehensive format in **Table 1**. Condensed data are presented in **Table 2**. Two examples of evaluated sets of photographs are presented in **Figure 5** and **Figure 6**.

Some trends were noted when the data were condensed. There were more than twice as many positive and equal responses as negative ones (21, 20, and 9, respectively). In general, a greater difference between the treated and untreated sides was observed for ecchymosis than for edema (13 positive, 9 equal, and 3 negative

Table 2. Condensed Data From Postoperative Photograph Review by Postoperative Visit*

Postoperative Visit	Edema			Ecchymosis		
	+	=	-	+	=	-
1	1 (1)	3	3	4 (2)	2	1 (1)
2	4 (2)	3	1	6 (6)	0	2
3	2 (1)	3	1	3 (3)	3	0
4	1	2 (1)	1	0	4 (2)	0
Total	8 (4)	11 (1)	6	13 (11)	9 (2)	3 (1)

*Plus sign indicates more edema or ecchymosis on the untreated side of the face (positive observation); equal sign, equal amounts of edema or ecchymosis on both sides of the face (equal observation); and minus sign, more edema or ecchymosis on the treated side of the face (negative observation). Numbers in parentheses indicate number with a unanimous observation by all 3 judges.

for ecchymosis vs 8 positive, 11 equal, and 6 negative for edema). Positive observations were clustered early in recovery and were most dense at the second visit; by the fourth postoperative visit, this trend had disappeared in favor of heavily equal observations (Table 2).

Data were further contracted by analysis only of observations where all 3 judges were in unanimous agreement. There were 15 unanimously positive observations (11 for ecchymosis, 4 for edema) vs 1 unanimously negative one (ecchymosis) and 3 unanimously equal scores (1 edema, 2 ecchymosis).

No trends were noted when data were analyzed 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.

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 al⁸ 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-



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).

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

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.

Accepted for publication August 15, 2001.

We wish to thank Blood Recovery Systems Inc of Fort Myers, Fla, for donating platelet sequestration equipment and technical expertise during the generation of APG for the patients in this study.

Corresponding author and reprints: David M. Powell, MD, Division of Facial Plastic and Reconstructive Surgery, Department of Otolaryngology, The Ohio State University, 4100 UHC, 456 W 10th Ave, Columbus, OH 43210 (e-mail: powell.210@osu.edu).

REFERENCES

1. Ganio C, Tenewitz FE, Wilson RC, Moyles BG. The treatment of chronic nonhealing wounds using autologous platelet-derived growth factors. *J Foot Ankle Surg.* 1993;32:263-268.
2. Slater M, Patava J, Kingham K, Mason RS. Involvement of platelets in stimulating osteogenic activity. *J Orthop Res.* 1995;13:655-663.
3. Hom DB, Maisel RH. Angiogenic growth factors: their effects and potential in soft tissue wound healing. *Ann Otol Rhinol Laryngol.* 1992;101:349-354.
4. Pierce GF, Berg JV, Rudolph R, Tarpley J, Mustoe TA. Platelet-derived growth factor-BB and transforming growth factor beta 1 selectively modulate glycosaminoglycans, collagen, and myofibroblasts in excisional wounds. *Am J Pathol.* 1991;138:629-646.
5. Lind M. Growth factors: possible new clinical tools. *Acta Orthop Scand.* 1996; 67:407-417.
6. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma growth factor enhancement for bone grafts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1998;85:638-646.
7. Korobelnik JF, Hannouche D, Belayachi N, Branger M, Guez JE, Hoang-Xuan T. Autologous platelet concentrate as an adjunct in macular hole healing. *Ophthalmology.* 1996;103:590-594.
8. Knighton DR, Ciresi K, Fiegel VD, Schummer S, Butler E, Cerra F. Stimulation of repair in chronic, nonhealing, cutaneous ulcers using platelet-derived wound healing formula. *Surg Gynecol Obstet.* 1990;170:56-60.
9. Hood AG, Hill AG, Reeder GD, et al. Perioperative autologous sequestration III: a new physiologic glue with wound healing properties. *Proc Am Acad Cardiovasc Perfusion.* 1993;14:126-129.
10. Welsh W. Platelet gel usage in cosmetic surgery. Presented at: American Academy of Cosmetic Surgery 16th annual scientific meeting; January 27-30, 2000; Orlando, Fla.
11. Knighton DR, Fiegel VD, Doucette MM, Fylling CP, Cerra FB. The use of topically applied platelet growth factors in chronic nonhealing wounds: a review. *Wounds.* 1989;1:71-78.
12. Hamra ST. *Composite Rhytidectomy.* St Louis, Mo: Quality Medical Publishing Inc; 1993.
13. Flemming I. Fibrin glue in face lifts. *Facial Plast Surg.* 1992;8:79-88.
14. Whitman DH, Berry RL, Green DL. Platelet gel: an autologous alternative to fibrin glue with applications in oral and maxillofacial surgery. *J Oral Maxillofac Surg.* 1997;55:1294-1299.