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The Effectiveness of Platelet Rich Fibrin as a Graft Material in Sinus Augmentation Procedures through Lateral Approach

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Abstract

Background: Rehabilitation of posterior maxilla is compromised by deficient residual bone height that inversely affects the primary dental implant stability. Sinus augmentation is a predictable surgery to provide additional bone volume. Natural bone regeneration can be improved with the use of platelet rich fibrin (PRF) that serves as a scaffold for new bone regeneration.

Aim: evaluation of effectiveness of PRF as a sole graft material with immediate or delayed implant placement.

Materials and methods: Simultaneous 17 implants placement with sinus augmentation (one-stage surgery) were done for 14 sinuses while augmentation with delayed implant placement (two-stage surgery) was performed for 5 sinuses with PRF as the sole filling biomaterial. Ten males and 6 females with mean age of 48.88 years (range: 29-65) were enrolled in this study. For each patient, a presurgical examination with orthopantomography (OPG) and cone beam computed tomography (CBCT) for initial assessment of the residual bone height. Twenty four weeks postsurgical radiographic examination was obtained with CBCT to assess the final height and density of submembranous bone.

Results: The submembraneous bone height for one-stage surgery ranged between 10.7 and 13.9 and for two-stage surgery ranged between 1.2-7.2 mm in proposed implant site, which was highly significant for both protocols. The mean density of gained bone in one-stage surgery cases 408.28±169.89 Hounsfield unit (HU), while for two-stage surgery was 183.60±97.67 HU. Postoperative period was uneventful and all implants were stable after 24 weeks.

Conclusion: Platelet rich fibrin is an easily obtained and cost effective biomaterial. PRF as the sole graft material with immediate implant placement provides stable, high level bone. However, despite PRF is able to form new bone in two-stage protocol but its capacity to maintain space is unclear.

Key words: platelet rich fibrin, sinus augmentation, sinus lift, dental implant.

INTRODUCTION

Edentulism of posterior maxilla results in deficient bone volume and vertical height between the floor of the sinus and the edentulous ridge, compromising the placement of dental implant with the necessary primary stability for long-term success. Sinus floor elevation to augment the maxillary sinus can be achieved by two main approaches: the external lateral window approach and the internal transalveolar approach[1].

The lateral window approach was first developed by Tatum in the mid-seventies and was published by Boyne and James in 1980. It is the most popular method to increase the residual bone height of the posterior maxilla with simultaneous or delayed implant placement[2].The other approach, established by **Summers** is the crestal technique. It is more conservative, less time consuming; but provides only limited augmentation. With both techniques a variety of augmentation material are used with successful results such as autogenous bone grafts, allografts, xenografts, and alloplastic materials [3]. Nowadays, platelet rich fibrin (PRF) has been used as sinus augmentation material. It was first prepared by Choukroun *et al*. in 2001 by simple collection of venous blood and centrifugation without any additives. It is characterized by its fibrin mesh that is enriched with platelets and growth factors, so accelerates physiologic wound healing and new bone formation [4]. For pre and postoperative assessment of sinus augmentation procedures cone beam computed tomography (CBCT) is potential and reliable diagnostic modality as reported in many literatures[5]. The objective of this clinical study was to assess the effectiveness of PRF clots as the sole filling material during lateral sinus lift with immediate or delayed implant placement using CBCT for radiographical analysis of height and density of neoformed bone.

MATERIALS AND METHODS

This prospective interventional non-controlled clinical study was conducted from October 2016 to September 2017 at the Department of Oral and Maxillofacial Surgery, College of Dentistry, Teaching Hospital, University of Baghdad, and Radiology Department of Al-Sadr Specialized Health Center.

A total of 16 patients aged 29-65 years, 10 males and 6 females who met the inclusion criteria were included in this study. Seventeen implants were placed simultaneously in 14 sinus lift procedures for 12 patients. Five cases (sinuses) underwent sinus augmentation only with delayed implant placement protocol for 4 patients. Three patients were treated bilaterally. All the cases underwent lateral sinus lift procedures in which PRF was used as the sole graft material. (Dentium Co., Korea) Dentium implant system was used in all procedures.

