Histomorphometric and cone beam computed tomography assessments on the influence a collagen membrane placed subjacent the sinus mucosa after maxillary sinus floor augmentation. A randomized clinical trial.

Authors

Dr. Atsuya Hirota, DDS, Doctor, Osaka Dental University, Osaka, Italy
Dr. Shigeo Fujiwara, DDS, Doctor, ARDEC Academy, Rimini, Italy
Dr. Mauro Ferri, DDS, Doctor, Corporación Universitaria Rafael Núñez, Cartagena de Indias, Colombia
Karol Alí Apaza Alccayhuaman, DDS, ARDEC Academy, Rimini, Italy
Niklaus Peter Lang, DDS, PhD, Center for Dental Medicine, University of Zurich, Zurich, Switzerland
Daniele Botticelli, BMBD, dentist, PhD, ARDEC Academy, Rimini, Italy
Dr. Natalia Fortich Mesa, DDS, Doctor, Corporación Universitária Rafael Núñez, Cartagena de Indias, Colombia

Corresponding author:

Dott. Karol Alí Apaza Alccayhuaman, DDS, ARDEC Academy, Viale Giovanni Pascoli 67 – 47923 RIMINI (ITALY) Tel.-Fax: +39 0541 393444
E-mail: caroline7_k@hotmail.com

Cartagena de Indias, April 4th, 2016

Conflict of Interest Statement

The authors declare no conflict of interest regarding this study.

Tecnoss srl, Giaveno, Italy will provide all biomaterials. Sweden & Martina SRL, Due Carrare, Padua, Italy and ARDEC Academy, Ariminum Odontologica s.r.l., Rimini, Italy will cover the costs of the study.

Abstract

Aim: to seek for differences in osseointegration at implants and dimensional variations of augmented maxillary sinuses with or without the placement of a collagen membrane subjacent the sinus mucosa.

Material and Methods: After the elevation of the maxillary sinus mucosa, a collagen membrane with standard dimensions will be placed at the test sites subjacent the sinus mucosa and the elevated space will be filled with a xenograft, both test and control groups. A collagen membrane will be placed to cover the antrostomy at both groups and sutures will be provided to close the wound. After six months of healing, mini-implants will be installed. After 9 months, biopsies containing the mini-implants will be harvested for histomorphometric analyses. CBCTs will be taken for all patients before surgery (T0), after 1 week from sinus floor augmentation (T1) and after 9 months of healing (T2). Osseointegration of the mini-implants and dimensional changes over time of soft and hard tissues will be evaluated on the CBCTs.

Introduction

The perforation of the sinus mucosa during sinus floor augmentation is a complication that has been reported in several clinical[1-4] and experimental studies[5,6] with an occurrence that varies between 10 and 55%. Dislodgement of the biomaterial and sinusitis may represent a consequence of the perforation.[2] Small perforations may not require any treatment because, after the elevation and relaxation of the sinus mucosa, the margin of the perforation may collapse together and close the defect.[7] Perforations of larger dimensions may be closed using sutures[1,8,9] or fibrin glue.[1,8,10] Collagen membranes were also used to protect the perforations of the sinus mucosa and good outcomes have been claimed.[3,4,11-16] Several experimental studies have bene performed to evaluate histologically the influence of a collagen membrane placed subjacent the sinus mucosa in the absence[5,16] or presence of perforation[17] and no differences were seen in the healing outcomes. However, there is still a lack of clinical information about how the placement of a collagen membrane between the sinus mucosa and the graft may influence the osseointegration of implants and the dimensional variations and healing at augmented maxillary sinuses. Hence, the aim of this randomized clinical trial will be to seek for differences in osseointegration at implants and dimensional variations of augmented maxillary sinuses with or without the placement of a collagen membrane subjacent the sinus mucosa.

Material and methods

The protocol was approved by the Ethical Committee of the University Corporation

Rafael Núñez, Cartagena de Indias, Colombia (protocol #03-2015; 4 December 2015) and the Declaration of Helsinki on medical protocols and ethics will be followed. This study will be submitted for registration to ClinicalTrials.gov PRS (https://clinicaltrials.gov) to obtain the NCT. The patients will be informed about the procedures and the possible complications and signed informed consents will be obtained. The Consort checklist will be followed for this study (http://www.consortstatement.org/).

