Alveolar Ridge Preservation Using a Bovine-derived Bone Graft in Association with Titanium Foil – A Prospective Case Series

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Abstract

Aims: To estimate the change in the alveolar ridge by means of a new alveolar ridge preservation (ARP) approach, using an anodized titanium foil (Tseal) associated with a bovine bone graft (BBG) by cone-beam computerized tomography.

Materials and Methods: Sixteen patients, each presenting one hopeless tooth, were selected and these teeth were carefully extracted. The alveolar socket was filled with BBG and the Tseal was trimmed and adapted to the bone crest. The primary outcome variable was the change in the alveolar dimension (AD) measurements between baseline (T1) and 6 months (T2) 1mm below the palatal bone.

Results: Imaging assessment of AD demonstrated a decreased value in all subjects. The absolute rate and percentage of absorption between T1 and T2 time point showed statistically significant differences. The mean AD varied from 9.88 ± 2.04 mm (T1) to 8.85 ± 1.92 mm (T2). On average, this ARP procedure maintained 89.55% ± 6.11% of the distance of between the buccal and palatal wall. No differences were observed between the maxilla and mandible ($p>0.05$).

Conclusion: The application of a bovine bone graft covered with Tseal resulted in clinically important horizontal preservation of the alveolar ridge at 6 months after extraction

Keywords: Bone augmentation, bone regeneration, titanium membrane, bone graft.

Introduction

Tooth extraction is a very common dental procedure, after which the alveolar bone healing is characterized by a rapid physiological process of bone remodeling and resorption (Amler *et al.,* 1969; Cardaropoli *et al.,* 2003; Araujo *et al.,* 2003; Araujo *et al.,* 2009; Ten *et al.,* 2011; Schropp *et al.,* 2003). The major changes that occur in an extraction site take place during the first 12 months after extraction, with 2/3 of these changes occurring in the first three months. The alveolar ridge thickness is reportedly reduced by 50% during this period, which could correspond to 5 to 7 mm of alveolar bone. In addition, several clinical studies have shown that the socket healing process occurs more rapidly to a greater extent on the buccal aspect than on the palatal/lingual side and a greater decrease in alveolar bone occurs in the molar area (Araujo *et al.*, 2005; Van Der Weijden *et al.*, 2009; Tan *et al.,* 2012). A systematic review, evaluating the change in the alveolar ridge during the first six months after tooth extraction and reported a mean reduction of 3.8 mm and 1.24 mm in width and in height, respectively (Tan *et al.,* 2012). Thus, these changes could alter the esthetic results of the final restoration, either with traditional rehabilitation or implant placement. Therefore, with the purpose of minimizing these changes, alveolar ridge preservation (ARP) techniques have become popular tools and important procedures in guided bone regeneration (GBR) procedures.

The goal of the ARP procedure is to keep an ideal ridge shape, and to prevent more extensive collapse of the alveolar ridge, thereby preserving adequate bone

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contour to promote correct three-dimensional implant placement and therefore, further oral rehabilitation (Darby *et al.,* 2008). Fortunately, innovations in surgical techniques and advances in the biological understanding of bone regeneration techniques have led to improved implant procedures and increased predictability in the reconstruction of alveolar ridge defects (Pelegrine *et al.,* 2018). Indeed, several systematic reviews have confirmed the efficacy of different ARP techniques for minimizing post-extraction dimensional changes in alveolar ridges (Ten *et al.,* 2011; Vignoletti *et al.,* 2012; Horvath *et al.,* 2013; Vittorini *et al.,* 2013, Avila-Ortiz *et al.,* 2019), which included socket grafting with autogenous bone (Bianchini *et al.,* 2009; Hanser *et al.,* 2014), demineralized freeze-dried bone allograft (DFDBA) (Becker *et al.,* 1994; Froum *et al.,* 2002; Bianchini *et al.,* 2009; Beck *et al.,* 2010; Clark *et al.,* 2018), xenografts (Araujo *et al.,* 2009; Mardas *et al.,* 2010), alloplasts (Ashman *et al.,* 2000; De Risi *et al.,* 2015), leucocyte- and platelet-rich fibrin (L-PRF) (Anwandter *et al.,* 2016; Temmerman *et al.,* 2016; Clark *et al.,* 2018). In addition, different guided bone regeneration (GBR) techniques, either associated with or without diverse bone grafts, have also been well documented (Mardas *et al.,* 2010; Avila *et al.,* 2014). In the majority of these ARP techniques, primary wound closure (also known as healing by primary intention) is fundamental to obtain a good outcome (Avila *et al.,* 2014). The basic idea reported for GBR procedures involves the use of an occlusive membrane that will act as a barrier to retain the blood clot, thus creating an ideal space around the bone defect, favoring the entry of bone cells without competition from other types of tissues during the healing process (Dahlin *et al.,* 1988). However, occasionally, primary wound closure, or healing by primary intention is not always possible due to anatomical and tissue conditions. Therefore, new products that can be used and perform well, even when exposed to the oral cavity, could be helpful during ARP procedures. In addition, some studies of ARP procedures have reported that ridge preservation, without primary flap closure, have shown better preservation of keratinized tissue and have resulted in less postoperative discomfort and swelling (Engler-Hamm *et al.,* 2011; Kim *et al.,* 2011).

