Luis Gustavo Jaime Paiva

Acompanhamento clínico, histológico, histomorfométrico e radiográfico de biomateriais utilizados no tratamento na maxila posterior atrófica – Ensaio clínico randomizado

Clinical, histological, histomorphometric and radiographic follow-up of biomaterials used in the treatment of atrophic posterior maxilla – Randomized clinical trial

Tese apresentada à

Faculdade de Odontologia da

Universidade Federal de Uberlândia,

como requisito parcial para obtenção

do Título de Doutor em Odontologia

na Área de Concentração de Clínica

Odontológica Integrada.

Uberlândia, 2022

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ATA DE DEFESA - PÓS-GRADUAÇÃO

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Reuniu-se em Web Conferência pela plataforma Zoom, em conformidade com a PORTARIA Nº 36, DE 19 DE MARÇO DE 2020 da COORDENAÇÃO DE APERFEIÇOAMENTO DE PESSOAL DE NÍVEL SUPERIOR - CAPES, pela Universidade Federal de Uberlândia, a Banca Examinadora, designada pelo Colegiado do Programa de Pós-graduação em Odontologia, assim composta: Professores Doutores: Flaviana Soares Rocha (UnB); Robson Rodrigues Garcia (UFG); Lívia Bonjardim Lima (UFU); Luiz Fernando Barbosa de Paulo (UFU); Darceny Zanetta Barbosa (UFU); orientador(a) do(a) candidato(a).

Iniciando os trabalhos o(a) presidente da mesa, Dr(a). Darceny Zanetta Barbosa, apresentou a Comissão Examinadora e o candidato(a), agradeceu a presença do público, e concedeu ao Discente a palavra para a exposição do seu trabalho. A duração da apresentação do Discente e o tempo de arguição e resposta foram conforme as normas do Programa.

A seguir o senhor(a) presidente concedeu a palavra, pela ordem sucessivamente, aos(às) examinadores(as), que passaram a arguir o(a) candidato(a). Ultimada a arguição, que se desenvolveu dentro dos termos regimentais, a Banca, em sessão secreta, atribuiu o resultado final, considerando o(a) candidato(a):

Aprovado.

Esta defesa faz parte dos requisitos necessários à obtenção do título de Doutor.

O competente diploma será expedido após cumprimento dos demais requisitos, conforme as normas do Programa, a legislação pertinente e a regulamentação interna da UFU.

Nada mais havendo a tratar foram encerrados os trabalhos. Foi lavrada a presente ata que após lida e achada conforme foi assinada pela Banca Examinadora.

Documento assinado eletronicamente por **Darceny Zanetta Barbosa**, **Professor(a) do Magistério Superior**, em 28/07/2022, às 18:16, conforme horário oficial de Brasília, com fundamento no art. 6º,

DEDICATÓRIA

Por todo amor e enorme suporte,

dedico este trabalho à vocês:

pai, mãe, Thais, Lucas e Theo.

AGRADECIMENTOS

Agradeço aos meus pais, Marco Aurélio e Cristiane, por não medirem esforços durante toda a minha vida, para que eu e meus irmãos pudéssemos priorizar nossa educação , sempre apoiando minhas decisões.

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Aos funcionários da FOUFU

À CAPES, ao CNPq e à FAPEMIG pelo apoio financeiro concedido para que as pesquisas dessa tese de doutorado pudessem ser desenvolvidas.

SUMÁRIO

RESUMO

Quando não há volume ósseo suficiente na região posterior da maxila, a elevação da membrana do seio maxilar com a utilização de enxertos ósseos pode permitir a instalação de implantes dentários e a reabilitação do paciente. Esse projeto de pesquisa buscou avaliar de maneira clínica, radiográfica, histológica e histomorfométrica a utilização de dois materiais substitutos ósseos, Boneceramic e Bio-Oss, ou da não utilização de biomateriais, nas cirurgias de levantamento da membrana do seio maxilar em humanos, com foco principal na quantidade e qualidade do tecido neoformado na região enxertada e nas repercussões clínica de possíveis diferenças encontradas entre os biomateriais. Para tal, foram avaliados 36 seios maxilares, tratados de forma aleatória com cada um dos biomateriais citados, dando origem a um estudo clínico randomizado controlado. O primeiro objetivo foi o de avaliar tomograficamente o osso neoformado a partir de cirurgia de elevação do assoalho do seio maxilar sem a utilização de biomateriais, apenas com o coágulo sanguíneo. Demonstramos um ganho em altura, área e volume satisfatórios para a reabilitação com implantes dentários osseointegráveis.

O segundo e terceiro objetivo foram avaliar e comparar histomorfometricamente e histologicamente o osso neoformado com dois diferentes biomateriais, um xenógeno (BioOss) e um sintético (BoneCeramic), além da não utilização de biomateriais. Demonstramos uma similaridade do percentual de osso neoformado.

Palavras-chaves: Elevação do assoalho do seio maxilar; transplante ósseo; teste de materiais, BioOss, Boneceramic**.**

ABSTRACT

Oral rehabilitation with osseointegrated dental implants can often be limited in situations of insufficient bone. Several techniques are described in order to restore an adequate amount of bone for the installation of dental implants. This research evaluate clinical, radiographic, histological and histomorphometric, the

use of two bone substitute materials, Boneceramic and Bio-Oss, or the clot, in maxillary sinus lift procedures. 36 maxillary sinuses were operated. For the first objective Computed tomography scans were performed, in blood clot group, preoperatively and 6 months postoperatively in order to measure bone height and volume in both periods. We demonstrated a satisfactory gain in height, area and volume for rehabilitation with osseointegrated dental implants. The second and third objectives were to evaluate and compare histomorphometrically and histologically the newly formed bone with two different biomaterials, one xenogenous (BioOss) and one synthetic (BoneCeramic), in addition to not using biomaterials. We demonstrated a similarity in the percentage of newly formed bone.
Keywords: Maxillary sinus floor elevation; bone transplantation; material testing, BioOss, Boneceramic

1. INTRODUÇÃO E REFERENCIAL TEÓRICO

Quando não há volume ósseo suficiente na região posterior da maxila, a elevação da membrana do seio maxilar com a utilização de enxertos ósseos pode permitir a instalação de implantes dentários e a reabilitação do paciente (1). A utilização do enxerto ósseo autógeno nestes procedimentos tem demonstrado propriedades osteogênicas, osteocondutivas e osteoindutivas, sendo considerada como o padrão-ouro para a correção destas deficiências ósseas.

O enxerto ósseo autógeno favorece uma situação viável para a instalação de implantes de titânio propiciando um aumento significativo na utilização destes implantes na última década. Entretanto, o osso autógeno necessita ser coletado de outra área do paciente podendo provocar desconforto e morbidade (2-4). Outro problema relacionado ao osso autógeno é a sua disponibilidade limitada na cavidade bucal e, de acordo com a região doadora, pode ser necessária a exploração de uma área doadora adicional (2-4).

Em uma tentativa de que tais problemas sejam evitados, diferentes materiais (denominados à partir daqui de biomateriais) têm sido utilizados com finalidade de recuperar o tecido ósseo perdido, procurando preencher as características do osso autógeno (2-4). Biomaterial compreende uma substância ou combinação de substâncias, farmacologicamente inertes, de origem natural ou sintética, utilizados com a finalidade de tratar, substituir ou aumentar a matéria viva (órgãos ou tecidos) cuja função foi perdida, e que podem ser usados tanto de maneira transitória como definitiva (5). Os biomateriais substitutos ósseos são rotineiramente classificados de acordo com o seu mecanismo de ação (*osteocondutores* - que atuam como substrato para neoformação óssea; *osteoindutores* - com a capacidade de recrutar e induzir a diferenciação de células ainda indiferenciadas em osteoblastos; *osteogênicos* - possuem osteoblastos ou demais células osteoprogenitoras viáveis, apresentando a capacidade de levar a ossificação direta), ou de acordo com sua origem (*autógenos* - obtido de áreas doadoras do próprio individuo; *homógenos* - obtido de indivíduos da mesma espécie do receptor; *xenógenos* - obtidos de indivíduos de espécies diferentes do receptor, sendo mais comumente obtidos de bovinos;

aloplásticos - podem ser de natureza metálica, cerâmica ou polimérica). Como já foi abordado, o enxerto ósseo autólogo continua sendo considerado como o padrão ouro atualmente, e é largamente empregado quando da necessidade de aumento do volume ósseo, visto que é o biomaterial que mais se aproxima de apresentar propriedades desejáveis como osteogênese, osteocondução e osteoindução, simultaneamente (6).

As vantagens da utilização de um biomaterial não autógeno para aumento ósseo são: facilidade de obtenção em quantidade desejada, redução do tempo cirúrgico e ausência da necessidade da manipulação de uma segunda área cirúrgica (doadora do enxerto), tornando-o uma alternativa viável nas cirurgias de reconstrução óssea prévias e posterior reabilitação com implantes osseointegráveis (2-4). Apesar do avanço nas pesquisas com a finalidade de incorporar todas as qualidades do osso autógeno, um biomaterial definido como "ideal" ainda não foi encontrado (2-4).

Dentre os biomateriais que são atualmente mais utilizados, além do enxerto ósseo autólogo, podemos um biomaterial aloplástico – cerâmico comercialmente chamado de Boneceramic (Straumann, Suíça)). O Boneceramic é um biomaterial sintético que consiste de 60% hidroxiapatita e 40% de Beta Tricálcio Fosfato, sendo que seus grânulos possuem 90% de porosidade para a intercomunicação e o tamanho de suas partículas varia entre 500 e 1000μm, com propriedades osteocondutivas (2-4). Estudos prévios demonstraram que o HA+β-TCP atua como excelente osteocondutor, quando instalado em seios maxilares (2-4). Podemos ainda citar um biomaterial substituto ósseo xenógeno, de origem bovina. O Bio-Oss (Geistlisch, Suíça). O Bio-Oss é uma hidroxiapatita natural constituída de matriz de osso bovino anorgânico e cristais de carbonato de cálcio. Não causa reação imunológica e é altamente osteocondutivo, fato que permite reparação óssea e pode ser usado em combinação com enxertos autógenos ou isoladamente (7). Embora diversos estudos com esses biomateriais utilizados de forma isolada estejam presentes na literatura, ensaios clínicos randomizados, abordando a remodelação das áreas enxertadas de forma histomorfométrica e radiográfica, além de avaliar os índices de sucesso dos implantes instalados sobre essas áreas são inexistentes até o momento.

Além disso, em alguns casos específicos, quando o remanescente ósseo da maxila posterior é insuficiente para instalação de implantes de comprimento adequando, mas suficiente para estabilização cirúrgica destes, a instalação de implantes é feita simultaneamente à elevação da membrana do seio maxilar. O espaço dentro do seio é mantido pela presença do implante e preenchido por coágulo sanguíneo, que seria responsável pela condução da formação óssea. Desta forma, esta técnica traz vantagens como a diminuição dos custos, pela não necessidade de colocação de biomateriais e redução do número de cirurgias, pois o implante e a elevação do seio maxilar são feitas em uma mesma etapa. Por outro lado, a literatura ainda é pobre em evidenciar os reais benefícios clínicos e biológicos dessa técnica (8).

O conhecimento aprofundado do processo de remodelação óssea e sobrevivência dos implantes, após a elevação da membrana do seio maxilar e reposição do osso perdido com diferentes biomateriais é essencial para uma indicação mais precisa deste protocolo e do biomaterial para substituição óssea, identificando as possíveis variáveis que possam influenciar na previsibilidade dos resultados.

2- PROPOSIÇÃO – OBJETIVO PRINCIPAL

O objetivo desta tese de doutorado é avaliar de maneira clínica, radiográfica, histológica e histomorfométrica a utilização de dois biomateriais subtitutos ósseos, Boneceramic, e Bio-Oss, ou da não utilização de biomateriais, nas cirurgias de levantamento da membrana do seio maxilar em humanos, com foco principal na quantidade e qualidade do tecido neoformado na região enxertada e nas repercussões clínica de possíveis diferenças encontradas entre os biomateriais.

OBJETIVOS ESPECÍFICOS

1. Avaliar tomograficamente o osso neoformado a partir de cirurgia de elevação do assoalho do seio maxilar sem a utilização de biomateriais.
2. Avaliar e comparar histomorfometricamente o osso neoformado com dois diferentes biomateriais, um xenógeno (BioOss) e um sintético (BoneCeramic)
3. Avaliar e comparar histomorfometricamente e histologicamente o osso neoformado com dois diferentes biomateriais, um xenógeno (BioOss) e um sintético (BoneCeramic), com a não utilização de biomateriais.

3. CAPÍTULOS

3.1. Capítulo 1
Artigo será submetido no periódico *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*

Tomographic analysis of non-grafted maxillary sinus submitted to implants placement. A prospective cohort study.

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Statement of Clinical Relevance

“For a greater scientific basis of less invasive protocols and lower financial costs to treat the posterior region of the maxilla, it is important to prove the accuracy of a surgical protocol for sinus mucosal lining elevation and simultaneous installation of osseointegrated implants without bone graft “

Abstract

Objective: A prospective clinical study of maxillary sinus floor lifting procedures without the use of any graft material, using only the blood clot, was conducted.

Study Design: 16 patients were selected, and a total of 21 maxillary sinuses were operated, installing two implants in each maxillary sinus, totaling 42 dental implants. The sinus membrane was elevated and supported superiorly by two implants. Computed tomography scans were performed preoperatively and 6 months postoperatively in order to measure bone height and volume in both periods.

Results: Of the 42 implants installed, one was considered lost (97% success rate). Bone height gain was 4.39 mm, and volume gain was 491.04 mm3 after 6 months.

Conclusion: The technique used in the present study was considered effective, being performed with a high success rate, and lower cost and morbidity in its performance.

