Introduction

Pneumatization of maxillary sinus towards alveolar crest due to tooth loss or horizontal-vertical resorption of alveolar bone decrease sufficient bone to place dental implants in the posterior maxilla. 1,2 The method proposed for placing implant with a standard length is use of sinus lift surgery with autogenous bone graft or bone substitute materials. The recent advances in surgical techniques, and graft materials have caused improved prognosis of implant treatment in the posterior maxillary region. 1,3 Also, due to the high success rate, it can be indicated for patients with bone deficiency in the posterior maxilla. 1 Various
Graft materials are used for sinus lift surgery including autologous bone, xenografts, mineralized and demineralized bone allografts, and alloplasts. However, in recent years, xenografts and allografts have been under greater use than bone autografts in sinus lift, which is mostly due to reducing the surgical complications associated with the graft donating region. Despite many studies have reported success in use of xenografts and allografts, higher treatment costs and the potential of disease transmission are still notable. Thus, the possibility of sinus lift without using bone-substitute materials can be desirable.

Ellegaard et al presented the first clinical report on sinus lift without any graft material. Also, Lundgren et al described open sinus lift method without graft materials and only with clot formation. Other studies have also reported that bone formation is not dependent on the graft material, and clot formation alone can lead to formation of bone in the space created under the membrane of the sinus. In this method, based on GBR principles, dental implant is also inserted, so that it keeps the membrane in elevated position as tent pegs, which can fill up the space with blood clot. The blood clot can act as a scaffold for bone formation.

To improve the clot stability, release more growth factors, accelerate the healing speed, improve the quality of the bone formed, and enhance the bone formation, some papers have used platelet-rich fibrin (PRF) in sinus lift surgery simultaneous with implant placement. PRF is prepared from venous blood with one time of centrifugation. After centrifugation, three parts are formed in the test tube, with the middle layer being PRF, which is a fibrin-rich platelet gel containing the minimum level of red blood cells, while the top layer is made of plasma and the bottom layer is composed of clot of RBCs. PRF contains coagulation factors forming a fibrin network, which keep different types of cytokines. PRF contains different cells including platelet, leukocyte, macrophages, granulocyte, and neutrophils. There is no need to delay PRF formation artificially by anti-coagulation agents, as this even does not initiate quickly. There is no need either to increase the extent of natural blood clotting and platelet activity, as the structure of the fibrin network develops through centrifugation along with large amounts of biological factors such as entrapped cytokines.

The present research with split-mouth design has dealt with radiographic investigation of the height and density of bone in sinus floor elevation surgery using PRF compared with sinus floor elevation without any graft material in order to assess the quality and quantity of bone.

Materials and methods

Patient selection and study design

In this research, 30-80-year-old patients participated visiting the implant ward of dentistry faculty at Tabriz University of Medical Sciences with bilateral partial edentulism or complete edentulism who needed sinus lift plus implant placement. In the present research, by designing the study as split-mouth, one side of the sinus of each patient was randomly assigned into the PRF test group, while the other side was considered as the control group without any graft materials. The inclusion criteria were complete edentulism or partial bilateral partial edentulism in maxilla, and remaining bone height between the alveolar crest and sinus floor of at least 4 mm and at most 8 mm. The exclusion criteria included: presence of systemic diseases such as uncontrolled diabetes, cardiovascular diseases, malignancy, head and neck radiotherapy, and auto-immune diseases with contraindication of surgery, individuals with poor oral hygiene, smoking, and history or presence of pathological signs in the sinus.

PRF preparation

PRF preparation was as with other papers, which was done according to instructions of Choukroun et al. Before the surgery, 20-40 ml of the venous blood of the patient was collected in sterilized glass tubes without anti-coagulation agent, and immediately placed inside the device and centrifuged at 3000 rpm for 10 min. Thus, activation of the coagulation cascade and formation of fibrin network of three layers including 1) the top layer or cell-free plasma (PPP), 2) the middle layer (PRF), and 3) the bottom layer which were red blood cells was evident in the test tube. The middle layer (PRF) was separated by scissors from the clot of red globules and used a filler material in the sinus space.

Surgical method

The surgery was done under local anesthesia. Access to the sinus wall was done in the crest of the edentulous ridge, where vertical releasing was done in the beginning and end of the flap, and full thickness elevation of flap was done. By using a diamond bone, the window was prepared in the lateral wall of the sinus. The bone window was gently separated off the membrane in order to facilitate the access to the membrane. Thereafter, the membrane was slowly dragged aside off the sinus floor up to the middle wall of the sinus, so that the membrane would be completely elevated. Then, preparation of the implant site was performed...
carefully, and overall all cases and given the ridge width, 41 implants with a length of 11.5 mm CMI IS-II active implant (Neobiotech Co., Seoul, Korea) were placed. Next, based on split-mouth method, 2-4 PRFs were used on the test side in the developed space, but in the control side of the same patient, this space only filled with clot. Absorbable membrane was used on the created window and the flap was sutured on its original site. All patients were prescribed Amoxicillin 500mg and Metronidazole 250mg every eight hours along with Gelofen 400mg every six hours up to one week. Further, Chlorhexidine 0.2% mouthwash was prescribed twice a day up to two weeks.