Thus, the aim of this prospective case series analysis was to investigate the effect of alveolar ridge preservation using a bovine bone graft associated with a titanium membrane on residual alveolar ridge dimensions at 6 months post-extraction.

Materials and Methods

Subject population

Sixteen healthy subjects, 8 women and 8 men in the age-range age from 27 to 66 years (mean age 41.2 ± 11.0; IC95%: 35.2 - 47.1), who were scheduled for tooth extraction and subsequent implant placement were selected for participation in this case series analysis. These subjects each received ARP treatment at the Oral Implantology Clinic during the period between September 2016 and September 2017. The Clinical Research Ethics Committee approved the study protocol and protection of humans was clearly described and complied with national and international protection guidelines. In addition, the protective measures adopted met or exceeded the requirements of the current WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. Accordingly, the study protocol was explained to each subject, and those that agreed to participate in the study signed the term of free and informed consent. All participants were prepared for the procedures in accordance with recognized dental practice guidelines, after appropriate demographic information and medical history had been collected and recorded.

Inclusion Criteria

All subjects were in good general health and presented with at least one tooth intended for extraction and subsequent implant placement. The inclusion criteria were as follows: patients between 20 and 70 years of age; anterior (incisor and canine) or posterior (pre-molar and molar) teeth; presenting a non-significant medical history and no current use of medications that might complicate results; an enclosed extraction site (without a buccal wall defect).

Exclusion Criteria

Subjects were excluded if they had healing disorders, i.e. HIV, diabetes mellitus, bone metabolic diseases, cancer, reported a history of tobacco use, or had received radiation therapy, systemic corticosteroids, immunosuppressive agents, and/or chemotherapy within the past 6 months. Subjects that received intramuscular or intravenous bisphosphonates or who had allergies or sensitivity to alginate, latex, acrylic or collagen or were also excluded.

Surgical Preservation Procedure

All subjects were treated by one trained and experienced dental surgeon (D.M.R). All patients received local anesthesia (Mepivalem Nova DFL, Rio de Janeiro, RJ, Brazil), after which the anterior or posterior tooth was carefully extracted using a non-invasive periotome (Hu-Friedy instruments, Chicago, IL, USA). An intrasucular incision was made using a 15C scalpel blade in the adjacent tooth. Subsequently, a full thickness flap was raised adjacent to gingival margin the only and all granulation tissue was removed. The extracted tooth alveolus was filled with a bovine bone substitute (Bionnovation Bonefill

Porous Medium, Bauru, SP, Brazil). According to the manufacturer, Bonefill porous is a biphasic xenograft bone substitute that consists of bovine hydroxyapatite produced without any thermal process. The sockets were then covered with new non-resorbable anodized titanium foil (Bionnovation Titanium Seal). According to the manufacturer, Titanium seal (Tseal), a 0.04mm thick titanium foil without porosity is produced by an anodization process without any electric charges. The titanium membrane was adapted, placed so that it extended 3 mm over the buccal and lingual bone plate and the flap was then sutured with 5-0 nylon sutures (Ethicon, Johnson & Johnson, São Paulo, Brazil), leaving the Tseal (Figure 1) exposed to the oral cavity.

Post-surgical procedures

After surgery, all patients received 500mg amoxicillin (T.I.D for 7 days), 750 mg Paracetamol (T.I.D. for 3 days) and 0.12% chlorhexidine digluconate solution (Periogard, São Paulo, SP, Brazil) for mouth rinsing twice a day for 14 days. In addition, all patients were instructed to suspend tooth brushing in the area of the tooth extraction during this period. Fourteen days after surgery, the nylon sutures were removed and 21 days after surgery the titanium membrane was removed without local anesthesia. On the same day that the titanium membrane was removed, a provisional fixed prosthesis was fitted.