Keywords: Schneiderian membrane; fibrin clot; maxillary sinus; sinus lifting.

Introduction

Oral rehabilitation with osseointegrated dental implants can often be limited in situations of insufficient bone. Several techniques are described in order to restore an adequate amount of bone for the installation of dental implants.[1,2] The presence of the maxillary sinus in the posterior region of the maxilla makes the rehabilitation of this area a challenge. The process of pneumatization of the sinus membrane (Schneiderian's membrane) after the loss of maxillary posterior

teeth can significantly limit the bone height availability . [2,3] Therefore, bone grafting procedures prior to implant placement surgery may be necessary. [2,4]

Various maxillary sinus floor augmentation techniques have been proposed for managing severe bone loss in the posterior maxilla [1,4,5,6]. The standard procedure for maxillary sinus floor elevation includes opening a bone window in the lateral region of the sinus, through which the Schneiderian membrane can be lifted, filling the generated space with some graft material. Dental implants can be installed during the grafting procedure or after 6-12 months after placement of the grafted material [1,2,3]. Various substitutes have been used to fill the resulting space of the sinus, including autogenous bone, allografts, xenografts, synthetics, blood clot and mixtures of various materials with similar results. [7,8]

The autogenous bone graft is considered the gold standard as a fill material in these procedures. This is due to its properties: osteogenesis, osteoconduction and osteoinduction, simultaneously. [6,7,8] However, autogenous bone requires an additional surgical area to obtain it, increasing the discomfort and morbidity of rehabilitation. [6,7,8] The non-autogenous biomaterials as xenografts, allografts, synthetics have some advantages : ease of obtaining the desired amount, reduction of surgical time and absence of the need to manipulate a second surgical area (graft donor) . [6,7,8] However, the absence of osteogenic and osteoinductive properties, added to the high cost, meant that other alternatives should be studied. [6,7,8,9]

There have been reports of successful bone formation with sinus floor elevation by simply elevating the maxillary sinus membrane and filling the sinus

cavity with a blood clot. [10,11,12,13] Boyne et al. (1993) [14] carried out the first experimental study, through the elevation of the sinus membrane, without the use of any graft material and immediate installation of implants in monkeys, obtaining satisfactory bone neoformation and implant stability. This technique was first described by Lundgreen ;Lundgren et al., (2004) [11] with an unexpected bone repair in the maxillary sinus, after the removal of an intra-sinusal mucous cyst, when new bone formation was observed. The protocol consists of the lateral approach to the maxillary sinus, creating a secluded space by lifting the membrane and maintaining the space through immediate implant placement, clot formation and subsequent repositioning of the bone window . [10] Radiographic evidence showed bone neo-formation in all 10 patients in the study. [11]

Thor et al. (2007) [15] evaluated 44 implants in the remaining alveolar bone ridges without bone graft. After a period of six months, periapical radiographs and CT scans were performed to measure bone formation. The results showed consistent bone formation with average bone gain of 6.51mm and survival rate of 97.7% during a period of 27.5 months.

Zenóbio et al. (2020) [16] showed new bone formation on all sites of implant placement with and without bone graft; Jensen et al. (2018) [17] in a systematic review showed that Sinus membrane elevation without the use of a graft material seems to enhance new bone formation with high implant survival; Zahedpasha et al. (2021) [18] demonstrate a Radiological bone gain similar between grafted and graftless groups. Pinchasov (2014) [19] shown in the review that the potential of the maxillary sinus to heal and to form new bone without bone grafts or substitutes is of high nature.

For a greater scientific basis of less invasive protocols and lower financial costs to treat the posterior region of the maxilla, this study describes and evaluates the surgical protocol for sinus mucosal lining elevation and simultaneous installation of osseointegrated implants without bone graft. For this, Cone beam tomography were made to analysed tomograpgys the bone formed.

Material and methods

This prospective cohort study was approved by the Research Ethics Committee of the Federal University of Uberlandia (CAAE:). Patients were informed about the objectives of this study, read, and signed the informed consent form. The study was carried out in accordance with the ethical norms established by the Declaration of Helsinki.

Patient selection

Patients were selected for this study if they presented clinical indications to install implants in the posterior region of the maxilla associated with reduced amount of bone availability, however, the remaining native bone enables the implants placement . In addition, it was necessary that there were no alveolar ridges in the healing phase in the area where the implants would to be installed, and patients should have good systemic health. The smokers, drug users or pathologies known to alter bone metabolism, pregnant and lactating women, and patients with chronic pathologies in the upper airways were excluded of this study.

Implants placement procedure

After performing local anesthesia, a full-thickness mucoperiosteum flap was detached to expose the lateral wall of the maxillary sinus. Using a spherical drill, an osteotomy was performed for access through the lateral wall of the maxillary sinus. After visualization of the mucosa of the maxillary sinus by transparency, the membrane was detached and the window formed by the lateral wall of the sinus was displaced into the maxillary sinus. Then, the surgical site was prepared for the implant's placement (SIN UNITITE – BRASIL) , and the formation of a blood clot was stimulate into the maxillary sinus. The surgical bed was covered with a resorbable collagen membrane and sutured using 5.0 nylon threads. It was prescribed for all patients during the postoperative period: amoxicillin (500mg) for 7 days, ibuprofen (600mg) for 5 days and sodium dipyrone (500mg) for 3 days for oral consumption. Additionally, 0.12% chlorhexidine gluconate-based mouthwash was prescribed for 14 days. The sutures were removed after 14 days (Figure 1).

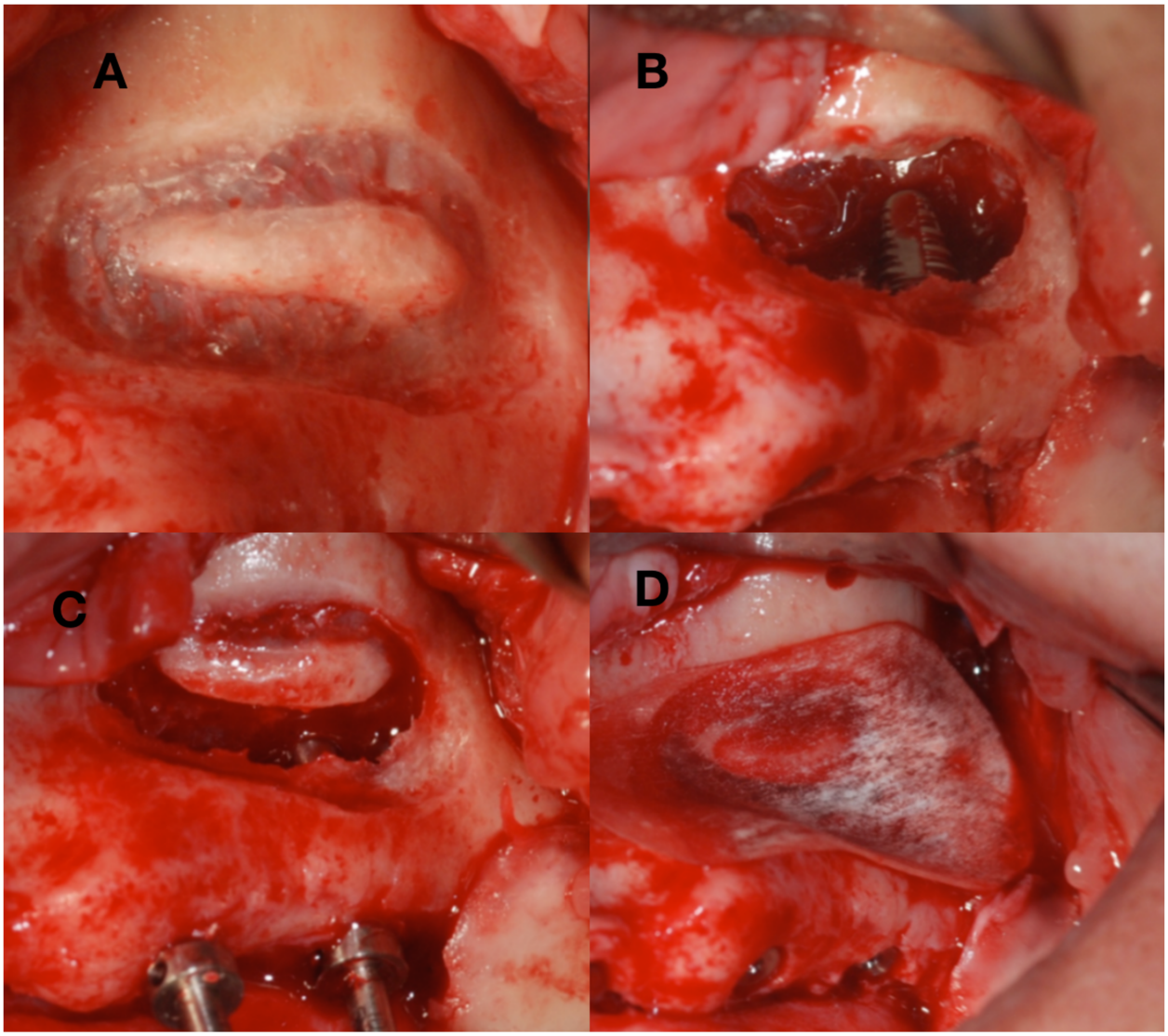

Figure 1 – Implants placement procedure

Tomographic analysis

All the patients were submitted for tomographic exams in three timepoints: prior to the grafting surgeries, 180 postoperative days. From these images using a dedicated software (OnDemand 3D 1.10.5, CyberMed, Seoul, South Korea), and with the help of an experienced operator, for each grafted maxillary sinus, 1 mm thick parasagittal sections (combination of 4 voxels of the image), were generated every 1 mm, throughout the grafted extension. Anatomical references

of the patient's maxilla were used to ensure that the beginning and end of imaging always occur in the same region, for the three volumes obtained from each patient, standardizing the same number of parasagittal slices generated for each moment of the study. This method were refined with the help of the “Fusion” module, from the same software, which aligns the volumes three-dimensionally, ensuring accuracy in the making of the cuts in the same places (Fugures 2 and 3) . The cuts obtained were exported to the TIF extension, without compression, and the images saved.

The images obtained were opened in another software (ImageJ, NIH, USA), and the highest bone height were accessed, in mm, for each image of the grafted region. At the end, the average height of each maxillary sinus were used to represent that sample. Additionally, in the images obtained in all observation periods, the bone area, in mm2, of the grafted region were measured, allowing the sum of the areas measured in all the images that represent a maxillary sinus to demonstrate the volume, in mm3, of each region treated, according to Cavalieri's principle. Based on these data, it were possible to evaluate the volumetric variation of the grafted areas over time (Figure 4).

Figure 2 - OnDemand 3D software screen with the Fusion module selected, showing the window where the volumes to be aligned are selected.

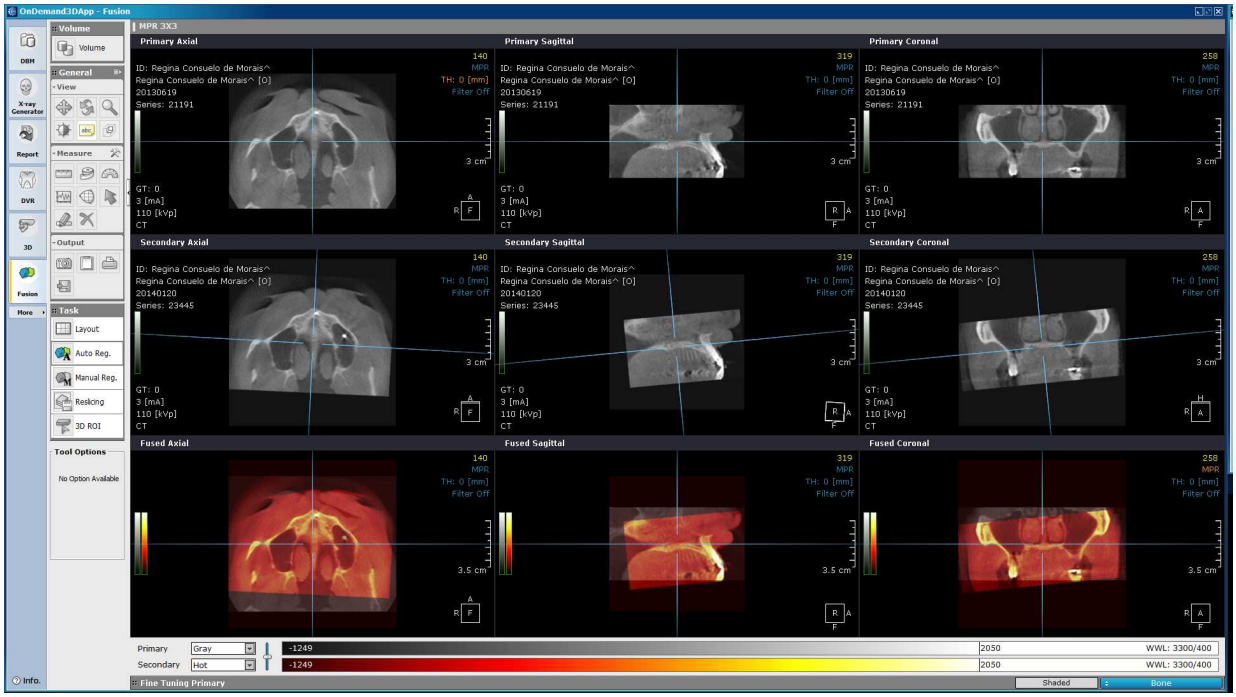

Figure 3 - OnDemand 3D software screen with the Fusion module selected, showing two volumes aligned three-dimensionally.

