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ORIGINAL ARTICLE

Effects of leukocyte-platelet rich fibrin on postoperative complications of direct sinus lifting

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ABSTRACT

BACKGROUND: Blood products have been widely used in soft tissue and bone regeneration in oral and maxillofacial surgery. The purpose of this study is to evaluate the effects of leukocyte-platelet rich fibrin (L-PRF) following direct sinus lifting procedure.

METHODS**:** Twenty-eight patients were included in the study. Direct sinus lifting was performed via lateral window approach under conscious sedation and local anesthesia. Bony window and sinus floor elevation were performed using piezosurgery device. Two groups were formed. In the first group an allogenous bone graft and L-PRF mixture was used as grafting material. The L-PRF membrane was used to close the lateral window. In the second group, only allogenous bone was used for grafting and resorbable collagen membrane was used to close the lateral window. Pain, swelling, sleeping, eating, phonetics, activities of daily living, missed work days and soft tissue healing were evaluated postoperatively.

RESULTS: Data of 24 patients were evaluated. Improvements were seen in the studied parameters in the L-PRF group; however, the difference was not significant between the two groups ($P>0.05$).

CONCLUSIONS: The use of L-PRF and allogenous bone graft in combination with L-PRF membrane does not significantly improve postoperative complications following direct sinus lifting.

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Platelet concentrates are increasingly being used in oral and maxillofacial surgery. Thrombin activated autologous platelet rich plasma (PRP) or platelet concentrate (PC), usually known as platelet gel has been used as either the sole material or in combination with other grafting materials. Previous studies have shown that platelet α-granules include high amounts of growth factors which play a critical role in both soft and hard tissue healing.[1]

The use of platelet rich fibrin (PRF) was introduced by Choukron *et al.* as a second generation platelet concentrate which contains leukocytes and does not require the use of anticoagulants.[2] PRF is not only a platelet concentrate but also acts similar to an immune node with the ability to stimulate defense mechanisms. The precise action of these defense mechanisms is unclear, but platelets are believed to have multiple functional effects in antimicrobial host defense.[2] PRF slowly releases a high concentration of cytokines and growth factors (GF) such as: platelet derived growth factor (PDGF), insulin like growth factor (IGF), transforming growth factor (TGF), and vascular endothelial growth factor (VEGF); this release occurs primarily during the first 7 days after application and shows a gradual decrease during the following 28 days.[3-5] Platelet derived cytokines which play

a critical role in healing and connective tissue remodeling, are gradually released as the fibrin matrix resorbs.[6]

Preparation of PRF requires a simple technique. Venous blood is collected in 10 mL dry tubes and centrifuged immediately without the addition of anticoagulants. After centrifugation three layers are formed: red blood cells at the bottom, PRF in the middle, and acellular plasma (platelet-poor plasma) at the top. It was reported that 97% of the platelets and 50% of the leukocytes from the original blood sample are concentrated in the PRF.[7]

Sinus lifting is a commonly preferred procedure that enables the practitioners to install a dental implant in the atrophic posterior maxilla. Either direct (lateral approach) or indirect (osteotome) technique may be used, depending on the residual alveolar bone height. As any other surgical procedure, sinus lifting may present complications.[8-10]

The purpose of this study was to evaluate the effect of leukocyte-platelet rich fibrin (L-PRF) on soft tissue healing and on postoperative self-assessed parameters of pain, swelling, sleeping, eating, phonetics, activities of daily living, missed work days following direct sinus lifting.

Materials and methods

Patients undergoing direct sinus lifting for placement of dental implants in the posterior maxilla were enrolled in the study. Inclusion criteria were; residual alveolar bone height of less than 5 mm, lack any systemic disease, no prior or present maxillary sinus pathology, smoking less than 10 cigarettes per day and no use of any antibiotics or anti-inflammatory drugs for at least 30 days prior to surgery. Only one side was included in the study even if the patient needed bilateral surgery. Participants were randomly assigned by coin toss to one of two groups: the study group and the control group. This study was approved by the Ethical Board of Istanbul Medipol University. Patients were informed regarding the study protocol and written consent was obtained. Each patient was examined by cone beam computed tomography (CBCT) preoperatively to measure residual alveolar bone height and to evaluate the maxillary sinus.