Study population

For the present randomized clinical trial, all recruitments, surgeries and follow-ups will be carried out at the University Corporation Rafael Núñez, in Cartagena de Indias (Colombia). To calculate the sample size, the data from an article that assessed the variations over time in height of the augmented sinuses were used.[18] It was calculated that an n=10 was sufficient to show differences, if exist. An author not involved in the surgeries will perform the randomization process (MF). The assignments will be sealed within opaque envelopes that will be opened after the completion of the elevation of the sinus mucosa.

The following inclusion criteria have to be fulfilled:

(i) presence of an edentulous atrophic zone in the posterior segment of the maxilla;

(ii) height of the sinus floor ≤4 mm;

(iii) desiring a prosthetic restoration of the zone using a fix prosthesis supported by implants;

(iv) ≥ 21 years of age;

(v) good general health;

(i) no contraindication for oral surgical procedures;

(ii) not being pregnant.

The patients will be excluded if they:

(iii) present a systemic disordered;

(iv) had a chemotherapic or radiotherapeutic treatment;

(v) are smokers >10 cigarettes per day;

(vi) have an acute or a chronic sinusitis;

(vii) had a previous bone augmentation procedures in the zone of interest.

Biomaterial used

The filler material will be a collagenated corticocancellous porcine bone granules (Gen-Os, 250–1000 µm, OsteoBiol, Tecnoss, Giaveno, Italy).

The membrane used subjacent the sinus mucosa at the test sites and to cover the antrostomy at both test and control sites the control sites will be an equine collagen membrane (Evolution, 0.3 mm, OsteoBiol, Tecnoss).

Clinical procedures

The lateral wall of the maxillary sinus will be exposed and osteotomies of about 6 mm in height and 10 mm long will be prepared using a diamond insert (SFS 109 029), Komet-Brasseler-GmbH, Germany) mounted on a sonic-air surgical instrument (Sonosurgery® TKD, Calenzano, Fi - Italy). The sinus mucosa will be elevated and, at the test sites, a collagen membrane will be placed subjacent the sinus mucosa. Subsequently, the elevated space will be filled with the xenograft

both at the test and control sites. A collagen membrane will be used to protect the antrostomies and the soft tissues wounds will be sutured.

After 6 months of healing, a mini-implant 2.4 mm of diameter and 8 mm of length (Sweden & Martina, Due Carrare, Padua, Italy), with a moderately rough surface (ZirTi, Sweden & Martina, Due Carrare, Padua, Italy) will be installed in the elevated area. After three months, the mini-implants were retrieved with custom-made trephine (GA33M, Bontempi Strumenti Chirurgici, San Giovanni in Marignano, RN, Italy), 3.5 mm and 4 mm of internal and external diameter, respectively. An eccentric method for retrieving biopsies was adopted and the specimens were fixed in 10% buffered formalin. A definitive implant will be installed in the site of the biopsy retrieval.

Amoxicillin 875 mg with clavulanic acid 125 mg twice a day for 6 days, nonsteroidal anti-inflammatory drugs as needed, and mouth rinses with 0.12% chlorhexidine three times a day for 10 days will be recommended after each surgery. The sutures will be removed after 7 days, and the patients will be enrolled in a maintenance program for the full extent of the study.

Histological preparation of the biopsies

The specimens will be dehydrated in an ascending series of alcohol and then included in a glycol-methacrylate resin (Technovit® 7200 VLC; Kulzer, Wehrheim, Germany) and polymerized. The biopsies were sectioned according to the longitudinal axis of the mini-implant, obtaining specimens of about 150 microns of width that were subsequently ground to about 30 μm of width. The staining will be performed with acid fuchsine and toluidine blue.

The Results Data Element Definitions for histomorphometric analyses

The histomorphometric evaluations will be performed at the ARDEC Academy facilities (Rimini, Italy) using an Eclipse Ci microscope (Nikon Corporation, Tokyo, Japan) connected to a digital video camera (Digital Sight DS-2Mv, Nikon Corporation, Tokyo, Japan). All histomorphometric evaluation will be performed x200 magnification from the most coronal to the most apical contact of the bone to the implant surface using the software NIS-Elements D 5.11 (Laboratory Imaging, Nikon Corporation, Tokyo, Japan).

Outcomes measures for the histomorphometric analyses

Primary outcome: New bone-to-implant contact

Description: Measurements will be assessed between the most coronal (B) and the most apical (A) contacts of new bone to the implant surface.