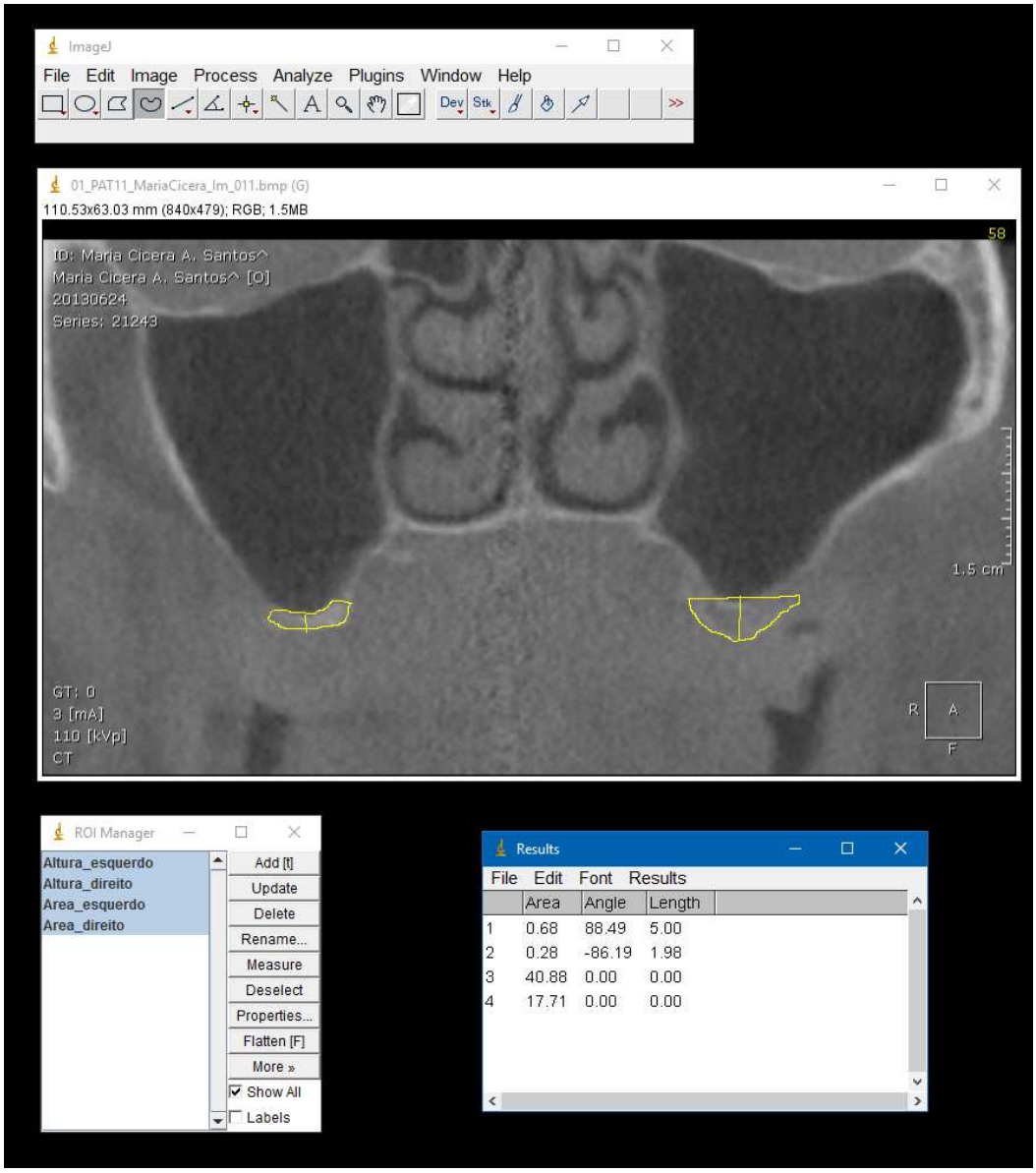

Figure 4 - ImageJ software screen, with the four measurements performed on each tomography slice exemplified (height and area, for each maxillary sinus). The measurements shown in the results were calibrated in mm.

Statistical Analysis

The distribution of the data was considered parametric, according to the Kolgomorov-Smirnov normality test. Statistical comparisons of the tomographic data between the initial and final periods were made using the paired t-test. The

histometric data was exposed by a descriptive analysis. The software used was SPSS 22 (IBM, USA). The graphs were created using the GraphPad Prism 6 software (GraphPad software Inc., USA). All tests were applied at the 95% confidence level.

Results

The study involved 16 patients which presented 21 maxillary sinuses that were submitted to the sinus floor elevation procedure associated with immediate the placement of 42 dental implants. One implant was lost giving a survival rate of 97.61%.

Regarding tomographic analysis, the new bone formation and the implants placement was associated with an increase in the total volume of osteodensity tissues inside the maxillary sinus on average of 491.04 mm3 (standard deviation of 307.86, range between -36.16 and 1223.58), increase in the average area of each parasagittal section of 41.29 mm2 (standard deviation) of 19.33, range between 4.52 and 81.57), and increase in the mean height of the ridge that varied on average 4.39 mm (standard deviation of 1.83, range between 0.54 and 7.62).

Considering the average difference (in percentage, proportionally to the initial value) measured for each of the evaluated parameters, an increase was verified in all evaluated parameters. The total volume of the radiodense area showed a mean increase of 90.37% (standard deviation of 52.11%, range between -6.90 and 173.25), the mean area of each parasagittal section increased

by 94.84% (standard deviation of 48.56%, range between 7.41 and 173.25).), and the mean height of the ridge increased by an average of 90.36% (standard deviation of 55.62%, range between 7.42 and 220.03).

Table 1 Mean, standard deviation, range, and p value (paired t-test) for the comparison between observation periods, for the total volume of the grafted area (mm3), mean area of each parasagittal section of the grafted area (mm2), and average height of the edge in the grafted area (mm)

Parameters	Period	Avarage	Standard deviation	Confidence interval	p
Volume	*Baseline*	580.76	234.04	166.78 – 1009.16	≤ 0.0001
	Final	1071.80	459.84	262.31 – 1974.35	
Area	*Baseline*	48.80	15.78	26.16 – 78.55	≤ 0.0001
	Final	90.10	22.63	43.72 – 131.62	
Height	*Baseline*	5.68	1.50	2.93 – 8.38	≤ 0.0001
	Final	10.07	1.32	7.61 – 12.39	

Discussion

The rehabilitation of the posterior region of the maxilla with osseointegrated dental implants often requires bone grafting procedures. [20,21,22] The search for techniques that provide a treatment with a lower cost and shorter

duration is constant. [3,5,12,16,17,20] The technique performed by the present study proved to be effective in terms of bone neoformation around the installed implants and their good survival.

Recently, some studies have evaluated bone height gain and newly formed bone density [7,8,9,10,11,12] including the bone volume variation with graftless maxillary sinus lift with simultaneous implants. [18,19] The present study used a methodology for tomographic analysis (Spin-Neto, 2013) [23], which guaranteed accuracy in measuring the same tomographic section at two different times. Our study analyzed and compared the variation in bone height and volume before and six months after maxillary sinus lift surgery.

The bone ridge height varied by 90.36% between the initial period and the 6-month postoperative period, which meant an average gain in bone height of 4.39 mm. Previous studies have demonstrated gains in height between 4-6 mm, corroborating the findings of the present study. [7,15,24] However, in a study evaluating the maxillary sinus lift without the placement of grafts, de Oliveira et al., (2013) [25] reported a bone formation considered insufficient for the posterior installation of dental implants. However the authors performed different procedures from the technique performed by the present study, such as use a titanium screw to hold the sinus membrane superiorly and no simultaneous implant placement. Possible membrane perforations and the absence of implants may not have guaranteed the maintenance of the space long enough for bone formation. In addition, recent studies have shown that the treatment surfaces of implants can provide better adhesion of the blood clot to the implants, which would stimulate the osteogenic cells migration. [7,11,12,15,18,19,24]

The volume variation of the present study was 90.37%, representing, in real values, a gain of 491.04 mm3 in 6 months. It is known that adequate bone volume and quality are essential factors for the dental implants osseointegration. [26,27] Different authors have demonstrated an increase in bone volume in maxillary sinus lift surgeries with different graft materials. [28,29] The present study demonstrated a similar gain in bone volume in 6 months through a technique without the use of any type of graft, thus substantially reducing the cost of treatment.

Implant survival in the present study was also evaluated. After placement of 34 implants and an average follow-up of 25 months, one implant was considered lost at the time of reopening surgery. In this way, a survival rate of 97% can be demonstrated, corroborating survival results demonstrated by other authors [7,15,18,18,24]

The absence of bone formation around the apices of some implants, qualitatively observed in the parasagittal sections of the present study, is in agreement with previous studies in animals and humans. [7,30]

Nevertheless, the absence of bone at the apices of the implants did not demonstrate any negative clinical imperative for implant success, as previously reported.[11,15,24]

More clinical studies with longer follow-up of implants under masticatory loads should be carried out, aiming at the sum of evidence that supports the technique evaluated in the present study.

Conclusion

Graftless maxillary sinus lift with immediate implants, demonstrated considerable increase in bone height and volume in a period of 6 months. A high survival rate of implants was observed. The time, cost and morbidity of the treatment decreased considerably due to the absence of graft material and the installation of implants simultaneously with the maxillary sinus lift surgery. More studies with longer follow-up are necessary, but the technique described in the present study showed good and promising results

Conflict of Interest: The authors declare that they have no conflict of interest

References

1- Verhoeven JW, Cune MS, Terlou M, et al: The combined use of endosteal implants and iliac crest onlay grafts in the severely atrophic mandible: A longitudinal study. Int J Oral Maxillofac Surg 1997:26:351. https://doi.org/10.1016/S0901-5027(97)80796-5

2- Garg AK: Augmentation grafting of the maxillary sinus for placement of dental implants: Anatomy, physiology, and procedures. Implant Dent 1999 :8:36. https://doi.org/10.1097/00008505-199901000-00004

3- Ungor C: Radiologic evaluation of putty versus powder form of demineralized bone matrix in sinus floor elevation. J Oral Implantol 2012:38:337. https://doi.org/10.1563/AAID-JOI-D-10-00017

4- Toffler M. Minimally invasive sinus floor elevation procedures for simultaneous and staged implant placement. N Y State Dent J 2004;70:38-44

5- Ahn JJ, Cho SA, Byrne G, Kim JH, Shin HI. New bone formation following sinus mem-brane elevation without bone grafting: histo-logic findings in humans. Int J Oral Maxillofac Implants 2011;26:83-90

6- Cordaro L, Bosshardt DD, Palattella P, Rao W, Serino G, Chiapasco M. Maxillary sinus grafting with Bio-Osss or Straumanns Bone Ceramic: histomorphometric results from a randomized controlled multicenter clinical trial. Clin. Oral Impl. 2008:796-803. https://doi.org/10.1111/j.1600-0501.2008.01565.x

7- Altintas NY, Senel FC, Kayipmaz S, Taske- sen F, Pampu AA. Comparative radiologic analyses of newly formed bone after maxillary sinus augmentation with and without bone grafting. J Oral Maxillofac Surg 2013:71:1520-30. https://doi.org/10.1016/j.joms.2013.04.036

8- Esposito M, Grusovin MG, Worthington HV, et al: Interventions for replacing missing teeth: Bone augmentation techniques for dental implant treatment. Cochrane Database Syst Rev: 2006. https://doi.org/10.1002/14651858.CD003607.pub2

9- Chiapasco, M., Zaniboni, M. & Boisco, M. Augmentation procedures for the rehabilitation of deficient edentulous ridges with oral implants. Clinical Oral Implants Research 2006 :17 :136-159. https://doi.org/10.1111/j.1600-0501.2006.01357.x

10- Lundgren S, Andersson S, Sennerby L. Spontaneous bone formation in the maxillary sinus after removal of a cyst: coincidental or expected reaction? Clin Implant Dent Relat Res 2003; 5:78-81. https://doi.org/10.1111/j.1708-8208.2003.tb00187.x

11- 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. https://doi.org/10.1111/j.1708-8208.2004.tb00224.x

12- Lundgren S, Cricchio G, Palma VC, Salata LA, Sennerby L.Sinus membrane elevation and simultaneous insertion of dental implants: a new surgical technique in maxillary sinus floor augmentation. Periodontol 2008; 47:193-205.
https://doi.org/10.1111/j.1600-0757.2008.00264.x

13- Palma VC, Magro-Filho O, de Oliveria JA, Lundgren S, Salata LA, Sennerby L. Bone reformation and implant integration follow- ing maxillary sinus membrane elevation: an experimental study in primates. Clin Implant Dent Relat Res 2006:8:11-24
https://doi.org/10.2310/j.6480.2005.00026.x

14- Boyne PJ: Analysis of performance of root-form endosseous implants placed in the maxillary sinus. J Long Term Eff Med Implants 1993:3:143.