L-PRF was produced by the protocol described by Dohan *et al.*[11] Four blood samples (10 cc each) were taken in 10 ml glass coated plastic tubes without the use of an anticoagulant. The blood samples were centrifuged at 2700 rpm for 12 minutes (IntraSpin™, Intra-Lock International-Inc., Baco Raton, FL, USA) (Figure 1). After centrifugation, each PRF clot was prepared in pieces (2 tubes) and membrane forms (2 tubes).

All patients underwent direct sinus lifting procedure (lateral window approach) performed by two experienced oral and maxillofacial surgeons. Sinus lifting was carried out

Figure 1.—Centrifugation of blood samples at 2700 rpm for 12 minutes.

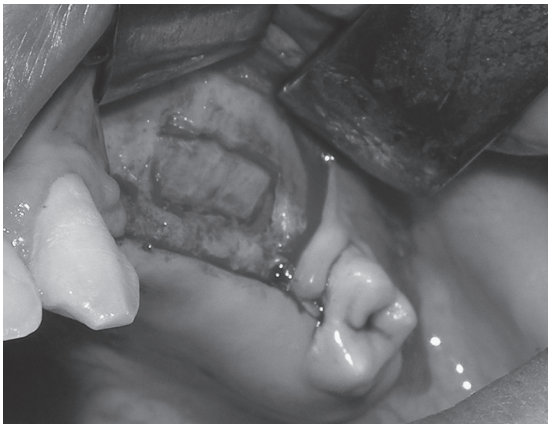

Figure 2.—Opening of lateral sinus window and sinus membrane elevation.

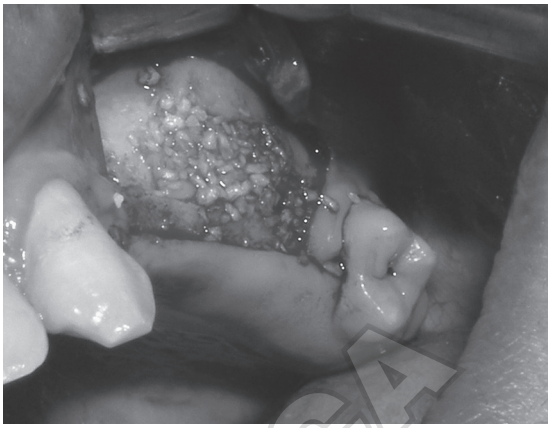

Figure 3.—Allogenous bone graft and L-PRF mixture for sinus grafting.

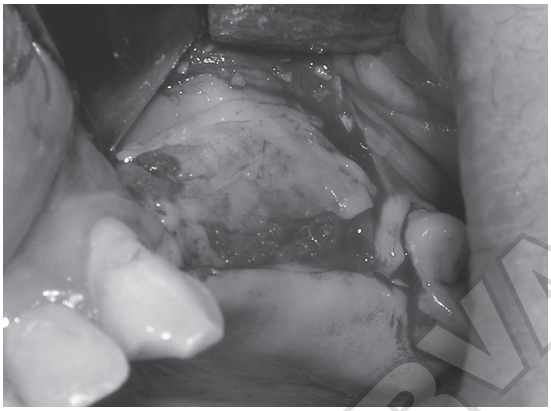

Figure 4.—Lateral window was covered with two layers of L-PRF membranes.

under conscious sedation (1 mg midazolam + 50 mg pethidine HCL) and local anesthesia (lidocaine HCL: 20 mg/mL, epinephrine HCL: 0.0125 mg/mL). After raising a mucoperiosteal flap, osteotomy and sinus membrane elevation were performed with the piezosurgery device (EMS Piezon Master Surgery®, Nyon, Switzerland) (Figure 2).

In the study group, after obtaining sufficient space by elevating the sinus membrane, allogenous freeze dried corticocancellous bone chips (MinerOss®, BioHorizons, Birmingham, AL, USA) mixed with L-PRF were used for grafting (Figure 3). Bony sinus windows were covered with two layers of PRF membranes (Figure 4). In the control group, subjects only received an allogenous bone graft. Bony sinus windows were covered with a resorbable collagen membrane (Bioteck® Bioteck S.p.A, Vicenza, Italy). Mucoperiosteal flaps were primarily closed with 3/0 silk suture. All subjects were prescribed 500 mg cephalexin twice daily, 500 mg paracetamol twice daily for five days and chlorhexidine mouthrinse twice daily for 15 days starting the day after surgery. Sutures were removed on the 7th postoperative day. The use of dentures was not permitted until they had been adjusted and refitted and no sooner than 2 weeks after surgery.