Inclusion criteria

1. Patients presented with partially or completely edentulous maxilla with pneumatized sinus seeking for dental implant placement.
2. Sinus augmentation with simultaneous implant placement were performed in cases of residual bone height (RBH) 3-6 mm while delayed implant placement in cases of RBH <3 mm.

Exclusion criteria

1. Local pathology or systemic diseases that compromise bone healing potential as radiotherapy, fibrous dysplasia, hyperparathyroidism, uncontrolled diabetes, etc…..
2. Clinical or radiographical features of rhinosinusitis and acute/chronic infection in the implant zone.
3. Parafunctional habits such as severe bruxism and clenching.
4. Alveolar ridge width <6 mm.
5. Previous sinus surgery.
6. Patients with recent history of radio or chemotherapy, receiving bisphosphonates, or other related drugs.

Preoperative assessment and surgical procedure

Preoperative OPG was taken for initial assessment. Cone beam CT is essential for assessment of alveolar bone height, width, and density of implant site, tooth proximity to implant site, septa, membrane thickness, antral pathology, ostium patency, sinus pneumatization, lateral wall thickness, and intraosseous alveolar antral artery, Figure (Fig.) 1(A). Surgery was done under local anasthesia. Reflection of full thickness mucoperiosteal three sided flap, followed by preparation of lateral osteotomy window with the first point of drilling is located at 3 mm from anterior and inferior border of the sinus wall, and can be adequately

determined with the aid of CBCT. Drilling was carried out in soft, intermitent, and sweeping motion with copious irrigation using round diamond bur attached to handpiece. Drilling was continued posteriorly according to the the length of edentolous area and amount of augmentation. Then again from the starting point, the drilling upward continued to a point that not exceed (if possible, depending on RBH) 16 mm from the alveolar ridge. Then the osteotomy preparation was continued to obtain the rectangular or oval shape window, Fig. 1(B). With contineous deepening of drilling the bluish hue of sinus membrane could be visible. Appropriate sinus membrane elevator was used from to start seperation of membrane from floor of sinus for only a few millimetres then mesial, distal, and apical separation of membrane. After that went back to the floor and complete elevation of sinus membrane according to amount of augmentation. Checking of Schneiderian membrane integrity was done at this stage by asking the patient to take deep breath and watching the upward and downward movement of the membrane with the attached bony island. Next, the preparation of implant osteotomy sites by subsequent drillng with gradually increasing size drills untill reaching the desired implant size but not to the full length for better primary stability[6] .

Platelet rich fibrin preparation

Twenty mL of whole blood was collected from one of the superficial veins in cubital fossa (cephalic, basilic, median cubital, and median antebrachial veins)[7] into two plain glass tubes and was immediately centrifuged at 3000 rpm for 10 minutes[8]. About one and a half of PRF clots were gently introduced into the created artificial space (sinus membrane space) ,Fig. 1(C), The implant was placed in its prepared bed to serve as a tentpeg then half of one of PRF clot was compressed slightly between two pieces of wet sterile gauze to be used as a membrane covering the lateral window. The flap was addapted to its position and wound closure was performed.

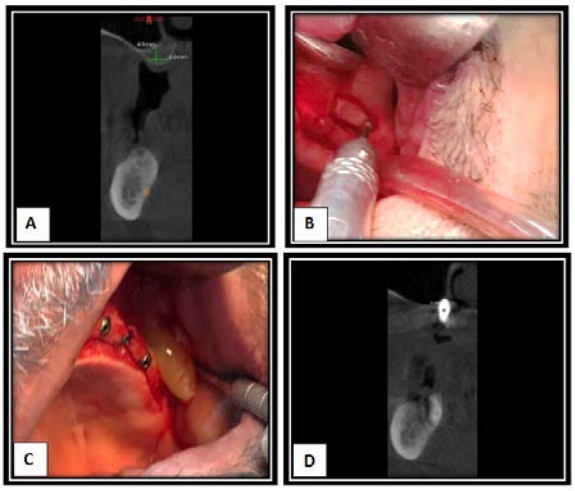

Figure 1: (A) Coronal view of CBCT revealed preoperative hight and width of residual alveolar bone. (B) Lateral osteotomy window preparation. (C) Insertion of PRF clot after implant placement. (D) Coronal view of CBCT 24 weeks after sinus augmentation reveals the dental implant is completely surrounded by bone.