**Radiographic assessment**

After six months, to investigate the density of the bone formed around the dental implants in the posterior maxillary region, CBCT radiography was taken from patient. The bone height from the sinus floor to the crest ridge in the baseline and six months after the sinus floor elevation surgery and placing the implant was also measured using CBCT.

**Data analysis method**

First, data normality was investigated to employ analyses in line with the data. Based on Kolmogorov-Smirnov test, it was found that the data had a normal distribution (p-value=0.05). Thus, paired t-test was utilized to compare the means of indices over time (before and after surgery) and between the two groups (with and without PRF). Further, to compare the height of the bones and bone density in the test and control groups, the values measured before the surgery in the two groups should not have a significant difference. In this way the mean difference of these indices after surgery between the two groups could be attributed to the intervention adopted. This comparison was done using paired t-test. This condition held and the mean measurements before the surgery had no significant difference between the two groups (p-value=0.706). All tests were statistically analyzed by SPSS 21. In this study, p-value<0.05 was considered significant. Note that to investigate the bone density, Hounsfield number was used with the help of Mimics 10.01 software.

**Ethical consideration**

All the subjects signed informed consent forms. The protocol of the study was approved by the Ethics Committee of Tabriz Faculty of Dentistry under the code IRCT20120702010155N4.

**Results**

In this study, which was done as clinical trial and split-mouth, 14 patients with complete edentulism or bilateral partial edentulism of the upper jaw were investigated. In each case, for the sinus lift surgery of the test side, PRF was used, while in the sinus lift surgery of the other side of the same patient, no graft materials was used. Before the second-stage surgery, CBCT was taken from the patients. All 41 implants had been osteointegrated in the second stage of surgery and were clinically stable. The extent of bone density formed in the two groups and the bone height prior to and after the sinus surgery were examined the groups with and without PRF. Comparison of the bone height before and after the sinus surgery is provided in Table 1. It is observed that the bone height in the group with PRF before the sinus surgery was 5.85±1.08 mm, while increased to 10.71±1.09 mm after the surgery. The difference between the pre- and post-surgery times in this index was 4.86 mm, which was statistically significant (p-value<0.001). Further, the bone height in the group without PRF was 5.67±1.03 before the surgery, which increased to 9.28±1.28 mm. The difference between pre- and post-surgery times in this index was 3.61 mm, which was significant (p-value<0.001). Comparison of the mean bone height and bone density between the two groups is provided in Table 2. It is observed that the bone height was 1.42 mm higher in the group with PRF than that group without PRF, which is statistically significant (p-value=0.004). Further, the bone density in the PRF group was 52.85 units larger than that of the group without PRF, which was statistically significant (p-value<0.001).

**Discussion**

In recent years, bone-substitute materials such as xenografts and allografts have been under wider applications more than bone autografts in enhancing the sinus floor, which are mostly due to diminished surgical complications associated with the graft donator site. Further, many studies have reported successful use of xenografts and allografts. However, the treatment cost

| Table 1. Comparing the height of bones before and after the sinus surgery |
|-----------------------------|----------------|-----------------|---------------|-----------------|-----------------|
| With PRF | Min | Max | Mean±SD | Mean difference between | P-value |
|Before | 4.05 | 7.37 | 5.85±1.08 | -4.86 | <0.001 |
|After | 8.69 | 12.06 | 10.71±1.09 | |
|Without PRF | Min | Max | Mean±SD | Mean difference between | P-value |
|Before | 4.11 | 7.18 | 5.67±1.03 | -3.61 | <0.001 |
|After | 07.11 | 10.78 | 9.28±1.28 | |
is higher and the disease transfer potential is still notable. Considering the costs and risk of infection, the possibility of elevating the sinus floor without using bone-substitute materials can be desirable. In the present research, using CBCT radiography, the bone height and density formed in the maxilla sinus were examined after sinus membrane elevation surgery simultaneously with implant placement without any graft material or use of PRF.

The present study in six-month follow-up of patients using CBCT radiography showed that in the sinus lift group, the bone forms beneath the membrane without any graft material and by only developing blood clot. In the sinus lift group, without any graft material which was present the control group here, the mean bone height from the crest to the sinus floor grew from 5.67 mm from pre-surgery to 9.28 mm at the post-surgery time.

In a first-of-its-kind experimental study, Boyne et al reported bone formation in implants which had been placed inside the sinus by 5 mm on monkeys.19 Ellegaard presented the first clinical report on bone formation around implants which had been placed inside the sinus space by 5 mm.4 Concurrent with sinus lift, Lundgren et al placed implants embedded into the sinus space by at least 5 mm, and reported clear formation of bone within a one-year follow-up.5 Chen et al,6 as well as Thor et al,7 also reported that bone formation in maxillary sinus does not need presence of biomaterial. Also, Riben et al proposed that preserving the space through implant for blood clot formation, its absorption, and deposition of bone cells with periosteum origin or the maxilla spongy bone are possibly responsible for bone formation in this region.20 In the study by Kim et al, extraction of stem cells from Schneiderian membrane and osteogenic differentiation potential of these cells were reported.21 Moreover, Srouji et al showed intrinsic osteogenic potential of Schneiderian membrane22 and the content of osteoprogenitor cells of Schneiderian membrane,23 which can be possibly the constituting origin of the new bone beneath the sinus membrane. Based on these studies, bone formation in the control group here can be justified and in line with other studies, the present research showed that if the collapse of sinus membrane is prevented by using dental implants, the formation of blood clots and periosteal osteogenic cells and the sinus floor bone may have the potential of bone formation.7,20,24-27