Patients were asked to fill out a questionnaire regarding the following parameters: postoperative pain, swelling, sleeping, eating, phonetics, activities of daily living, and missed work days. These factors were self-assessed on a 4-point scale ranging from 0 to 3: 0-little/none, 1-some, 2-quite a bit, 3-very much. Patients were asked to complete the form at the 8th, 24th, 48th, and 72nd postoperative hours and on the 7th postoperative day. Clinical evaluation of soft tissue healing was assessed by using the Healing Index (HI) described by Landry *et al.*[12] Recordings of HI were performed on the 7th and 14th postoperative days by a surgeon who was blinded to the treatment of patients. A score of 1 to 5 was given, with 1 being associated with very poor healing and 5 with excellent healing.

Statistical analysis of the data was done using SPSS Statistics 22 program (IBM®, Armonk, NY, USA). Mann-Whitney U Test was

used for between group comparisons, and Wilcoxon Signed-Rank Test was used for intragroup comparisons. P-value≤0.05 was considered significant.

Results

Twenty-eight patients were included in the study. Four patients were excluded from the analyses due to postoperative maxillary sinusitis developing in two patients and sinus membrane perforation occurred in two patients during surgery. Study treatment was continued in the excluded patients. In total, 24 patients (14 male, 10 female) aged 23 to 66 years with a mean of 47.8 years were assessed. Each group consisted of 12 patients (study group: 8 male and 4 female with a mean age of 46.3 years and the control group: 7 male and 5 female with a mean age of 49.3 years). There were gradual improvements in postoperative pain, swelling, sleeping, eating, phonetics, activities of daily living, and missed work days in the L-PRF group, but the differences between the groups were not significant (P>0.05) (Table I). Wound healing in both study and control groups was uneventful. HI scores of the L-PRF group (4.2±0.9) were higher than that of the control group (3.6±0.7) on the 7th (4.7±0.4) and 14th postoperative days (4.4±0.5); however, these differences were not statistically significant (P=0.127 and P=0.189, respectively).

Discussion

PRF is a second generation platelet concentrate consisting of a fibrin matrix that contains platelets, leukocyte, cytokines and circulating stem cells. It was demonstrated that platelets in PRF releases high quantities of growth factors for at least 7 days after application.[13] Leukocytes in the fibrin clot are activated during centrifugation. Inflammatory and anti-inflammatory cytokines are incorporated into the fibrin network. The gradual release of these molecules may play a significant role in inflammatory and infectious reactions.[6]

The use of PRF presents multiple advantages. Firstly, PRF forms a gel-like matrix that contains high concentrations of functional platelets that release growth factors. Secondly, it can be easily reshaped to form a membrane which serves as a matrix to accelerate wound healing. Thirdly, PRF is easy to prepare and manipulate, and is inexpensive.[14]

Dohan *et al.* reported that PRF also plays an important role in suppressing inflammatory reactions, thus acting as an immune regulation node, and attributed these effects to the release of anti-inflammatory cytokines.[15] The ability to release GF and cytokines makes PRF an attractive biologic agent in oral and maxillofacial surgery. Simonpieri *et al.* emphasized that PRF reduces pain and edema and also limits minor infectious phenomena. These authors also suggested that leucocytes and cytokines enable PRF to play an important role in immunity and inflammation. The gradual release of these molecules affects the self-regulation of inflammatory and infectious processes.[6]

Studies have reported improved tissue healing and increased patient comfort during the early wound healing period (the first 7 postoperative days) when PRF is used as graft material and membrane;[16-18] therefore, we hypothesized that the use of PRF in direct sinus lifting may enhance wound healing and reduce postoperative complications. The healing of oral