15- Thor A, Sennerby L, Hirsch JM, Rasmusson L. Bone formation at the maxillary sinus floor following simultaneous elevation of the mucosal lining and implant installation without graft material: an evaluation of 20 patients treated with 44 Astra Tech implants. J Oral Maxillofac Surg 2007: 65:64-72. https://doi.org/10.1016/j.joms.2006.10.047

16- Zenóbio EG, Mendes LD, Bustamante RP, Vidigal BC, Favato MN, Manzi FR, Cosso MG,. Effect of amount of biomaterial used for maxillary sinus lift on volume maintenance of grafts. J Clin Exp Dent. 2020

17- 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 Surg. 2018 https://doi.org/10.1016/j.ijom.2017.05.001

18- Zahedpasha A, Ghassemi A, Bijani A, Haghanifar S, Majidi MS, Ghorbani ZM. Comparison of Bone Formation After Sinus Membrane Lifting Without Graft or Using Bone Substitute "Histologic and Radiographic Evaluation". J Oral Maxillofac Surg. 2021 https://doi.org/10.1016/j.joms.2020.12.040

19- Pinchasov G, Juodzbalys G. Graft-free sinus augmentation procedure: a literature review. J Oral Maxillofac Res. 2014 https://doi.org/10.5037/jomr.2014.5101

20- Astrand P, Nord PG, Branemark PI: Titanium implants and onlay bone graft to the atrophic edentulous maxilla: A 3-year longitudinal study. Int J Oral Maxillofac Surg 1996: 25:25. https://doi.org/10.1016/S0901-5027(96)80007-5

21- Kühl S, Payer M, Kirmeier R, Wildburger A, Acham S, Jakse N.The influence of particulated autogenous bone on the early volume stability of maxillary sinus grafts with biphasic calcium phosphate: a randomized clinical trial. Clin Implant Dent Relat Res. 2015 :17:173-8. https://doi.org/10.1111/cid.12086

22- Sul SH, Choi BH, Li J, et al: 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 2008:105:684. https://doi.org/10.1016/j.tripleo.2007.09.024

23- Spin-Neto, R., A. Stavropoulos, L. A. Pereira, E. Marcantonio, Jr. & A. Wenzel. Fate of autologous and fresh-frozen allogeneic block bone grafts used for ridge augmentation. A CBCT-based analysis. Clin Oral Implants Res. 2013 Feb;24(2):167-73. https://doi.org/10.1111/j.1600-0501.2011.02324.x

24- Bassi AP, Pioto R, Faverani LP, Canestraro D, Fontão FG. Maxillary sinus lift without grafting, and simultaneous implant placement : a prospective clinical study with a 51-month follow-up.Int J Oral Maxillofac Surg. 2015:44:902-7. https://doi.org/10.1016/j.ijom.2015.03.016

25- de Oliveira GR, Olate S, Cavalieri-Pereira L, Pozzer L, Asprino L, de Moraes M, et al. Maxillary sinus floor augmentation using blood without graft material Preliminary results in 10 patients. J Oral Maxillofac Surg 2013:71:1670-5. https://doi.org/10.1016/j.joms.2013.05.025

26- Raja SV. Management of the posterior maxilla with sinus lift : Review of techniques. J Oral Maxillofac Surg 2009:67;1730-4 https://doi.org/10.1016/j.joms.2009.03.042

27- Woo I, Le BT: Maxillary sinus floor elevation: Review of anatomy and two techniques. Implant Dent 2004:13:28. https://doi.org/10.1097/01.ID.0000116369.66716.12

28- Berberi A, Bouserhal L, Nader N, Assaf RB, Nassif NB, Bouserhal J, Salameh Z Evaluation of Three-Dimensional Volumetric Changes After Sinus Floor Augmentation with Mineralized Cortical Bone Allograft. J Maxillofac Oral

Surg. 2015 :14:624-9
https://doi.org/10.1007/s12663-014-0736-3

29- Kirmeier R, Payer M, Wehrschuetz M, Jakse N, Platzer S, Lorenzoni M Evaluation of three-dimensional changes after sinus floor augmentation with different grafting materials. Clin Oral Implants Res. 2008 :19:366-72. https://doi.org/10.1111/j.1600-0501.2007.01487.x

30- Jeong SM, Choi BH, Li J, Xuan F: A retrospective study of the effects of sinus membrane elevation on bone formation around implants placed in the maxillary sinus cavity. Oral Surg Oral Med Oral Pathol Oral Radiol Endod . 2009:107:364.
https://doi.org/10.1016/j.tripleo.2008.05.032

3.2 Capítulo 2

Artigo será submetido no periódico *Journal of Periodontology*

Histomorphometric analysis of maxillary sinuses grafted with different osteoconductive bone substitutes. A case-control study.

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Abstract

Background: This investigation was designed to compare the histomorphometric results from sinus floor augmentation with anorganic bovine bone (ABB) and a new biphasic calcium phosphate, Straumann Bone Ceramic (BCP).

Methods: 20 maxillary sinuses were treated in 20 patients. Residual bone height was < 5 mm. .Lateral sinus augmentation was used, with grafting using either DBB (10 sinuses) or HA/TCP), (10 sinuses). After 180 days of healing, implant sites were created and biopsies taken for histological and histomorphometric analyses. The parameters assessed were area fraction of new bone, soft tissue, and graft substitute material in the grafted region;

Results: Histology showed close contact between new bone and graft particles for both groups, with no significant differences in the amount of mineralized bone 31.84 ± 6.36 % in the DBB group and 27.11 ± 10.16 % in the HA/TCP group. Soft tissue amounts were observed in the DBB (52.26 ± 6.76%) and HA/TCP (56.05 ± 9.86 %) groups (p <0.001). The percentage of residual graft material was not different between the DBB (16.05 ± 6.71 %) and HA/TCP (16.84 ± 4.99 %) groups.

Conclusion: Both DBB anda HA/TCP produced similar amounts of newly formed bone, with similar histologic appearance, indicating that both materials are suitable for sinus augmentation for the placement of dental implants.

Key words: biphasic calcium phosphate, bone grafting, bone substitute, bovine bone, histology, histomorphometry, maxillary sinus augmentation, sinus floor elevation

Introduction

A maxillary sinus lift procedure is an established method used to provide a sufficient bone volume for implant placement in patients with a severely atrophied posterior maxilla [1,2,3] A wide variety of graft materials have been used to augment the maxillary sinus floor . The use of autogenous bone in sinus augmentation is considered the gold standard because of the reproducible healing mechanism of osteogenesis, osteoinduction, and osteoconduction. [4,5,6] However, there are several disadvantages including donor site morbidity, limping when the graft is taken from the iliac crest, prolonged healing time, second surgical intervention, requirement of general anesthesia and hospitalization, increased cost of treatment, and unpredictable resorption of the graft.[7,8] These disadvantages have led to a search for suitable graft materials that are a biocompatible and osteoinductive or at least osteoconductive alternative to autogenous bone substitute in sinus floor augmentation procedure. [1,3,5,7]

Various bone-grafting materials such as alloplasts (hydroxyapatite, b-tricalcium phosphate, bio- active glass),[9,10,11,12,13] xenografts (bovine or coralline hydroxyapatite),[14,15,16,17] or allografts (freeze-dried de- mineralized bone)[18] are currently being used as alternatives or supplements to autogenous bone. These biomaterials act as a scaffold for further bone formation.[19]

Deproteinized bovine bone (DDB), one type of xenograft, has been shown to be a safe and biocompatible bone graft material with osteo- conductive properties.[20,21,22] Also, several experimental and clinical studies have shown

successful results of BHA graft materials when used for maxillary sinus floor augmentation.[13,14,15,21,22]

Biphasic ceramic based on hydroxyapatite and β-tricalcium phosphate (HA/TCP), a ceramic alloplast, is another popular graft material that has shown promising results with osteoconductive properties.[23,24,25] Several authors have reported HA/TCP as a satisfactory graft material for augmentaion of the maxillary sinus.[11,12,13,19]

The choice of augmentation material is a crucial factor in sinus augmentation surgery. DDB and HA/TCP have been used successfully in sinus augmentation procedures.[11,20,24,25] Choosing one of these materials for sinus augmentation is still controversial, and no consensus has yet been reached.

The aim of this clinical study was to compare the biological performances of two different graft material, a xenograft (BioOss) and an alloplast (BoneCeramic), in the sinus augmentation procedure by using histomorphometry.

Material and methods

This case-control clinical study was approved by the Research Ethics Committee of the Federal University of Uberlandia (CAAE:). Patients were informed about the objectives of this study, read, and signed the informed consent form. The study was carried out in accordance with the ethical norms established by the Declaration of Helsinki.

Patient selection

Patients were selected for this study if they presented clinical indications to install implants in the posterior region of the maxilla, however they also presented no enough bone to undergo this type of procedure. In addition, it was necessary that there were no alveolar ridges in the healing phase in the area where the implants were to be installed, and patients should have good systemic health.

Smokers, drug users or users of pathologies known to alter bone metabolism, pregnant and lactating women, and patients with chronic pathologies in the upper airways were excluded of this study.

Sinus augmentation procedure

After performing local anesthesia, a full-thickness mucoperiosteum flap was detachated to expose the lateral wall of the maxillary sinus. Using a spherical drill, an osteotomy was performed for access through the lateral wall of the maxillary sinus. After visualization of the mucosa of the maxillary sinus by transparency, the membrane was detached and the window formed by the lateral wall of the sinus was displaced into the maxillary sinus. The grafts were inserted with a varied volume depending on the volume and anatomy of the maxillary sinus. The maxillary sinuses were exerted with deproteinized bovine bone (10 patients) and with biphasic ceramic based on hydroxyapatite and β-tricalcium phosphate (10 patients). After insertion of the biomaterials, the surgical bed was covered with a resorbable collagen membrane and sutured using 5.0 nylon threads. It was prescribed for all patients during the postoperative period: amoxicillin (500mg) for 7 days, ibuprofen (600mg) for 5 days and sodium dipyrone

(500mg) for 3 days for oral consumption. Additionally, 0.12% chlorhexidine gluconate-based mouthwash was prescribed for 14 days. The sutures were removed after 14 days (Figure 01).

Biopsy retrieval

Patients from both groups (DBB and HA/TCP) were called for implantation 6 months after sinus augmentation and the bone biopsies were removed at the place where the implants were installed. Bone was measured and biopsies were harvested using a 2 mm inner diameter trephine drill. prior to implant placement with abundant sterile saline irrigation. One to two vertical biopsies were taken from each sinus at the site where dental implants would be placed. After biopsy removal the dental implants (Unitite®, SIN, São Paulo, Brazil) were placed and the insertion torque was measured. The flap was sutured and the post-operation care was the same executed in the first surgery. The biopsies were designated for histological description and histomorphometric analysis (Figure 2) .

Histologic and histomorphometric analysis

For the histomorphometric evaluation, the bone biopsies were immediately fixed paraformaldehyde 4% for 48 days and decalcified in EDTA 7% for 60 days. Then, the samples were dehydrated in alcohol and xylol, embedded in paraffin, sectioned in the vertical axis (5-um thickness), and stained with the Hematoxylin and Eosin technique. Histologic images were obtained using a digital microscopic camera (Leica ICC50, Leica Microsystems. Heerbrugg, Switzerland) coupled to a microscope (Leica DM500, Leica Microsystems®, Heerbrugg, Switzerland).

Histomorphometric measurements were performed using QuPath. The region of interest was defined excluding the residual native bone. The percentage of new bone formation (area of new bone/total area), the percentage of soft tissue (area of soft tissue/total area) and the graft particle area (area of bone graft residual/total area) in the region of interest were measured at x100 magnification. The sinus were considered the sample unit so the data provided by different biopsies in the same sinus were establish as an average of each sinus. Analyses were carried out by the same investigator who was blinded to which group a specimen was assigned.

Statistical analysis

All statistical analyses were carried out using the GraphPad Prism 6 (San Diego, CA, USA)) considering the significance level of α=0.05. The results were expressed as the mean ± standard deviation. The Shapiro-Wilk test was performed to test normality ($p < .05$). The data were analyzed by ANOVA and Tukey HSD tests.

Results

The study involved 20 patients (13 women and 7 men), which presented 20 maxillary sinuses that were submitted to the sinus floor elevation procedure associated with the placement of 40 dental implants. One implant was lost in a maxillary sinus filled with HA/TCP. Regarding the treatment in each maxillary sinus, 10 patients and 10 maxillary sinuses were treated with DBB or with

HA/TCP, with 20 implants installed in each group with 100% survival in areas grafted with DBB and 95% in HA/TCP grafted areas (Table 1)

Primary stability

Implants installed in maxillary sinuses grafted with the bone substitutes DBB and HA/TCP presented, respectively, an insertion torque of 16.51 ± 24.24 Ncm and 19.82 ± 27.76

Histomorphometric analysis

The percentage of new bone was 31.84 ± 6.36 % in the DBB group and 27.11 ± 10.16 % in the HA/TCP group, and no differences were detected between the groups. Soft tissue amounts were observed in the DBB (52.26 ± 6.76%) and HA/TCP (56.05 ± 9.86 %) groups ($p < 0.001$). The percentage of residual graft material was not different between the DBB (16.05 ± 6.71 %) and HA/TCP (16.84 ± 4.99 %) groups (Table 1)

Discussion

Technological evolution and better understanding of bone-healing biology have helped to clarify the optimum makeup of bone substitutes, including the source, preparation methods, and particle size, in order to improve their osteoconductive potential. When associated with the refinement of the sinus lift surgical technique occurred in recent years, this allows for predictable placement

of implants in atrophic maxillae bone regenerated with various graft materials. [26, 27,28] . In the present study, the survival rate of implants placed after a sinus augmentation procedure was 100% in areas grafted with DBB and 95% in HA/TCP grafted areas which is comparable with the pre-existing literature data. [26, 29 30]

Deproteinized bovine bone and Biphasic ceramic based on hydroxyapatite and β-tricalcium phosphate has been found suitable to repair bone defects [31,32]. Deproteinized bovine bone (DBB) is similar to human cancellous bone both in terms of its crystalline and morphological structure. It is also biocompatible and osteoconductive but has no osteoinductive property.[16,19] However, the rate and mechanism of its resorption are still unclear.[20,33,34,35] Sartori et al,[33] in their 10-year follow-up study, reported that resorption of DBB was a slow but continuous process. Also, they found that the resorption rate was 3.6% per year for the initial 2 years and then decreased consistently in the following 8 years, with a mean value of 0.58% per month. Schlegel and Donath[36] identified the presence of DDB 6 years after the grafting procedure. They reported DDB as a permanent implant.