Postoperative management

All patients were given medications including cefixime trihydrate, 400 mg tab orally once/day, for 5 days, metronidazole 250 mg tab orally three times/day , for 5 days, phenylephrine 0.5% nasal drops 2-3 drops every 4 hours for 5 days, acetaminophen500 mg tab, orally on need, and chlorhexidine digluconate 0.2% mouthwash twice/day for 2 weeks.

Evaluation method (six months after surgery)

1. The neoformed bone was measured in submillimeters using special CBCT software tools by substracting the preoperative RBH (measure X) from the postoperative submembraneous bone height (SBH) (measure Y) which was calibrated from alveolar bone to the uppermost point of bone above the DI, Fig. 1(D) Neoformed bone = measure Y – measure X .
2. Density of neoformed bone was measured at three points; mesial, distal, and apical to the implant, and mean density was calculated. Density estimation was performed utilizing CBCT (Carestream Health Inc., USA) depending on misch scale for density estimation as follow: D1>1250 HU, D2= 850-1250 HU, D3= 350-850 HU, D4 =150-350 HU, and D5 <150 HU[9] .
3. Ossseointegration of implant is assessed according to Albrektsson criteria of success (immobility, asymptomatic, no peri-implant radiolucency).
4. Sinus was evaluated for any complications or pathological changes clinically and radiographically.

Fixtures exposure was done by using tissue punch at speed 300 rpm and the cover screw was removed and replaced by healing abutment for about 10-14 days, thereafter the patient was referred to the prosthodontic department for fabrication of the final prosthesis. Statistical analysis using Statistical Package for social Science (SPSS version 21) was presented as Frequency, percentage, mean, and standard deviation. Two independent samples T-test: test the significant differences of means between two groups. Paired sample T test: the data may consist of two measurements taken on the same subject or one measurement taken on a matched pair of subjects. Pearson Correlation (r): test the correlation between two quantitative variables. Level of significance as: not significant P>0.05, significant P<0.05, highly significant P<0.01.

RESULTS

The SBH (RBH+ neoformed bone) for one-stage surgery in each implant site ranged between 10.7 and 13.9 mm (mean±SD 12.44±0.99) and for two-stage surgery ranged between 1.2-7.2 mm (mean 4.93±1.61) in proposed implant site, which was highly significant for both protocols, table (1).

Table 1: Descriptive and statistical test of postoperative SBH (mm) among stages.

Description	Stages		Independent Sample T test		
	One-Stage	Two-Stage	T	DF	P-value
Min.	10.70	1.20	15.021	25	0.000 HS
Max.	13.90	7.20			
Mean	12.44	4.93			
SD	0.99	1.61			
SE	0.24	0.51			

HS: highly significant at P<0.01.

The mean of gained bone in one-stage surgery was 7.98±1.70 mm and 3.01±1.63 mm in two-stage surgery which was also highly significant. The density of gained bone was measured for each treatment protocol and it was found that the density in the one-stage surgery cases was 408.28±169.89 HU which falls in D3 category according to Misch scale of density, while for two-stage surgery the mean of gained bone density was 183.60±97.67 HU which falls in D4 category. For one-stage surgery there was 5.88% of cases were located in D2 category followed by 35.29% D3, and 58.82% D4. For two-stage surgery 80% of cases fall in D4 category and 20% in D5. Bone density of D1 category was not obtained in one or two-stage surgery, table (2).

Table 2: Descriptive and statistical test of density change within stages.

Stage		Subantral bone density (HU)	Gained bone density (HU)	Paired sample Test		
				T	DF	P-value
One-Stage	Min.	110.00	236.10	4.457	16	0.001 HS
	Max.	623.00	863.60			
	Mean	256.59	408.28			
	SD	135.99	169.89			
	SE	32.98	41.20			
Two-Stage	Min.	113.00	.00	0.675	9	0.517 NS
	Max.	341.00	244.00			
	Mean	222.20	183.60			
	SD	95.74	97.67			
	SE	30.28	30.89			
Total	Min.	110.00	.00	2.351	26	0.027 Sig.
	Max.	623.00	863.60			
	Mean	243.85	325.07			
	SD	121.82	182.46			
	SE	23.45	35.11			

NS=not significant at P>0.05,Sig.=significant at P<0.05,HS=highly significant at P<0.01.