In contrast, in an animal research, Kim et al showed that when no graft material is used in sinus lift surgery, bone formation becomes limited.28 In line with the previous study, Sul et al reported limited bone formation around implants penetrated into the sinus.29 Based on the present research and the studies in line with it, it may be stated that in the research by Kim et al as well as Sul et al, the membrane collapse in response to air pressure, no formation of stable clot, or not elevating the membrane properly in the animal samples might be the reason of the limited bone formation around the implants.28,29

The implant placed concurrent with sinus lift can act as tent pegs. In this method, based on GBR principles, the implant is embedded concurrent with sinus lift, and no material is used beneath the space developed between the membrane and sinus floor. Indeed, the end of implants keeps the sinus membrane at elevated position causing the space developed to be filled by blood clot, which becomes a scaffold for bone formation, cellular migration, differentiation, and osteogenesis.7,20,24,26,30 Some papers have used PRF in sinus lift surgery concurrent with implant placement for greater release of growth factors, increasing the healing speed, improving the quality of the bone formed, and increasing bone formation.8-13,17,18 In the test group of the present study, the surgery of sinus lift was performed concurrent with implant placement along with use of PRF as the only graft material under the sinus membrane. In this group, the mean height of bone before the sinus surgery was 5.85 mm, which increased to 10.71 mm after the surgery. As with the present research, in three studies,11,12,31 PRF had been used as the only graft material in open sinus lift surgery concurrent with implant placement. Mazor et al performed 22 sinus lift surgeries along with implant placement. The mean initial bone height was 2.9 mm, which in the six-month radiographic evaluation from the operator sinuses, the mean bone height was reported as 10.1 mm, showing a significant increase in the bone height.11 Simonpieri et al and Tajima et al reported that the mean final height of the sinus bone when using PRF as the only graft material in sinus lift surgery concurrent with implant placement was 10.4
and 11.8 mm, respectively. Nevertheless, in a systematic review by Ali, it was found that these studies had no control group in order to demonstrate the advantage of PRF as compared with sinus lift without any graft material. In the present research, with the design of the study as split-mouth, along with control group, investigation of PRF effect on the height and density of bone formation in sinus lift surgery was performed. In other words, in the sinus lift surgery of the test group, PRF was used, while on the other side of the sinus of the same patient as the control group, no graft material was utilized. The results of CBCT investigation of the patients six months after the surgery represented the mean height of the sinus bone in the control group without graft material as 9.28 mm, while the mean bone height of the test group (PRF) was reported as 10.71 mm. It is observed that the mean bone height in the group with PRF was 1.42 mm higher than that of the group without any graft material, with this difference being reported a significant (p-value=0.004).

Bone density can be evaluated by Hounsfield unit. Applying this parameter, a relative scale is defined which has been valued for different types of bone including very high density cortical bone (>600 HU), cortical bone plus a medium density spongy bone (400 to 600 HU), and cortical bone plus low density spongy bone (<200 HU). As mentioned previously, although various studies have reported bone formation in sinus lift surgeries whether by PRF or without graft material, there are limited studies on the density of the bone formed after elevating the Schneiderian membrane. In the present study, the mean density of the bone formed around the dental implants of the test group (PRF) was 310.35 HU, while the mean density of the bone formed around the dental implants in the control group without graft material was 257.5 HU. Under these conditions where the bone density in the PRF group has been 52.85 units significantly higher than that of the control group, yet in the present study, the density of the formed bone whether by PRF or without any graft material is comparable to the values reported for the normal bone present in the posterior maxillary region. In line with the results of the present research, Tajima et al reported that mean density of a newly formed bone six months after sinus lift surgery using PRF as the only graft material as large as 323 HU.

Altintas et al reported bone density after sinus lift with and without PRF as being higher than that of the group without any graft material. In the present research, since the bone density is higher when PRF is used, it is advisable to consider it for enhancing the bone quality in sinus lift surgery.

Conclusion

Considering the limitations of the study and based on the results obtained here, one can possibly say that open sinus lift using PRF and even without PRF can be reliable to place implants. Nevertheless, based on the present research, PRF is suggested to enhance the bone quantity and quality of bone formation. It is recommended that future studies consider the extent of newly formed bone based on histological investigations.

Authors’ contributions

The study was planned by MCh and HK. Data collection was carried out by HK; statistical analyses and interpretation of data were carried out by AHD. The manuscript was prepared by AB and SA, and edited by HK. All the authors have read and approved the final manuscript for submission.

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Competing interests

The authors declare that they have no competing interests with regards to authorship and/or publications of this paper.
Ethics approval
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