TABLE I.—*The results of self assessed parameters in L-PRF and control groups.*

	8th hour		24th hour		48th hour		72nd hour		7th day	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
Pain	1.7±0.95	1.7±0.67	0.8±0.63	0.9±0.57	0.5±0.71	0.9±0.99	0.4±0.52	0.6±1.26	0.1±0.32	0.5±0.85
Swelling	1.21±1.03	1.2±0.63	1.5±0.85	1.5±0.53	1.2±0.79	1±0.82	0.5±0.71	0.7±0.95	0.2±0.42	0.2±0.42
Sleeping	0.9±0.99	1.3±0.67	0.5±0.53	0.8±0.63	0±0	0.5±0.97	0±0	0.4±0.97	0±0	0.2±0.42
Eating	1.6±0.84	1.6±0.84	1±0,94	1.2±0.79	0.5±0.85	0.9±0.99	0.3±0.67	0.7±1.25	0.2±0.63	0.5±1.08
Phonetics	1.2±1.03	1.2±0.79	0.6±0.84	1±0.67	0.4±0.52	0.6±0.84	0.1±0.32	0.3±0.67	0.1±0.32	0.2±0.42
Activities of daily living	1.6±0.97	1.1±0.88	1±0.94	0.8±0.79	0.5±0.71	0.7±0.95	0.3±0.67	0.6±0.97	0.2±0.63	0.2±0.42
Missed work days	2±0.94	1.3±1.06	0.9±0.74	0.6±0.7	0.5±0.71	0.7±0.95	0.4±0.7	0.6±0.97	0.4±0.7	0.4±0.52

soft tissue was predominantly investigated in periodontal surgery research. The use of PRF in combination with coronally advanced flap was compared with enamel matrix derivative in combination with coronally advanced flap in gingival recession treatment. It was found that HI scores were significantly higher in the PRF group one week postoperatively, whereas as scores of both groups were similar after two postoperative weeks.[17] Jankovic *et al.* used PRF in the treatment of gingival recessions with a coronally advanced flap and they reported higher gingival HI and less pain in the PRF group. In another study, Jankovic *et al.* compared PRF membrane and connective tissue graft in gingival recession treatment and found not a significant difference between the groups on treatment outcomes. However, HI scores in the first and second postoperative weeks were significantly better in the PRF group. Similarly, patients in the PRF group reported lower intensity of pain in the first 7 days after the operation. They concluded that improvement in early wound healing provided less patient discomfort postoperatively.[18] The strength of the L-PRF membrane provides protection against unfavorable forces demonstrating its mechanical role as a barrier membrane.[6, 16]

The effect of PRF on bone regeneration after direct sinus lifting procedure has been investigated. Xuan *et al.* compared PRF combined with anorganic bovine bone particles with commercial fibrin combined with anorganic bovine bone in canine model. They found that bone formation in the PRF group was significantly greater than in the fibrin group.[19] Zhang *et al.* compared PRF combined anorganic bovine bone (Bio-Oss) particles and Bio-Oss alone in direct sinus lifting. Histological and histomorphometric evaluatios revealed similar percentages of new bone formation, residual bone substitute and contact length between newly formed bone and bone substitute. They concluded that there is neither advantage nor disadvantage in adding PRF to Bio-Oss for bone regeneration in direct sinus lifting.[20] In our study we did not evaluate bone healing, hence were unable to determine the effects of L-PRF on bone regeneration.

We found higher HI scores in the PRF group than in the control group although the difference was not significant. Favorable effects of PRF on wound healing may be related to dense fibrin fibers observed in the PRF membrane and the activity of growth factors leading to increased angiogenesis and matrix biosynthesis.[17] L-PRF is not only a simple fibrin membrane but also a matrix containing all the molecular and cellular elements allowing optimal healing. The matrix contains all favorable components found in the blood.[6]

In this study the parameters assessing postoperative patient comfort did not show significant differences between the groups. Pain and swelling are the most frequent seen complications after sinus lifting surgery. In this study the L-PRF group showed less pain and swelling than the control group; however, the differences were not statistically significant. Piezosurgery device was used in all operations for the creation of lateral sinus window. In a previous study, piezosurgery device was found to cause less pain and swelling postoperatively compared with conventional technique.[21] There are other reported complications related to sinus lifting which we did not investigate in this study.[22-24]

Conclusions

The results of this study demonstrates better wound healing and patient comfort following direct sinus lifting although the difference did not reach significance. Studies with larger number of patients or using different parameters to evaluate patient comfort following oral surgery procedures may yield significant results.

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Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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