Strong positive correlation was found between implant length and gained bone (r=0.65) and this is highly significant (0.005) at p<0.01, while non significant correlation was found between implant length and density. No statistically significant correlation was found between implant diameter, gained bone and density. Intraoperative complications were reported as bleeding from injured alveolar antral artery in 3 cases (15.79%) and Schneiderian membrane perforation occurred in 4 cases (21.05%). Neither postoperative complications such as infection, wound dehiscence, nor implant failure were recorded. For both treatment protocols, the total mean of preoperative membrane thickness was 3.17 mm and 2.46 mm postoperatively. There were no statistically significant changes in membrane thickness (P-value=0.53).

DISCUSSION

The result of this study reveals that PRF clot is effective when used as a sole filling material during a lateral sinus lift with immediate implant placement and less effective when delayed implant placement protocol is performed, utilizing CBCT for radiographical analyses of height and density of neoformed bone.The final SBH 6 months after surgery for each implant site was highly significant. For one-stage surgery; the SBH ranged between 10.7 mm and 13.9 mm (mean 12.44±0.99 mm). On clinical examination all implants were stable at the time of surgical exposure and radiographically the end of implant was in continuity with the sinus floor. This is comparable with other available studies in the same topic[10-12] . Although in these studies greater amount of PRF clots were used (72 mL of whole blood withdrawn to prepare 8 PRF membranes). The placement of PRF clot in close relation with Schneiderian membrane may be responsible for more stable bone at the level of implant apex due to stimulation of periosteal-like layer of Schneiderian membrane as it is documented that PRF clot has a great potential for intense osteoblast stimulation[13] **.**The implant serves as a space maintainer, i.e. keeps the *Schneiderian membrane* elevated and prevents its collapse, so the natural bone regeneration is highly stabilized in the submembraneous space up to the implant apex[10]. Graftless sinus lift is well documented procedure and published by many authors, but ends up with limited bone volume that results in embedment of implant apex in thick connective tissue of sinus "not osseoitegrated" [14,15]. The use of PRF simply and safely allows placement of the preferable length of implant if primary stability can be obtained clinically (in this study the minimum RBH was 3 mm provided good clinical primary stability). Sohn (2011)[16] reported the advantages of such augmentation material as no cross infection, no donor site morbidity, no reported infection and more gained bone with reducing operation cost. In this study sinus augmentation depending on two-stage protocol was done when RBH being <3 mm (mean 1.92 ±1.08 mm) and the mean gained bone at time of second stage surgery was 3.01±1.63 mm. This bone gain is statistically significant but clinically the mean final SBH was 4.93±1.61 mm so the sinus augmentation still insufficient for adequate implant placement. This may be explained by the limited capacity of PRF clot to keep the artificial space created during membrane elevation that results in membrane collapse; and could be avoided if space maintainer is to be used. It is documented that PRF clot dissolves gradually during 1-2 weeks[17]. Another explanation is that insufficient PRF clots were used in the two-stage surgery while it was sufficient when placed with dental implant as the implant occupied the space and splinted PRF. However, the space maintaining capacity of PRF clot need further studies and more PRF clots can be used for stronger evidence. To the best of author's knowledge, there was only one case report published by Aoki *et al.* (2016)[18] in which 2 PRF membranes were used in sinus augmentation without implant placement and the results were comparable to this study. One sinus augmentation procedure failed and no bone was formed after 24 weeks (the case was from the two-stage group). In this patient severe intra and immediate postoperative bleeding from branch of the superior labial artery encountered that necessitated wound re-exploration to identify the source of bleeding and cauterization with hot Ash 49 was done. The bleeding washing effect is documented[19]. It may be that PRF clot is washed out and dislodged from the submembraneous space particularly the clot was not supported by implant. In this study, the mean density of gained bone in one-stage surgery cases was 408.28±169.89 HU which falls in D3 category according to Misch scale of density. That was comparable to the density of posterior maxilla which falls in D4 category [20] and this result is in agreement with study published by Tajima *et al.* (2013)[12] in which the autors reported that the density of gained bone was 323±156.2 HU. In two-stage surgery the mean density of gained bone was 183.60±97.67 HU which is categorized as D4. This difference between densities of gained bone among stages may be explained by the compactness of PRF clot in the artificial space created after membrane elevation, that mean when the implant is placed simultaneously with PRF clot in the submembraneous space, it may help in keeping PRF clot well condensed, supported, and confined between the sinus walls around it, while in two-stage surgery there is no implant to support the elevated membrane that gradually compress the PRF clot with respiration movement result in rolling out of the clot making it not to be confound in a precise area. Taking in consideration the degree of sinus pneumatization which may also influence the degree of compactness of PRF clot in space particularly a standardized amount of PRF clots were used in this study (2 PRF clots for all procedures) regardless the volume to be augmented . In a histological examination of the gained bone around implant 6 months after sinus augmentation with PRF, Mazor *et al.* (2009) and Sohn (2011)[10,16] found that the bone is dense and mature and this was attributed to formation of architecturally strong bone matrix begins from PRF fibrin matrix and high concentration of growth factors. Fibrin matrix is well organized scaffold supporting bone morphogenic protein[21].