Biphasic ceramic based on hydroxyapatite and β-tricalcium phosphate (HA/TCP) is a derivative of hydroxyapatite, which is the inorganic component of bone. This alloplast is osteoconductive and biocompatible, but it is not an osteoinductive material. Osteoconductive properties are responsible for appositional bone growth on the surface or into pores, channels, or pipes without evidence of toxic reaction.[19,22,37] Since it is ceramic in nature, there is no risk of transmission of certain infectious diseases, which is theoretically possible with xenograft materials. [19]

The impact of the resorption rate on the amount of newly formed bone in augmented sites is still unclear. It has been demonstrated that, unlike DBB , HA/TCP is extensively resorbed in 12 to 18 months and is replaced by bone that is similar both functionally and anatomically to the original bone.[35,38,39] In an animal study, Artzi et al[38] reported that HA/TCP was completely resorbed in 24 months, whereas DBB particles still occupied a remarkable area fraction without significant resorption even after 6 months. In the present study, the mean percentage of residual graft particle after an average of 6 months of healing in the DBB group was 16.05 ± 6.71 % and in the HA/TCP group was 16.84 ± 4.99 %, showing no different between the groups.

In the present study, The percentage of new bone was 31.84 ± 6.36 % in the DBB group. Sartori et al[33] reported 29.8% new bone formation in sinus augmentation by using DBB after 8 months of healing. Similarly, Simunek et al[19] reported 34.2% and Piattelli et al[40] reported 30% new bone formation by using DBB in sinus augmentation procedures. On the other hand, this result was superior to the 14.7% rate reported by Yıldırım et al[16] and the 21% rate reported by Valentini et al.[26]

The mean new bone formation was 27.11 ± 10.16 % in the HA/TCP group. This result was comparable to the 21.4% rate reported by Simunek et al.[19] On the other hand, this result was superior to the 17% rate reported by Zerbo et al[37] and Zijderveld et al[13] and inferior to the 36% rate and the 29% rate reported by Szabo et al.[11,12]

There are some studies that compare the effect of DBB and HA/TCP as sinus graft materials. In an experimental study, Artzi et al[38] used DBB and HA/TCP to restore the mandibular bony defects in dogs and compared bone healing. They reported that the HA/TCP bone area fraction was significantly greater than DBB sites at 6 months. Simunek et al[19] compared the efficacy of DBB and HA/TCP in sinus augmentation surgery in a prospective human study. They found that new bone formation in the DBB group was significantly greater than in the HA/TCP group. In this clinical study both graft materials demonstrated successful biocompatibility in the sinus augmentation procedure with a similar amount of newly formed bone 180 days post-grafting, corroboting other studies [41,42,43,44] Additionally both group did not show higher amounts of soft tissue components than the native bone of the residual maxillary bone, and no diference was found between the two groups.

When designing the protocol of this clinical multicenter study, it was considered important to include patients with residual alveolar ridge dimensions within a clearly defined range, in this case a bone height of < 5 mm. This was considered important in evaluating the clinical differences between the two grafting materials. In the present study, two groups with similar residual ridge dimensions treated with an identical surgical protocol with the exception of the grafting material used were compared. This is particularly important since the amount of new bone and residual graft may be dependent on the distance of the grafted area from the residual bone [34] and possible explain the reason we found different results in others studies, that do not design this protocol.

In this study, comparison of DBB and HA/TCP was not performed in the same patients because the patients underwent unilateral sinus augmentation procedure. This is the limitation of this study. Another study can be conducted with patients who need a bilateral sinus augmentation procedure in order to compare these 2 graft materials in the same patients. Also, further studies should be done to evaluate the longterm success of the implants placed into these graft materials.

Conclusions

The results of this randomized prospective clinical trial demonstrate that there was no difference in the amount of newly formed bone between Deproteinized bovine bone (Biooss) and Biphasic ceramic based on hydroxyapatite and β-tricalcium phosphate (Boneceramic) when used as a grafting material for sinus floor elevation. Both materials are, therefore, suitable for bone augmentation in this situation.. It may be concluded that, with respect to the histomorphometric aspect after 180 days of healing both bone graft substitute materials appear to be equally suitable for the use of sinus floor elevation.

Conflict of Interest: The authors declare that they have no conflict of interest.

REFERENCES

1. Esposito M, Felice P, Worthington HV. Interventions for replacing missing teeth: augmentation procedures of the maxillary sinus. Cochrane Database Syst Rev. 2014 May 13;5 https://doi.org/10.1002/14651858.CD008397.pub2

2. Del Fabbro M, Wallace SS, Testori T. Long-term implant survival in the grafted maxillary sinus: a systematic review. Int J Periodontics Restorative Dent. 2013 Nov-Dec;33(6):773-83 https://doi.org/10.11607/prd.1288

3. Duttenhoefer F, Souren C, Menne D, Emmerich D, Schön R, Sauerbier S. Long-term survival of dental implants placed in the grafted maxillary sinus: systematic review and meta-analysis of treatment modalities. PLoS One. 2013 Sep 18;8(9). https://doi.org/10.1371/journal.pone.0075357

4. Boyne PJ, James RA. Grafting of the maxillary sinus floor with autogenous marrow and bone. J Oral Surg. 1980;38:613-616.

5. Jensen SS, Shulman LB, Block MS, Iacono VJ. Report of the sinus consensus conference of 1996. Int J Oral Maxillofac Implants 1998;13:11-45.

6. Pejrone G, Lorenzetti M, Mozzati M, Valente G, Schierona GM. Sinus floor augmentation with autogenous iliac bone block grafts: a histological and histomorphometrical report on the two- step surgical technique. Int J Oral Maxillofac Surg. 2002;31:383-388 https://doi.org/10.1054/ijom.2002.0286

7. Younger EM, Chapman MW. Morbidity at bone graft donor sites. J Orthop Trauma 1989;3:192-195. https://doi.org/10.1097/00005131-198909000-00002

8. Kalk WWL, Raghoebar GM, Jansma J, Boering G. Morbidity from iliac crest bone harvesting. J Oral Maxillofac Surg. 1996;54: 1424-1429. https://doi.org/10.1016/S0278-2391(96)90257-8

9. Tadjoedin ES, de Lange GL, Lyaruu DM, Kuiper L, Burger EH. High concentrations of bioactive glass material (BioGran) vs. autogenous bone for sinus floor elevation. Clin Oral Implants Res. 2002;13:428-436. https://doi.org/10.1034/j.1600-0501.2002.130412.x

10. Quinones CR, Hu¨rzeler MB, Schu¨pbach P, et al. Maxillary sinus augmentation using different grafting materials and osseoin- tegrated dental implants in monkeys. Part II: evaluation of porous hydroxyapatite as a grafting material. Clin Oral Implants Res. 1997;8: 487-496. https://doi.org/10.1034/j.1600-0501.1997.080607.x

11. Szabo G, Suba Z, Hrabak K, Barabas J, Nemeth Z. Autogenous bone versus beta tricalcium phosphate graft alone for bilateral sinus elevations (2- and 3-dimensional computed tomographic, histologic, and histomorphometric observations): preliminary results. Int J Oral Maxillofac Implants. 2001;16:681-692.

12. Szabo G, Huys L, Coulthard P, et al. A prospective multicenter randomized clinical trial of autogenous bone versus b-tricalcium phosphate graft alone for bilateral sinus elevation: histologic and histomorphometric evaluation. Int J Oral Maxillofac Implants. 2005;20:371-381.

13. Zijderveld SA, Zerbo IR, van den Bergh JP, Schulten EA, ten Bruggenkate CM. Maxillary sinus floor augmentation using a beta- tricalcium phosphate (Cerasorb) alone compared to autogenous bone grafts. Int J Oral Maxillofac Implants. 2005;20:432-440.

14. Hu¨rzeler MB, Quinones CR, Kirsch A, et al. Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part I. Evaluation of anorganic bovine-derived bone matrix. Clin Oral Implants Res. 1997;8:476-486.
https://doi.org/10.1034/j.1600-0501.1997.080606.x

15. Valentini P, Abensur DJ. Maxillary sinus grafting with anorganic bovine bone: a clinical report of long-term results. Int J Oral Maxillofac Implants 2003;18:556-560.

16. Yıldırım M, Spiekermann H, Biesterfeld S, Edelhoff D. Maxillary sinus augmentation using xenogenic bone substitute material Bio-Oss in combination with venous blood: a histologic and histomorphometric study in humans. Clin Oral Implants Res. 2000;11:217-229.
https://doi.org/10.1034/j.1600-0501.2000.011003217.x

17. Haas R, Donath K, Fo¨dinger M, Watzek G. Bovine hydroxyapatite for maxillary sinus grafting: comparative histomor- phometric findings in sheep. Clin Oral Implants Res. 1998;9:107-116.
https://doi.org/10.1034/j.1600-0501.1998.090206.x

18. Avila G, Neiva R, Misch CE, et al. Clinical and histologic outcomes after the use of a novel allograft for maxillary sinus augmentation: a case series. Implant Dent 2010;19:330-341.
https://doi.org/10.1097/ID.0b013e3181e59b32

19. Simunek A, Kopecka D, Somanathan RV, Pilathadka S, Brazda T. Deproteinized bovine bone versus beta-tricalcium phosphate in sinus augmentation surgery: a comparative histologic and histomorphometric study. Int J Oral Maxillofac Implants. 2008; 23:935-942.

20. Berglundh T, Lindhe J. Healing around implants placed in bone defects treated with Bio-Oss: an experimental study in the dog. Clin Oral Implants Res. 1997;8:117-124.
https://doi.org/10.1034/j.1600-0501.1997.080206.x

21. Hammerle CH, Olah AJ, Schmid J, et al. The biological effect of natural bone mineral on bone formation on the rabbit skull. Clin Oral Implants Res. 1997;8:198-207.
https://doi.org/10.1034/j.1600-0501.1997.080306.x

22. Peetz M. Characterization of xenogenic bone material. In: Boyne PJ, Evensen L, eds. Osseous Reconstruction of the Maxilla and the Mandible: Surgical Techniques Using Titanium Mesh and Bone Mineral. Carol Stream, Ill: Quintessence; 1997;87-100.

23. Breitbart AS, Staffenberg DA, Thorne CH, et al. Tricalcium phosphate and osteogenin: a bioactive onlay bone graft substitute. Plast Reconstr Surg. 1995;96:699-708.
https://doi.org/10.1097/00006534-199509000-00024

24. Buser D, Hoffmann B, Bernard JP, Lussi A, Mettler D, Schenk RK. Evaluation of filling materials in membrane protected bone defects: a comparative histomorphometric study in the mandible of miniature pigs. Clin

Oral Implants Res. 1998;9:137-150. https://doi.org/10.1034/j.1600-0501.1998.090301.x

25. Ohsawa K, Neo M, Matsuoka H, et al. The expression of bone matrix protein mRNAs around beta-TCP particles implanted into bone. J Biomed Mater Res. 2000;52:460-466. https://doi.org/10.1002/1097-4636(20001205)52:3<460::AID-JBM3>3.0.CO;2-U

26. Valentini P, Abensur D, Densari D, Graziani JN, Hämmerle C. Histological evaluation of Bio-Oss in a 2-stage sinus floor elevation and implantation procedure. A human case report. Clin Oral Implants Res. 1998 Feb;9(1):59-64 https://doi.org/10.1034/j.1600-0501.1998.090108.x

27. Wallace SS, Froum SJ. Effect of maxillary sinus augmentation on the survival of endosseous dental implants. A systematic review. Ann Periodontol. 2003 Dec;8(1):328-43 https://doi.org/10.1902/annals.2003.8.1.328

28. Wallace SS, Froum SJ, Tarnow DP. Histologic evaluation of a sinus elevation procedure: a clinical report. Int J Periodontics Restorative Dent. 1996 Feb;16(1):46-51.

29. Chiapasco M, Zaniboni M, Rimondini L. Dental implants placed in grafted maxillary sinuses: a retrospective analysis of clinical outcome according to the initial clinical situation and a proposal of defect classification. Clin Oral Implants Res. 2008 Apr;19(4):416-28. https://doi.org/10.1111/j.1600-0501.2007.01489.x

30. Pjetursson BE, Tan WC, Zwahlen M, Lang NP. A systematic review of the success of sinus floor elevation and survival of implants inserted in combination with sinus floor elevation. J Clin Periodontol. 2008 Sep;35(8 Suppl):216-40 https://doi.org/10.1111/j.1600-051X.2008.01272.x

31. Saito, M., Shimizu, H., Beppu, M., Takagi, M.,. The role of beta-tricalcium phosphate in vascularized periosteum. J. Orthop. Sci. 2000. 5, 275-282 https://doi.org/10.1007/s007760050163

32. Galois, L., Mainard, D., Delagoutte, J.P.,. Beta-tricalcium phosphate ceramic as a bone substitute in orthopaedic surgery. Int. Orthop. 2002, 26, 109-115.
https://doi.org/10.1007/s00264-001-0329-x

33. Sartori S, Silvestri M, Forni F, Icaro Cornaglia A, Tesei P, Cattaneo V. Ten-year follow-up in a maxillary sinus augmentation using anorganic bovine bone (Bio-Oss): a case report with histomorphometric evaluation. Clin Oral Implants Res. 2003;14: 369-372.
https://doi.org/10.1034/j.1600-0501.2003.140316.x

34. Artzi Z, Kozlovsky A, Nemcovsky CE, Weinreb M. The amount of newly formed bone in sinus grafting procedures depends on tissue depth as well as the type and residual amount of the grafted material. J Clin Periodontol. 2005;32:193-199.
https://doi.org/10.1111/j.1600-051X.2005.00656.x

35. Artzi Z, Givol N, Rohrer MD, Nemcovsky CE, Prasad HS, Tal H. Qualitative and quantitative expression of bovine bone mineral in experimental bone defects. Part 2: morphometric analysis. J Periodontol. 2003;74:1159-1160.
https://doi.org/10.1902/jop.2003.74.8.1153

36. Schlegel AK, Donath K. Bio-Oss: a resorbable bone substitute? J Long Term Eff Med Implants. 1998;8:201-209.

37. Zerbo IR, Zijderveld SA, de Boer A, et al. Histomorphometry of human sinus floor augmentation using a porous beta-tricalcium phosphate: a prospective study. Clin Oral Implants Res. 2004;15: 724-732. https://doi.org/10.1111/j.1600-0501.2004.01055.x

38. Artzi Z, Weinreb M, Givol N, et al. Biomaterial resorption rate and healing site morphology of inorganic bovine bone and beta-tricalcium phosphate in the canine: a 24-month longitudinal histologic study and morphometric analysis. Int J Oral Maxillofac Implants 2004;19:357-368.