Timeframe: Mini-implants will be installed six months after sinus lifting and retrieved after three months of healing.

Secondary outcome: New bone density around the mini-implant, from B to A and up to a distance of 400 μm from the implant surface.

Description: Measurements will be assessed using a point counting procedure, superposing a lattice with squares of 50 μm over the histological image.

Timeframe: Mini-implants will be installed six months after sinus lifting and retrieved after three months of healing.

Other pre-specified outcomes for histometric assessments: old-bone (pre-existing), marrow bone and residual xenograft.

Description: Measurements will be assessed between the most coronal (B) and the most apical (A) contacts of new bone to the implant surface

Timeframe: Mini-implants will be installed six months after sinus lifting and retrieved after three months of healing.

Other pre-specified outcomes for morphometric assessments: old-bone (pre-existing), marrow bone, residual xenograft, and vessel.

Description: Measurements will be assessed using a point counting procedure, superposing a lattice with squares of 50 μm over the histological image.

Timeframe: Mini-implants will be installed six months after sinus lifting and retrieved after three months of healing.

Comparisons among test (membrane sites) and control groups will be performed.

CBCT imaging procedures

Cone bean computed tomographies (CBCTs) will be taken at three different periods: before the sinus floor elevation (T0); one week (T1) and 9 months (T2) after surgery.

CBCT imaging analyses

All radiographic evaluations will be performed with the software i-Dixel 2.0 (J. Morita Corporation, Kyoto, Japan). As references, a line drew following the floor of

the nose will be used both in the coronal view (axis X) and in the lateral view (axis Z).

The Results Data Element Definitions for CBCTs

The following parameters will be evaluated: mucosa thickness, bone crest height, nasal floor height from the base of the sinus, superior posterior alveolar artery height and diameter, sinus width, distance between the inferior margin of the antrostomy and the base of the sinus, antrostomy height, sinus length in the lateral view, the largest length of the xenograft/ hard tissue in the lateral view.

The variation in height and area of the elevated region will be evaluated among the CBCT taken in the various periods of healing

Outcomes measures for the CBCTs analyses

Primary outcome: Changing in height of the elevated zone.

Description: Measurements will be assessed in the medial, middle and lateral regions of the elevated zone using the cone beam computerized tomographies (CBCTs) taken in various periods. Comparisons among the CBCTs of each participants will be performed.

Timeframe: The CBCTs will be taken before surgery (T0) and 1-week (T1) and 9 months (T2) after surgery.

Secondary outcome: Changing in mucosa thickness.

Description: Measurements will be assessed in the cone beam computerized tomographies (CBCTs) taken in various periods. Comparisons among the CBCTs of each participant will be performed.

Timeframe: The CBCTs will be taken before surgery (T0) and 1-week (T1) and 9 months (T2) after surgery.

Other pre-specified outcomes: (C-F) bone crest height, (X-F) nasal floor height, (AC) anastomosis height and (AD) its diameter, (XW) sinus width, (LM-F) balcony height, (LM-UM) window height, (ZW) sinus length, (ZE) the largest length of the xenograft/ hard tissue, T0 X-area and T0 Z-area.

Description: Measurements will be assessed in the medial, middle and lateral regions of the elevated zone using the cone beam computerized tomographies (CBCTs) taken in various periods. Comparisons among the CBCTs of each participants will be performed.

Timeframe: The CBCTs will be taken before surgery (T0) and 1-week (T1) and 9 months (T2) after surgery.

Data analysis

The histomorphometric and radiographic measurements will be performed twice by well-trained researchers that will be blinded about the differences in the protocols. Mean values will be obtained between the two measurements and used for analyses.

Mean values and standard deviations (SD) will be calculated for each outcome variable. Differences between the groups will be analyzed using the Mann-Whitney test. The level of significance will be set at $\alpha=0.05$.