The tissue biopsy in case of two-stage surgery revealed woven bone around mature lamellar bone[18]. That is supportive explanation to the low density obtained in delayed implant placement protocol for this study. Hussein and Hassan (2017)[22] conducteded a study utilizing surgicel as a non-autogenous graft material for indirect sinus lift procedure (crestal approach) and the

density of gained bone was 489.62 HU which is very comparable to the density obtained with PRF clot but it is worth to point out the privilege of PRF as an autogenous, inexpensive, and easily prepared graft material. Schneiderian membrane perforation occurred in 4 sinus lift procedures (21.05%) may be due to the presence of septa and/or irregular sinus floor that interfered with the smoothness of membrane dissection. The presence of septa was reported as a risk factor for membrane perforation[23]. Many authors reported that it is the most common complication during lateral sinus augmentation and its incidence ranges between 11% and 56% [24]. Other studies reported perforation incidence about 19.5-41% in lateral sinus lift procedure [25].In this study the perforation in the 4 cases, was < 2 mm (according to Fugazzotto *et al.* (2015)[25], class II A) and was managed successfully by application of the easily adapted PRF membrane. Intraoperative bleeding from injured alveolar antral artery associated with 3 procedures (15.79%) during lateral osteotomy window preparation and this is reported as one of the most common intraoperative complications of lateral sinus lift procedure[25]. In two cases the bleeding was not so severe and stopped spontaneously while proceeding in the operation. The researcher encountered one case with profuse bleeding of injured alveolar antral artery, it is documented by Valente *et al.* (2015)[26] that the incidence of injury is increased when diameter of alveolar antral artery >0.5 mm.In this case the bleeding was severe so that cauterization with diamond bur attached to turbine without water irrigation was done; this maneuver was confirmed by Resnik and Misch (2017)[27]. Intact alveolar antral artery and Schneiderian membrane are important for proper revascularization of the area and neoangiogenesis[28].No postoperative infection was reported in this study, this is coincident with other studies[29]. This is may be related to the well established anti-infectious and immune regulation properties of leukocyte entrapped in fibrin mesh of PRF[30].Platelets are responsible for releasing modulator proteins of humoral and cellular immunity. Antibacterial and fungicidal proteins also stored in platelets granules[31].Survival rate of DI 6 months after surgery was 100%; all implants were clinically stable at the time of 2nd stage surgery (implant uncoverage). In a systematic review by Ali *et al.* (2015)[20], a total of 57 sinus augmentation using PRF as a sole graft material were done and 110 implants were placed in 46 patients, in all cases during uncovering time, the 110 implants placed were clinically stable. PRF application improves implant stability during the early healing period owing to faster osseointegration[32].For both treatment protocols, the total mean preoperative membrane thickness was 3.17 mm and 2.46 mm postoperatively. There were no statistically significant changes in membrane thickness (P-value=0.53). The minimum radiographically detected mucosal thickness is 2 mm and the greater thickness is considered pathological thickening. It was reported that the preoperative CBCT for patients who need sinus augmentation procedure greatly revealed mucosal thickening >2 mm[1] **.** This is in acceptance with the preoperative findings of this study as the mean preoperative MT was 3.17 mm.