39. Wiltfang J, Merten HA, Schlegel KA, et al. Degradation characteristics of alpha and beta tricalciumphosphate (TCP) in minipigs. J Biomed Mater Res. 2002;63:115-121
https://doi.org/10.1002/jbm.10084

40. Piattelli M, Favero GA, Scarano A, Orsini G, Piattelli A. Bone reactions to anorganic bovine bone (Bio-Oss) used in sinus augmentation procedures: a histologic long-term report of 20 cases in humans. Int J Oral Maxillofac Implants. 1999;14:835-840.

41. Mordenfeld A, Lindgren C, Hallman M. Sinus Floor Augmentation Using Straumann® BoneCeramic™ and Bio-Oss® in a Split Mouth Design and Later Placement of Implants: A 5-Year Report from a Longitudinal Study. Clin Implant Dent Relat Res. 2016 Oct;18(5):926-936. https://doi.org/10.1111/cid.12374

42. Lindgren C, Mordenfeld A, Hallman M. A prospective 1-year clinical and radiographic study of implants placed after maxillary sinus floor augmentation with synthetic biphasic calcium phosphate or deproteinized bovine bone. Clin Implant Dent Relat Res. 2012 Mar;14(1):41-50. https://doi.org/10.1111/j.1708-8208.2010.00224.x

43. Schmitt CM, Doering H, Schmidt T, Lutz R, Neukam FW, Schlegel KA. Histological results after maxillary sinus augmentation with Straumann® BoneCeramic, Bio-Oss®, Puros®, and autologous bone. A randomized controlled clinical trial. Clin Oral Implants Res. 2013 May;24(5):576-85 https://doi.org/10.1111/j.1600-0501.2012.02431.x

44. Lei L, Han J, Wen J, Yu Y, Ke T, Wu Y, Yang X, Chen L, Gou Z. Biphasic ceramic biomaterials with tunable spatiotemporal evolution for highly efficient alveolar bone repair. J Mater Chem B. 2020 Sep 21;8(35):8037-8049 https://doi.org/10.1039/D0TB01447H

Table 1. Mean and standard deviation values (%) of the histomorphometric analysis

	Newly formed bone (%)	Residual grafted material (%)	Soft tissue (%)
Bio-Oss	31.8 ± 6.5	16.0 ± 6.9	52.2 ± 6.9 ^{A}
BoneCeramic	27.2 ± 10.1	16.8 ± 5.1	55.8 ± 9.8 ^{A}

Different letters indicate statistically significant differences verified by Tukey HSD test ($p<0.05$) for soft tissue component comparison between the groups

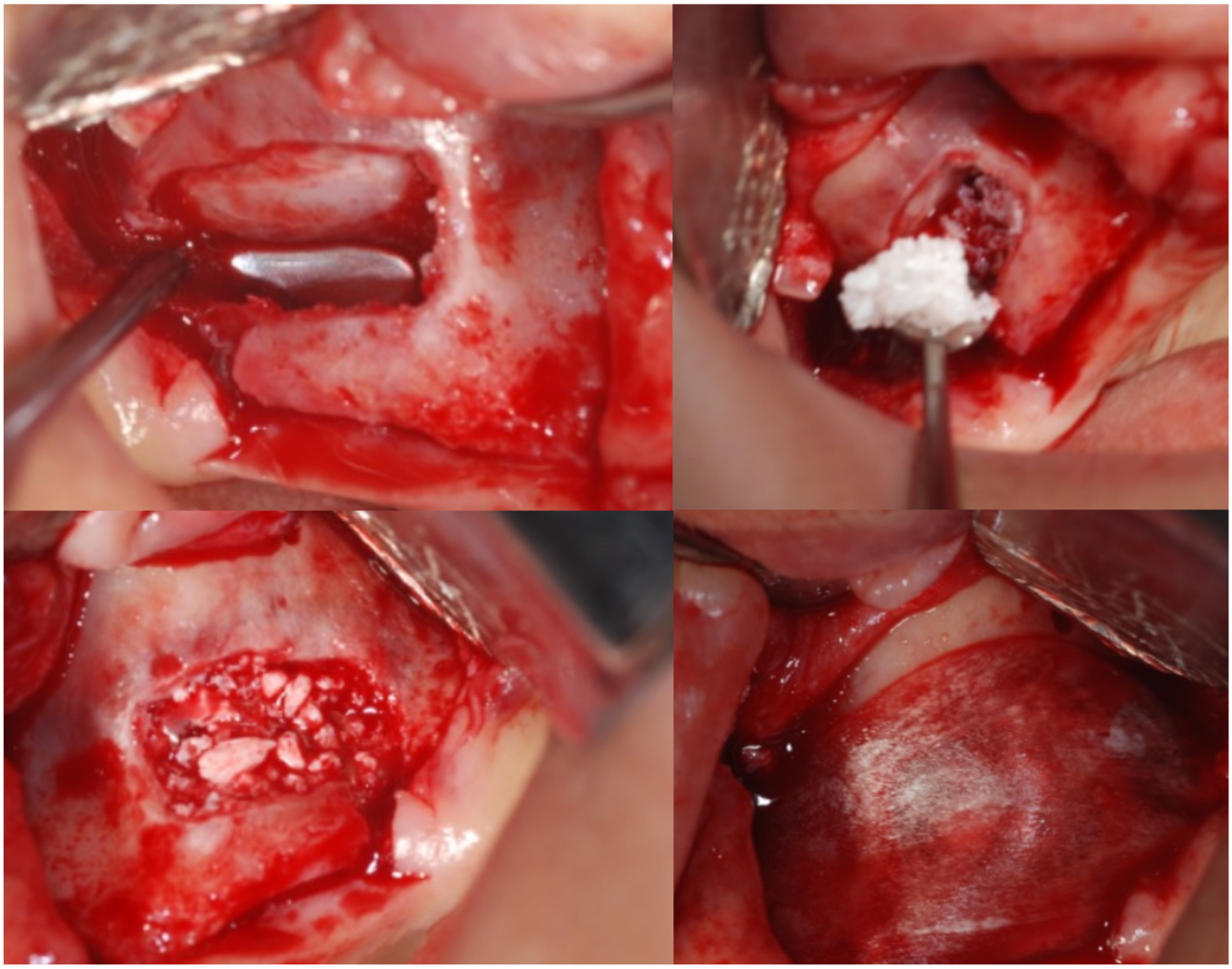

Figure 1 – Clinical images of the surgical procedure

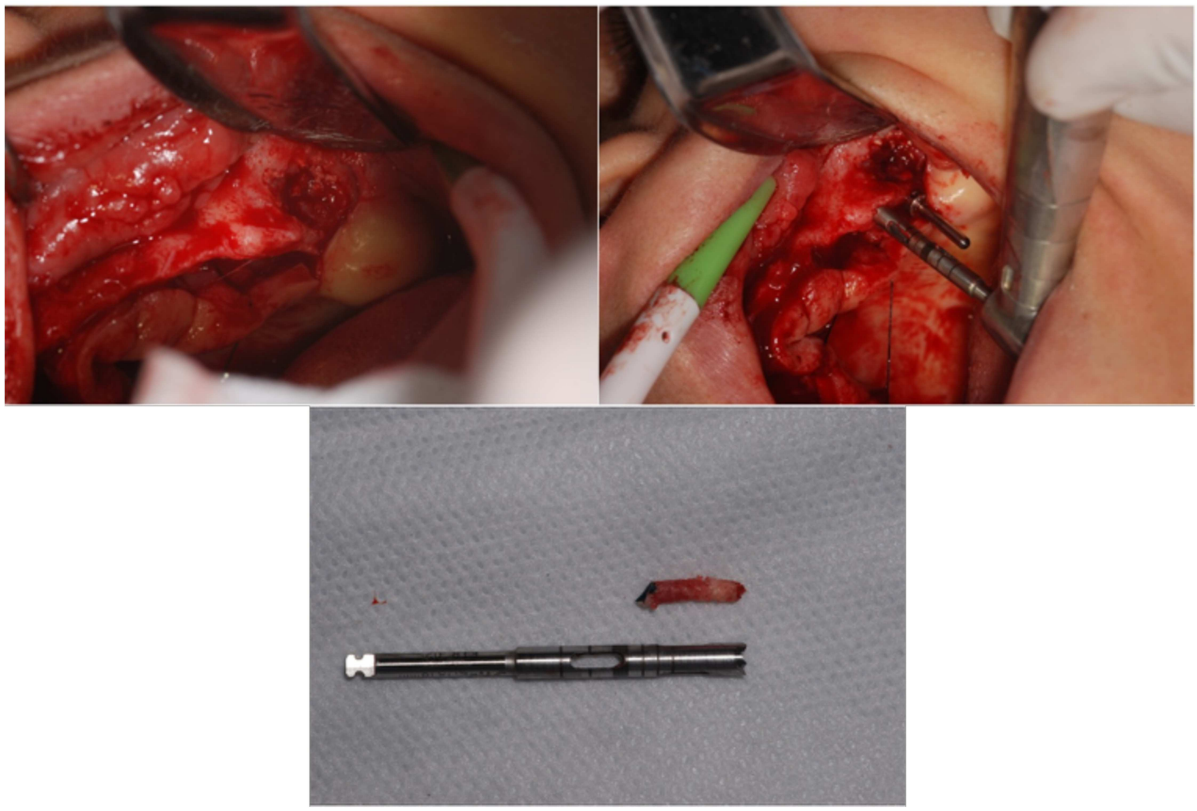

Figure 2 – Clinical images of the Biopsy retrieval

3.3 Capítulo 3

Artigo será submetido no periódico *Revista de Odontologia da UNESP*

Avaliação histológica e histomorfométrica de diferentes biomateriais e coágulo sanguíneo em cirurgias de elevação do seio maxilar : estudo caso-controle

Histologic anda Histomorphometric analysis of maxillary sinuses grafted with different osteoconductive bone substitutes and blood clot. A case-control study.

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RESUMO

INTRODUÇÃO: Quando a altura do osso alveolar residual é insuficiente na região posterior da maxila, a elevação do assoalho do seio maxilar visando viabilizar a instalação de implantes dentários é um procedimento indicado. O enxerto autógeno (ABG) de regiões intra ou extra-oral é considerado o padrão ouro para esse procedimento. Novas opções de substitutos ósseos vêm surgindo, como o Straumann® BoneCeramic(BCP) 100% sintética, enxertos xenógenos como o BioOss, além de técnicas sem nenhuma material de enxerto ósseo. OBJETIVO: Avaliar e comparar histologicamente e histomorfometriamente, o comportamento de dois substitutos ósseos e apenas o coágulo sanguíneo em cirurgias de elevação do assoalho do seio maxilar. MATERIAL E MÉTODO: Trinta pacientes saudáveis e parcialmente desdentados na região posterior da maxila foram submetidos à elevação do assoalho do seio maxilar previamente a instalação de implantes dentários osseointegráveis, sendo destes, 10 com BCP, 10 com BO e 10 com coágulo. Após 6 meses, as amostras foram coletadas por uma trefina e avaliadas histologicamente e histomorfometricamente. RESULTADOS: Todos os implantes osseointegráveis apresentaram boa estabilidade primária. A análise histológica demonstrou tecido ósseo neoformado em todos os grupos, além de um íntimo contato do tecido ósseo mineralizado recém formado com as partículas do BCP e BO. A análise histomorfométrica demonstrou tecido ósseo neoformado com 31.8 ± 6.5% no grupo Bio-Oss; 27.2 ± 10.1 no grupo BoneCeramic; e 28.3 ± 9.5 no grupo coágulo.. CONCLUSÃO: os três grupos avaliados demonstraram tecido ósseo

neoformado estatisticamente similares, As técnicas utilizadas demonstraram serem indicados para procedimentos de elevação de seio maxilar.

Descritores: Elevação do assoalho do seio maxilar; transplante ósseo; teste de materiais.

ABSTRACT

INTRODUCTION: Sinus lift to permit insertion of implants when alveolar residual bone height is insufficient may be considered an effective procedure. The use of autogenous bone from intraoral or extraoral sources is considered as the gold standard for this procedure. New techniques have been sought and investigated. OBJECTIVE: This investigation was designed to compare the histomorphometric and histologic results from sinus floor augmentation with anorganic bovine bone (ABB) , a biphasic calcium phosphate, Straumann Bone Ceramic (BCP), and graftless technique METODS AND MATERIALS: 30 maxillary sinuses were treated in 30 patients. Lateral sinus augmentation was used, with grafting using either DBB (10 sinuses) or HA/TCP), (10 sinuses) and immediate implant with graftless technique (10 sinuses) . After 180 days of healing biopsies taken for histological and histomorphometric analyses.

Results: Histology showed close contact between new bone and graft particles for both grafted groups. No significant differences in the amount of mineralized bone 31.84 ± 6.36 % in the DBB group , 27.11 ± 10.16 % in the HA/TCP group, and 26.92 ± 10.05 % in the graftless group . The percentage of residual graft material was not different between the DBB (16.05 ± 6.71 %) and HA/TCP (16.84 ± 4.99 %) groups.