References

1. Schwartz-Arad, D., Herzberg, R. & Dolev, E. (2004) The prevalence of surgical complications of the sinus graft procedure and their impact on implant survival. Journal of Periodontology 75: 511–516.
2. Nolan, P.J., Freeman, K. & Kraut, R.A. (2014) Correlation between Schneiderian membrane perforation and sinus lift graft outcome: a retrospective evaluation of 359 augmented sinus. Journal of Oral and Maxillofacial Surgery 72: 47–52.
3. Kawakami S, Lang NP, Iida T, Ferri M, Apaza Alccayhuaman KA, Botticelli D. Influence of the position of the antrostomy in sinus floor elevation assessed with cone-beam computed tomography: A randomized clinical trial. J Investig Clin Dent. 2018 Nov;9(4):e12362.
4. Kawakami S, Lang NP, Ferri M, Apaza Alccayhuaman KA, Botticelli D. Influence of the height of the antrostomy in sinus floor elevation assessed by cone beam computed tomography- a randomized clinical trial. Int J Oral Maxillofac Implants. 2019 January/February;34(1):223–232.
5. Iida T, Carneiro Martins Neto E, Botticelli D, Apaza Alccayhuaman KA, Lang NP, Xavier SP. Influence of a collagen membrane positioned subjacent the sinus mucosa following the elevation of the maxillary sinus. A histomorphometric study in rabbits. Clin Oral Implants Res. 2017 Dec;28(12):1567-1576.
6. Omori Y, Ricardo Silva E, Botticelli D, Apaza Alccayhuaman KA, Lang NP, Xavier SP. Reposition of the bone plate over the antrostomy in maxillary

sinus augmentation: A histomorphometric study in rabbits. Clin Oral Implants Res. 2018 Aug;29(8):821-834.

7. Aimetti M, Romagnoli R, Ricci G,Massei G.Maxillary sinus elevation: The effect of macrolacerations and microlacerations of the sinus membrane as determined by endoscopy. Int J Periodontics Restorative Dent 2001;21:581–589.
8. Khoury, F. (1999) Augmentation of the sinus floor with mandibular bone block and simultaneous implantation: a 6-year clinical investigation. The International Journal of Oral & Maxillofacial Implants 14: 557–564.
9. Lundgren S, Andersson S, Gualini F, Sennerby L. Bone reformation with sinus membrane elevation: A new surgical technique for maxillary sinus floor augmentation. Clin Implant Dent Relat Res 2004;6:165–173.
10. Choi BH, Zhu SJ, Jung JH, Lee SH, Huh JY.The use of autologous fibrin glue for closing sinus membrane perforations during sinus lifts.Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:150–154.
11. Pikos, M.A. (1999) Maxillary sinus membrane repair: report of a technique for large perforations. Implant Dentistry 8: 29–34.
12. Proussaefs P, Lozada J.The “Loma Linda pouch;” A technique for repairing the perforated sinus membrane. Int J Periodontics Restorative Dent 2003;23:593–597.
13. Proussaefs P, Lozada J, Kim J. Effects of sealing the perforated sinus membrane with a resorbable collagen membrane: A pilot study in humans. J Oral Implantol 2003;29:235–241.

14. Testori, T., Wallace, S.S., Del Fabbro, M., Taschieri, S., Trisi, P., Capelli, M. & Weinstein, R.L. (2008) Repair of large sinus membrane perforations using stabilized collagen barrier membranes: surgical techniques with histologic and radiographic evidence of success. The International Journal of Periodontics & Restorative Dentistry 28: 9–17.
15. Kim, Y.K., Yun, P.Y., Oh, J.S. & Kim, S.G. (2014) Prognosis of closure of large sinus membrane perforations using pedicled buccal fat pads and a resorbable collagen membrane: case series study. Journal of the Korean Association of Oral and Maxillofacial Surgeons 40: 188–194.
16. Scala A, Lang NP, Velez JU, Favero R, Bengazi F, Botticelli D. Effects of a collagen membrane positioned between augmentation material and the sinus mucosa in the elevation of the maxillary sinus floor. An experimental study in sheep. Clin Oral Implants Res. 2016 Nov;27(11):1454-1461.
17. Favero V, Lang NP, Canullo L, Urbizo Velez J, Bengazi F, Botticelli D. Sinus floor elevation outcomes following perforation of the Schneiderian membrane. An experimental study in sheep. Clin Oral Implants Res. 2016 Feb;27(2):233-40.
18. Zijderveld SA, Schulten EA, Aartman IH, ten Bruggenkate CM. Long-term changes in graft height after maxillary sinus floor elevation with different grafting materials: radiographic evaluation with a minimum follow-up of 4.5 years. Clin Oral Implants Res. 2009 Jul;20(7):691-700.