Surprisingly 5 sinuses (26.32%) with preoperative membranous thickening >2 mm were found to resolve completely. This may be attributed to the anti-inflammatory effect of (IL-4) secreted by activated leukocyte of PRF clot[33] .To the best of author's knowledge there is no published study discuss such changes in membrane when PRF used as graft material.

CONCLUSION

The use of PRF as the sole graft material during sinus lift with simultaneous implant placement (one-stage surgery) provides stable, high level of natural bone which is comparable to normal bone density of posterior maxilla in the submembraneous cavity in continuity with the tip of the implant, however, sinus augmentation with PRF alone without implant placement (two-stage surgery) results in a limited bone formation.

REFERENCES

1. Kao DW, editor. Clinical Maxillary Sinus Elevation Surgery. 9600 Garsington Road, Oxford, OX4 2DQ, UK:John Wiley & Sons; 2014.
2. Starch-Jensen T, Aludden H, Hallman M, Dahlin C, Christensen AE, Mordenfeld A. A systematic review and meta-analysis of long-term studies (five or more years) assessing maxillary sinus floor augmentation. *Int J Oral Maxillofac Sur*g. 2018; 47(1):103-16.
3. Batal H, and Norris O. Lateral antrostomy technique for maxillary sinus augmentation. *Implants*. 2013 :1, pp.12-20.
4. Zhao JH, Tsai CH, Chang YC. Clinical application of platelet-rich fibrin as the sole grafting material in maxillary sinus augmentation. *J Formos Med Assoc*.2015;114(8):779-80.
5. Benavides E, Rios HF, Ganz SD, An CH, Resnik R, Reardon GT, Feldman SJ, Mah JK., Hatcher D, Kim MJ and Sohn DS. Use of cone beam computed tomography in implant dentistry: the International Congress of Oral Implantologists consensus report. *Implant dent*, 2012;*21*(2):78-86.
6. Mohammed DH and Alnakkash WA. Biomechanical evaluation of porous titanium implants (CpTi) fabricated by powder technology. *J Bagh Coll Dent*. 2015;*27*(1):18-25.
7. Lee H, Lee SH, Kim SJ, Choi WI, Lee JH and Choi IJ. Variations of the cubital superficial vein investigated by using the intravenous illuminator. *Anat cell boil*. 2015;*48*(1):62-65.
8. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J and Gogly B. Platelet- rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006; *101*(3),e37-e44.
9. Misch CE.Contemporary implant dentistry.MosbyElsevier.2008.Ch:3P48
10. Mazor Z, Horowitz RA, Del Corso M, Prasad HS, Rohrer MD and Dohan Ehrenfest DM. Sinus floor augmentation with simultaneous implant placement using Choukroun's platelet-rich fibrin as the sole grafting material: a radiologic and histologic study at 6 months. *J Periodontol*. 20009; *80* (12): 2056-2064.
11. Simonpieri A, Choukroun J, Del Corso M, Sammartino G and Ehrenfest DMD. Simultaneous sinus-lift and implantation using microthreaded implants and leukocyte-and platelet-rich fibrin as sole grafting material: a six-year experience. *Implant Dent*. 2011; *20*(1):2-12.
12. Tajima N, Ohba S, Sawase T, Asahina I. Evaluation of sinus floor augmentation with simultaneous implant placement using platelet-rich fibrin as sole grafting material. Int J Oral Maxillofac Implants. 2013; *28*(1):77-83.
13. Ehrenfest DMD, Doglioli P, Giuseppe M, Del Corso M and Charrier JB. Choukroun's platelet-rich fibrin (PRF) stimulates in vitro proliferation and differentiation of human oral bone mesenchymal stem cell in a dose-dependent way. *Arch Oral Biol*. 2010; *55*(3):185-194.
14. Sul SH, Choi BH, Li J, Jeong SM and Xuan F. Histologic changes in the maxillary sinus membrane after sinus membrane elevation and the simultaneous insertion of dental implants without the use of grafting materials. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2088a;*105*(4):e1-e5.
15. Sul SH, Choi BH, Li J, Jeong SM and Xuan F. Effects of sinus membrane elevation on bone formation around implants placed in the maxillary sinus cavity: an experimental study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008b; *105*(6): 684-
16. Sohn D S, Heo JU, Kwak D H, KimD E Kim JM, Moon JW Lee JH and Park I S. Bone regeneration in the maxillary sinus using an autologous fibrin-rich block with concentrated growth factors alone. *Implant Dent* . 2011;20:389–395.
17. Borie E, Oliví DG, Orsi IA, Garlet K, Weber B, Beltrán V and Fuentes R. Platelet-rich fibrin application in dentistry: a literature review. *Int J Clin Exp Med*. 2015; *8*(5):7922-7929.
18. Aoki N, Kanayama T, Maeda M, Horii K. Miyamoto H, Wada K, Ojima Y, Tsuchimochi T and Shibuya Y. Sinus augmentation by platelet-rich fibrin alone: A report of two cases with histological examinations. *Case Rep Dent, 2016*;.7 pages.
19. Rosano G, Taschieri S, Gaudy JF, Weinstein T and Del Fabbro M. Maxillary sinus vascular anatomy and its relation to sinus lift surgery. *Clin Oral Implants Res*. 2011; *22*(7): 711-715.