CONCLUSION: All the groups produced similar amounts of newly formed bone, with similar histologic appearance, indicating that the three techniques are suitable for sinus augmentation for the placement of dental implants.

Descriptors: Maxillary sinus floor augmentation; bone transplantation; materials testing.

1. INTRODUÇÃO

A elevação do assoalho do seio maxilar é um procedimento cirúrgico previsível e que permite a instalação de implantes dentários quando se utiliza enxertos ou materiais, no preenchimento do espaço entre o rebordo alveolar e a nova posição da membrana sinusal. [1]

O enxerto ósseo pode ser classificado em autógeno(quando o doador e o receptor são o mesmo indivíduo, ou seja, é removido do próprio paciente); homógenos (enxerto proveniente de um doador que pertença à mesma espécie do receptor); heterógeno (obtidos de um doador de espécie diferente do receptor); e sintéticos (produzido em laboratório). [1,2]

O enxerto ósseo autógeno tem se mostrado a melhor alternativa para as cirurgias de levantamento do assolho do seio maxilar, sendo considerado o padrão ouro. [1,2,3] Os ótimos resultados com esse tipo de enxerto são explicados pela ausência de antigenicidade, pequena reação inflamatória, fácil revascularização, e potencial de osseoindução, osteogênese e osseocondução. [1,2,3] Apesar dessas vantagens, apresenta algumas desvantagens como: maior morbidade, mair tempo cirúrgico; maiores riscos de complicações pós-operatórias; quantidade limitada; reabsorção imprevisível; formato ou contorno

diferentes do sítio receptor. Estes fatores contribuem com a necessidade de se desenvolver algum tipo de material, que quando empregado, evite a necessidade de enxerto autógeno. [1,2,3,4]

Dentre os biomateriais que são atualmente mais utilizados, além do enxerto ósseo autólogo, podemos citar dois biomateriais aloplásticos – cerâmicos comercialmente chamados de Boneceramic (Straumann, Suíça) . O Boneceramic é um biomaterial sintético que consiste de 60% hidroxiapatita e 40% de Beta Tricálcio Fosfato, sendo que seus grânulos possuem 90% de porosidade para a intercomunicação e o tamanho de suas partículas varia entre 500 e 1000μm, com propriedades osteocondutivas [2,3,4]. Estudos prévios demonstraram que o HA+β-TCP atua como excelente osteocondutor, quando instalado em seios maxilares [2,3,4,5,6]. Podemos ainda citar um biomaterial substituto ósseo xenógeno, de origem bovina. O Bio-Oss (Geistlisch, Suíça). O Bio-Oss (BO) é uma hidroxiapatita natural constituída de matriz de osso bovino anorgânico e cristais de carbonato de cálcio. Não causa reação imunológica e é altamente osteocondutivo, fato que permite reparação óssea e pode ser usado em combinação com enxertos autógenos ou isoladamente [4,5,6.] Embora diversos estudos com esses biomateriais utilizados de forma isolada estejam presentes na literatura, ensaios clínicos randomizados, abordando a remodelação das áreas enxertadas de forma histomorfométrica e radiográfica, além de avaliar os índices de sucesso dos implantes instalados sobre essas áreas são inexistentes até o momento. [4,5,6,7]

Além disso, em alguns casos específicos, quando o remanescente ósseo da maxila posterior é insuficiente para instalação de implantes de comprimento

adequando, mas suficiente para estabilização cirúrgica destes, a instalação de implantes é feita simultaneamente à elevação da membrana do seio maxilar. [8,9,10,11] O espaço dentro do seio é mantido pela presença do implante e preenchido por coágulo sanguíneo, que seria responsável pela condução da formação óssea. [8,9,10,11] Desta forma, esta técnica traz vantagens como a diminuição dos custos, pela não necessidade de colocação de biomateriais e redução do número de cirurgias, pois o implante e a elevação do seio maxilar são feitas em uma mesma etapa. [8,9,10,11] Por outro lado, a literatura ainda é pobre em evidenciar os reais benefícios clínicos e biológicos dessa técnica.

Considerando os dados da literatura científica, e, sobretudo diante da necessidade de se obter um material substituto ósseo que proporcione um resultado tão bom quanto o proporcionado pelo enxerto autógeno, o presente estudo teve como objetivo avaliar e comparar, histologicamente e histomorfométricamente o comportamento de dois substitutos ósseos , BCP e BO, e do coágulo sanguíneo, quando utilizados em cirurgias de levantamento do assoalho do seio maxilar previamente a instalação de implantes dentários osseointegráveis.

2. MATERIAIS E MÉTODOS

O estudo foi desenvolvido de acordo com as normas do Comitê de Ética em pesquisa da Universidade Federal de Uberlândia (UFU), parecer de aprovação protocolo 1.042.781. Todos os pacientes participantes do projeto aceitaram e assinaram um termo de consentimento livre e esclarecido, previamente a realização das cirurgias de levantamento do assoalho do seio

maxilar, todas elas com indicação clínica baseada nos protocolos atuais da implantodontia.

Foram selecionados 10 pacientes para cada grupo, que foram submetidos a cirurgias de levantamento do assoalho do seio maxilar, com enxertos ósseos do tipo 100% material sintético - Straumann® BoneCeramic (BCP), Suíça, (10 pacientes) , 100% osso xenógeno BioOss (10 pacientes), e com implante imediato e coágulo sanguíneo (10 pacientes). Após 6 meses do tempo de integração do enxerto/material, durante a fase cirúrgica de instalação de implantes osseointegráveis, foram coletadas amostras com uma broca trefina (2 mm de diâmetro interno e 10 mm de comprimento) em direção vertical no local da instalação de implantes.). Nos seios maxilares com altura óssea remanescente entre 5 e 7 mm, em que foram feitos a elevação da membrana do seio maxilar e instalação imediata de implantes, sem utilização de biomaterial, foi realizado a coleta com trefina 6 meses pós cirurgia no momento da reabertura, em direção horizontal entre os dois implantes instalados.

As amostras coletadas no interior da trefina foram coradas pelo método pela Hematoxilina de Harris e Eosina aquosa a 1% (HE) para avaliação microscópica, que se deu com auxílio de microscópio óptico (CARL ZEISS, Germany). A análise microscópica qualitativa e comparativa entre os grupos, obedeceu os parâmetros microscópicos: presença de áreas de necrose ou reação inflamatória; presença de área de deposição óssea e incorporação das partículas do biomaterial ao osso. A análise histomorfométrica foi realizada utilizando o software QuPath . A região de interesse foi definida excluindo o osso residual. A porcentagem de osso neoformado (área de osso neoformado / área

total) e a área de partículas residuais de material de enxerto (enxerto residual / área total) nas regiões de interesse foram medidas em magnificação x 100. Todas as análises foram realizadas pelo mesmo avaliador , sem saber qual espécime de grupo era avaliada.

A análise estatística foi realizada utilizando o GraphPad Prism 6 (San Diego, CA, USA) considerando o nível de significância de α=0.05. Os resultados foram expressos pela media com desvio padrão. O teste de normalidade Shapiro-Wilk foi realizado ($p < .05$). Os dados foram analizados pelos testes ANOVA e Tukey HSD .

3. RESULTADOS

Todos os pacientes que foram incluídos no trabalho apresentaram um processo de cicatrização normal e satisfatório após as cirurgias de levantamento do assoalho do seio maxilar e as de colocação dos implantes dentários osseointegráveis. Nenhum processo inflamatório ou infeccioso foi observado. No momento da reabertura para coleta das amostras, a área enxertada apresentou-se bem vascularizada, com uma dureza e resistência semelhante ao tecido ósseo maxilar. Todos os implantes osseointegráveis inseridos apresentaram uma boa estabilidade primária.

Histologicamente, osso neoformado e partículas do biomaterial (exceto para o grupo coágulo) foram encontrados em todos os grupos. Nenhum reação inflamatória e necrose foram encontrados. Partículas de biomaterial foram facilmente identifcadas pelo seu formato geométrico. Mais osteoclastos foram encontrados nos grupos enxertados, tendo sido notado um íntimo contato do

tecido ósseo mineralizado recém formado com as partículas dos biomateriais (Figura 01).

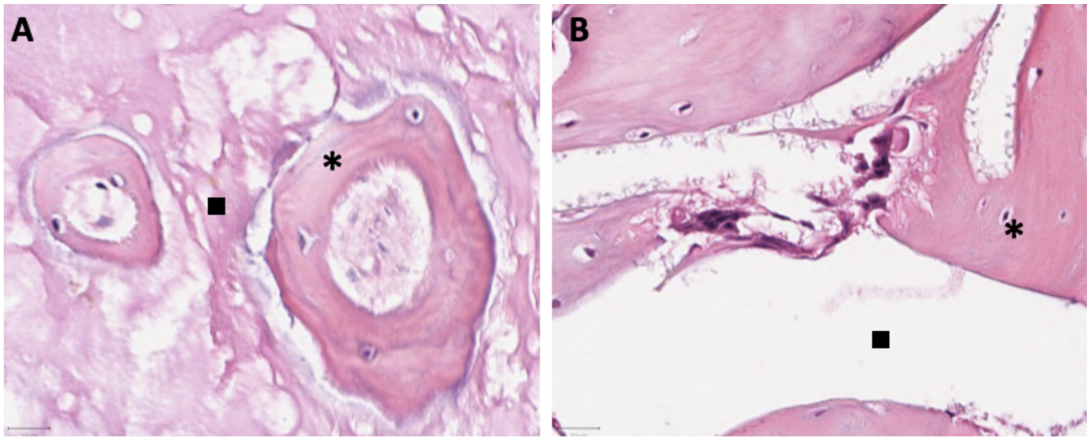

Figura 1 - (A) Grupo Bio-Oss e (B) BoneCeramic (aumento orirginal x40): osso neoformado (*) ao redor das particulas de biomaterial (■).

O percentual de osso neoformado foi de 31.8 ± 6.5% no grupo Bio-Oss; 27.2 ± 10.1 no grupo BoneCeramic; e 28.3 ± 9.5 no grupo coágulo. Não havendo diferença estatisticamente significativa entre os grupos (*P*=0.09). O percentual de material residual de enxerto foi de 16.0 ± 6.9 no grupo Bio-Oss e 16.8 ± 5.1 no grupo BoneCeramic , não havendo diferença estatística (*P*=0.1) (Tabela 01).

	Osso neoformado (%)	Partículas de biomaterial (%)
Bio-Oss	31.8 ± 6.5	16.0 ± 6.9

BoneCeramic	27.2 ± 10.1	16.8 ± 5.1
Coágulo	28.3 ± 9.5	NA

Tabela 01 – Valores e desvio padrão (%) da análise histomorfométrica.

4. DISCUSSÃO

Algumas condições anatômicas podem limitar a reabilitação oral com implantes na região posterior da maxila. Dentre essas condições, pode-se destacar a pneumatização do seio maxilar. [3,6] Nesta circunstância, alguns procedimentos de elevação do seio maxilar, visando correção desta deficiência e a possibilidade de colocação de implantes osseointegráveis na região, são necessários, sendo inclusive muito bem descritos há muito tempo na literatura. [1,2]

Devido às suas propriedades osteogênicas, osteoindutoras e osteocondutoras o uso do enxerto ósseo autógeno no seio maxilar, é tido como uma técnica cirúrgica segura, confiável e com excelentes índices de sucesso, comprovados por estudos com controles superiores há 10 anos. [6,7,8] Porém, devido à necessidade de um sítio doador, e as suas desvantagens, como morbidade, gradualmente outros biomateriais vêm sendo usados, apresentando índices de sucesso convincentes. Muitos são os substitutos ósseos utilizados atualmente e apresentam resultados muito semelhantes ao enxerto autógeno, inclusive em períodos superiores há 10 anos. [4,5,9,10,11] Os materiais de enxertia, utilizados neste trabalho foram o BCP, um substituto ósseo 100% sintético, cuja

composição é basicamente uma mistura de hidroxiapatita e fosfato de cálcio, e o BO, um substituto ósseo de origem bovina. Segundo os fabricantes, ambos biomateriais possuem uma reabsorção gradativa, elevado grau de porosidade, são biocompatíveis, osteocondutor e permitem uma estrutura de suporte para adesão do tecido ósseo durante o processo de osteogênese. [4,5,9]

Nesse contexto o presente estudo avaliou histologicamente e clinicamente o comportamento do BCP , BO, e coágulo quando utilizados em cirurgias de levantamento do assoalho do seio maxilar. Na avaliação clinica, nossos resultados mostraram-se semelhantes ao achados de outros trabalho [11,12,13,14,15,16] que observaram integração dos biomateriais no osso maxilar original, e altura óssea adequada, na área enxertada para sustentar implantes dentários, com ausência de processo inflamatório ou infeccioso, e com a área receptora bem vascularizada, com uma dureza e resistência semelhante ao tecido ósseo maxilar. Além disso, todos os implantes osseointegráveis inseridos apresentaram também uma boa estabilidade primária.

Quando comparado o comportamento entre BCP, BO e coágulo nossos resultados demonstram uma grande similaridade histológica do tecido ósseo formado. Caracterizando pela presença de trabéculas ósseas bem estruturadas e viáveis, com uma matriz óssea homogênea e grande quantidade de osteócitos viáveis no seu interior, além dos espaços medulares estarem preenchidos com tecido conjuntivo frouxo. Resultados similares ao demonstrado em cirurgias com enxerto ósseo autógeno, tido como o padrão ouro para esse tipo de procedimento [18,19,20]

Analisando a proximidade das partículas dos dois biomateriais , BCP e BO, com o tecido ósseo mineralizado recém formado, foi observado um íntimo contato entre os mesmos, de modo que as partículas estavam rodeadas por tecido ósseo viável. Esses resultados vão de acordo com os encontrados por Froum et al.[21] (2008), Cordaro et al.[4] (2008), Frenken et al.[5] (2010), e Daculsi et al. [20] (2003) o que, segundo os mesmos, demonstra histologicamente as propriedades osteocondutoras dos biomateriais.

No presente estudo, ambos os biomateriais demonstraram estatisticamente o mesmo percentual de particulas do material de enxerto, grupo BO 16.05 ± 6.71 % e grupo BCP 16.84 ± 4.99 %. Demonstrando assim uma grande similiaridade nesse quesito, sendo o seu impacto clínico ainda desconhecido .[17,22,23]

Histomorfometricamente foi demonstrado um percentual de osso neoformado similar entre os três grupos. 31.84 ± 6.36 % no grupo BO, 27.11 ± 10.16 % no grupo BCP e 26.92 ± 10.05 % no grupo coágulo. Tal resultado vai contra o demonstrado por Sohn [24] et al (2010) , que demonstraram , em um estudo animal, uma maior área de osso neoformado no grupo com coágulo quando comparado ao grupo BO. Por outro lado, nossos achados quantitativos de osso neoformado, similar em todos os grupos avaliados no presente trabalho, vão de encontro com diversos autores[13,15,25,26] Tais achados sugerem uma neoformação óssea adequada para reabilitação de regiões edêntulas maxilares, com a possibilidade da não utilização de material de enxerto ósseo em casos com altura óssea residual entre 4 e 7 mm.

5. CONCLUSÃO

Todos os grupos avaliados no presente trabalho demonstraram uma neformação óssea adequada para a reabilitação de áreas edêntulas posterior maxilar. Ambos os biomateriais foram similares em todos os parâmetros avaliados, demonstrando seu potencial osteocondutor. O coágulo sanguíneo, apresentou a mesma taxa de osso neoformado comparado com os biomateriais, demonstrando ser uma técnica promissora, e quando indicada, com a vantagem de um menor custo e menor tempo de tratamento. Novos trabalhos, com maior número de pacientes e mais tempo de acompanhamento são necessárias, para que se possa indicar com segurança tal técnica.

Conflito de interesses: Os autores declaram não haver confilto de interesses.

REFERÊNCIAS

1- Fugazzotto PA, Vlassis J. Long-term success of sinus augmentation using various surgical approaches and grafting materials. Int J Maxillofac Implants. 1998; 13: 52-8.

2- Furst G, Gruber R, Tangl S, Zechner W, Haas R, Maila Th.G, Sanroman F, Watzek G. Sinus grafting with autogenous plated-rich plasma and bovine hydorxiapatite. A histomorphometric study in minipigs. Clin Oral Implants Res. 2003; 14: 500-8. https://doi.org/10.1034/j.1600-0501.2003.00859.x

3- John HD, Wenz B. Histomorphometric analysis of natural bone mineral for maxillary sinus augmentation. Int J Oral Maxillofac Implants. 2004; 19: 199-207.

4- Cordaro L, Bosshardt DD, Palattella P, Rao W, Serino G, Chiapasco M. Maxillary sinus grafting with Bio-Oss or Straumann Bone Ceramic: histomorphometric results from a randomized controlled multicenter clinical trial. Clin Oral Implants Res. 2008; 19: 796-803. https://doi.org/10.1111/j.1600-0501.2008.01565.x

5- Frenken JWFH, Bouwman WF, Bravenboer N, Zijderveld SA, Schulten EAJM, Ten Bruggenkate CM. The use of Straumann® Bone Ceramic in a maxillary sinus floor elevation procedure: a clinical, radiological, histological and histomorphometric evaluation with a 6-month healing period. Clin Oral Implants Res. 2010; 21: 201-8. https://doi.org/10.1111/j.1600-0501.2009.01821.x

6- Van Der Bergh JP, Ten Bruggenkate CM, Dish FJ, Tuinzing DB. Anatomical aspects of sinus floor elevations. Clin. Oral Impl. Res. 2000; 11: 256-65.
https://doi.org/10.1034/j.1600-0501.2000.011003256.x

7- Boyne PJ, James RA. Grafting of the maxillary sinus floor with autogenous marrow and bone. J. Oral Surg. 1980; 38: 613-16.

8- Lundgren S, Andersson S, Sennerby L. Spontaneous bone formation in the maxillary sinus after removal of a cyst: coincidental or expected reaction? Clin Implant Dent Relat Res 2003; 5:78-81. https://doi.org/10.1111/j.1708-8208.2003.tb00187.x

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. https://doi.org/10.1111/j.1708-8208.2004.tb00224.x

10- Lundgren S, Cricchio G, Palma VC, Salata LA, Sennerby L.Sinus membrane elevation and simultaneous insertion of dental implants: a new surgical technique in maxillary sinus floor augmentation. Periodontol 2008; 47:193-205.
https://doi.org/10.1111/j.1600-0757.2008.00264.x

11- Palma VC, Magro-Filho O, de Oliveria JA, Lundgren S, Salata LA, Sennerby L. Bone reformation and implant integration follow- ing maxillary sinus membrane elevation: an experimental study in primates. Clin Implant Dent Relat Res 2006:8:11-24
https://doi.org/10.2310/j.6480.2005.00026.x

12- Thor A, Sennerby L, Hirsch JM, Rasmusson L. Bone formation at the maxillary sinus floor following simultaneous elevation of the mucosal lining and implant installation without graft material: an evaluation of 20 patients treated with 44 Astra Tech implants. J Oral Maxillofac Surg 2007: 65:64-72. https://doi.org/10.1016/j.joms.2006.10.047

13- Zenóbio EG, Mendes LD, Bustamante RP, Vidigal BC, Favato MN, Manzi FR, Cosso MG,. Effect of amount of biomaterial used for maxillary sinus lift on volume maintenance of grafts. J Clin Exp Dent. 2020

14 - 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 Surg. 2018 https://doi.org/10.1016/j.ijom.2017.05.001

15- Zahedpasha A, Ghassemi A, Bijani A, Haghanifar S, Majidi MS, Ghorbani ZM. Comparison of Bone Formation After Sinus Membrane Lifting Without Graft or Using Bone Substitute "Histologic and Radiographic Evaluation". J Oral Maxillofac Surg. 2021 https://doi.org/10.1016/j.joms.2020.12.040

16- Chiapasco M, Zaniboni M, Rimondini L. Dental implants placed in grafted maxillary sinuses: a retrospective analysis of clinical outcome according to the initial clinical situation and a proposal of defect classification. Clin Oral Implants Res. 2008 Apr;19(4):416-28 https://doi.org/10.1111/j.1600-0501.2007.01489.x

17- Artzi Z, Kozlovsky A, Nemcovsky CE, Weinreb M. The amount of newly formed bone in sinus grafting procedures depends on tissue depth as well

as the type and residual amount of the grafted material. J Clin Periodontol. 2005;32:193-199.
https://doi.org/10.1111/j.1600-051X.2005.00656.x

18- Becker W, Urist M, Becker BE, Jackson W, Perry DA, Bartold M, Vincenzzi G, De Georges D, Niederwang M. Clinical and histologic observations of sites implanted with intraoral autologous bone grafts or allografts: 15 human case reports. J Periodontol. 1996;67: 1025-33. https://doi.org/10.1902/jop.1996.67.10.1025

19- Buser D, Hoffmann B, Bernard JP, Lussi A, Mettler D, Schenk RK. Evaluation of filling materials in membrane-protected bone defects. A comparative histomorphometric study in the mandible of miniature pigs. Clin Oral Implants Res. 1998; 9: 137-50. https://doi.org/10.1034/j.1600-0501.1998.090301.x

20- Daculsi G, Laboux O, Malard O, Weiss P. Current state of the art of biphasic calcium phosphate bioceramics. Journal of Materials Science: Materials in Medicine. 2003; 14: 195-200. https://doi.org/10.1023/A:1022842404495

21- Froum SJ, Wallace SS, Cho SC, Elian N, Tarnow DP. Histomorphometric Comparison of a Biphasic Bone Ceramic to Anorganic Bovine Bone for Sinus Augmentation: 6- to 8-Month Postsurgical Assessment of Vital Bone Formation. A Pilot Study. Int J Periodontics Restorative Den. 2008; 28: 273-81.

22- Artzi Z, Givol N, Rohrer MD, Nemcovsky CE, Prasad HS, Tal H. Qualitative and quantitative expression of bovine bone mineral in experimental bone defects. Part 2: morphometric analysis. J Periodontol.

2003;74:1159-1160.
https://doi.org/10.1902/jop.2003.74.8.1153

23- Wiltfang J, Merten HA, Schlegel KA, et al. Degradation characteristics of alpha and beta tricalciumphosphate (TCP) in minipigs. J Biomed Mater Res. 2002;63:115-121.
https://doi.org/10.1002/jbm.10084

24- Sohn DS, Kim WS, An KM, Song KJ, Lee JM, Mun YS. Comparative histomorphometric analysis of maxillary sinus augmentation with and without bone grafting in rabbit. Implant Dent. 2010 Jun;19(3):259-70
https://doi.org/10.1097/ID.0b013e3181df1406

25- Sartori S, Silvestri M, Forni F, Icaro Cornaglia A, Tesei P, Cattaneo V. Ten-year follow-up in a maxillary sinus augmentation using anorganic bovine bone (Bio-Oss): a case report with histomorphometric evaluation. Clin Oral Implants Res. 2003;14: 369-372.
https://doi.org/10.1034/j.1600-0501.2003.140316.x

26- Simunek A, Kopecka D, Somanathan RV, Pilathadka S, Brazda T. Deproteinized bovine bone versus beta-tricalcium phosphate in sinus augmentation surgery: a comparative histologic and histomorphometric study. Int J Oral Maxillofac Implants. 2008; 23:935-942.

4. CONCLUSÕES

Com base nas metodologias utilizada e nos resultados obtidos destes estudos, pode-se concluir que:

- Atualmente o procedimento de elevação do assoalho do seio maxilar pode ser considerado reprodutível. Porém, a técnica utilizada bem como o material substituto ósseo escolhido, devem ser corretamente indicados.
- A técnica de levantamento do seio maxilar sem material de enxerto e com instalação imediata de implantes, demonstrou, tomograficamente, considerável aumento em altura e volume ósseos em um período de 6 meses. Foi observada alto índice de sobrevivência dos implantes. O tempo, custo e morbidade do tratamento diminuíram consideravelmente em virtude da não necessidade de material de enxerto e da instalação dos implantes simultânea à cirurgia de levantamento do seio maxilar.
- A análise histomorfométrica de dois dos principais biomateriais substitutos ósseos utilizados atualmente, BioOss e BoneCeramic, demonstrou uma quantidade de osso neoformado adequada para reabilitação com implantes dentários osseointegráveis.
- Em nossos estudos não encontramos fatores que pudessem indicar uma vantagem de um biomaterial em relação ao outro. Ambos os biomateriais, demonstraram o mesmo percentual de osso neoformado , bem como características histológicas similares ao osso autógeno, tido como o padrão ouro na literatura.
- A análise histomorfométrica do osso neoformado a partir do coágulo sanguíneo, não demonstrou diferença significativa em relação aos biomateriais. Somado ao resultado tomográfico, esses resultados validam a utilização dessa técnica, em situações de rebordo ósseo remanescente maior ou igual a 5 mm.

5.REFERÊNCIAS

Cordaro L, Bosshardt DD, Palattella P, Rao W, Serino G, Chiapasco M. Maxillary sinus grafting with Bio-Oss or Straumann Bone Ceramic: histomorphometric results from a randomized controlled multicenter clinical trial. Clin Oral Implants Res. 2008 Aug;19(8):796-803. https://doi.org/10.1111/j.1600-0501.2008.01565.x

Albert A, Leemrijse T, Druez V, Delloye C, Cornu O. Are bone autografts still necessary in 2006? A three-year retrospective study of bone grafting. Acta Orthop Belg. 2006 Dec;72(6):734-40.

Buser D, Dula K, Belser U, Hirt HP, Berthold H. Localized ridge augmentation using guided bone regeneration. 1. Surgical procedure in the maxilla. Int J Periodontics Restorative Dent. 1993;13(1):29-45.

Contar CM, Sarot JR, Bordini J, Jr., Galvao GH, Nicolau GV, Machado MA. Maxillary ridge augmentation with fresh-frozen bone allografts. J Oral Maxillofac Surg. 2009 Jun;67(6):1280-5. https://doi.org/10.1016/j.joms.2008.11.010

Williams KR, Blayney AW. Tissue response of several polymeric materials implanted in the rat middle ear. Biomaterials. 1987 Jul;8(4):254-8. https://doi.org/10.1016/0142-9612(87)90112-8

Amrani S, Anastassov GE, Montazem AH. Mandibular ramus/coronoid process grafts in maxillofacial reconstructive surgery. J Oral Maxillofac Surg. Mar;68(3):641-6. https://doi.org/10.1016/j.joms.2009.09.100

Pinholt EM, Bang G, Haanaes HR. Alveolar ridge augmentation in rats by Bio-Oss. Scand J Dent Res. 1991 Apr;99(2):154-61. https://doi.org/10.1111/j.1600-0722.1991.tb01878.x

Piero B, Mario V, Niccolo N, Marco F. Implant placement in combination with sinus membrane elevation without biomaterials: a 1-year study on 15 patients. Clin Implant Dent Relat Res. 2012Oct;14(5):682-9. https://doi.org/10.1111/j.1708-8208.2010.00318.x

Spin-Neto R, Stavropoulos A, Dias Pereira LA, Marcantonio E, Jr., Wenzel A. Fate of autologous and fresh-frozen allogeneic block bone grafts used for ridge augmentation. A CBCT-based analysis. Clin Oral Implants Res. 2013 Feb;24(2):167-73. https://doi.org/10.1111/j.1600-0501.2011.02324.x