20. Ali S, Bakry S A and Abd-Elhakam H. Platelet-rich fibrin in maxillary sinus augmentation: a systematic review. *J Oral Implantol*.2015; *41* (6): 746-753.
21. Naik B, Karunakar P, Jayadev M and Marshal VR. Role of Platelet rich fibrin in wound healing: A critical review. *J Conserv Dent: JCD*.2013; *16*(4):284-293.
22. Hussein LA and Hassan TA. The Effectiveness of Oxidized Regenerated Cellulose as a Graft Material in Transalveolar Osteotome Sinus Lift Procedure. *J Craniofac Surg*.2017; *28*(7):1766-1771.
23. Nolan PJ, Freeman K and Kraut RA.Correlation between Schneiderian membrane perforation and sinus lift graft outcome: a retrospective evaluation of 359 augmented sinus. *J Oral Maxillofac Surg*. 2014; *72*(1):47-52.
24. Froum S. ed. *Dental implant complications: etiology, prevention, and treatment*. 2121 State Avenue, Ames, Iowa 50014-8300, USA John Wiley & Sons. 2015.
25. Fugazzotto P, Melnick PR and Al-Sabbagh M. Complications when augmenting the posterior maxilla. *Dent Clin North Am*. 2015; *59*(1):97-130.
26. Valente NA, Harogiannis K and Andreana S. Alveolar antral artery management during sinus elevation: A case report of a novel approach with review of the literature. *Int J Contemp Dent Med Rev, 2015*.
27. Resnik R and Misch CE. 2017. Avoiding Complications in Oral Implantology. Elsevier. 1st ed. Ch:7.p. 290.
28. Rysz M, Ciszek B, Rogowska M and Krajewski R. Arteries of the anterior wall of the maxilla in sinus lift surgery. *Int j oral maxillofac surg*. 2014;*43*(9):1127-1130.
29. Bastami F and Khojasteh A. Use of leukocyte-and platelet-rich fibrin for bone regeneration: a systematic review. *Regen. Reconstr. Restor*. 2016;*1*(2):47-68.
30. Bielecki T, M Dohan Ehrenfest D, A Everts P and Wiczkowski A. The role of leukocytes from L- PRP/L-PRF in wound healing and immune defense: new perspectives. *Curr Pharm Biotechnol*. 2012; *13*(7):1153-1162.
31. Joshi CP, Patil AG, Karde PA, Khedkar SU, Mahale SA and Dani NH. Autologous Platelet Rich Fibrin as a potential antiperiopathogenic agent: An in-vitro study. *Int J Periodontol Implantol. 2016;1*(2):50-54.
32. Öncü E and Alaaddinoðlu E. Effect of platelet-rich fibrin on osseointegration. *Int J Oral Maxillofac Surg*.2013; *42*(10):1265-1266.
33. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J and Gogly B. Platelet- rich fibrin (PRF): a second-generation platelet concentrate. Part III: leucocyte activation: a new feature for platelet concentrates. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;,101*(3):e51-e55.