Cone-beam computerized tomography analysis

One week before the surgery, cone-beam computerized tomography (CBCT) was taken (T1—baseline; Figure 2 and 3) using a plastic photographic retractor (Januario *et al.,* 2008). At 6 months after surgery, a second CBCT was taken (T2—6 months postoperative, Figure 2 and 3), as previously described. A single calibrated (Kappa test > 90%) examiner evaluated the following tomographic parameters: the horizontal width measurements of the alveolar socket (HW), evaluating the distance between buccal and palatal bone plates. This measurement was always performed in the center of the alveolus (distance between the two lateral teeth), 1mm above the palatal crestal bone (Jung *et al.,* 2013) (Figure 2). All CBCT assessments were obtained with a scanner (model iCat Classic, Imaging Sciences International, LCC, Hatfield, PA, USA), using a 0.25 mm slice thickness; reconstruction interval of 0.25mm, and exposure factors of 120 KV and 36.12 mAs were used. To analyze the reproducibility of the data (intra-observer) all samples were measured twice (duplicate) and the intraclass correlation coefficient analysis was used to test the mean differences (Spin-Neto *et al.,* 2013). All files were saved in DICOM format and the Ez3D Plus software (Vatech Global, Fort Lee, NJ, USA) was used to analyze the data.

Statistical analysis

The mean HW (mm) value at baseline and 6 months post-extraction, and the mean change between time points were assessed for each subject and then averaged across subjects. The percentage of mean changes between time points was also evaluated. Shapiro-Wilk test was done in order to understand the distribution of the data. In order to detect statistically significant differences between the two time points the paired Student's t test. was used. Differences in HW measurements between teeth in the mandible and maxilla were sought by using a Student's t-test. The data presented in this study were independently analyzed by an independent statistician (H.D). The level of significance was set at 5%.

Results

Sixteen patients participated in the study during the whole study period and met all the inclusion criteria, according to the study protocol for this case series analysis. No postoperative problems were reported by any of the subjects or observed by the clinical operator during

Figure 1. Teeth were carefully extracted using a periotome. All alveolar sockets were filled with a bovine bone substitute. The sockets were then covered with a new non-resorbable anodized titanium membrane.

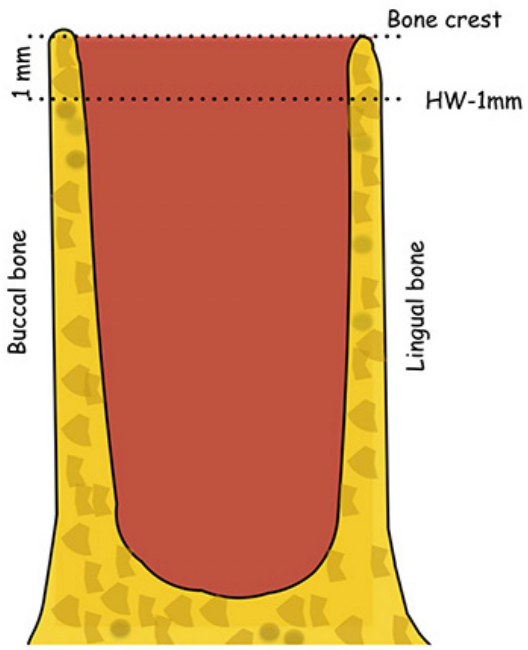

Figure 2. Schematic representation of a slice section of the cone-beam computerized tomography (CBCT) radiographic analysis at baseline and 6 months post-extraction. HW-1mm represents measurements performed below the bone crest at baseline and at 6 months post surgery.

the experimental period. All patients had the titanium foil removed at 21 days post-surgery without any pain.

Nine maxillary teeth and seven mandibular teeth were selected for this clinical study and data are presented in Table 1. The imaging assessment of HW demonstrated a decreased value in all subjects. Intergroup analysis showed statistically significant differences in the absolute rate and percentage of absorption between baseline and at the 6-month evaluation. The mean HW ranged from 9.88± 2.04 mm (baseline) to 8.85 ± 1.92 mm (6 months). This mean alteration of 1.02 ± 0.66 mm corresponded to 9.82% ± 17.29% of the distance between the buccal and the lingual alveolar wall. On average, the ARP procedure maintained 89.55% ± 6.11% of the distance from the buccal to the lingual wall after tooth extraction.

The mean values of the absolute rate and percentage of horizontal width of the alveolar socket, when the alveolar sockets were subdivided into mandible and maxilla, are presented in Table 2. The mean HW ranged between 9.34 ± 1.82 mm and 10.57 ± 2.23 at baseline to 8.08 ± 1.61 mm and 9.86 ± 1.93 mm at 6 months for the mandible and maxilla, respectively. This mean absorption of 1.30 ± 0.46 mm and 0.95 ± 0.80 were equivalent to 13% and 7%, respectively. On an average, this treatment protocol preserved 86.48% ± 4.42% of the distance from the buccal and lingual wall in the maxilla and 93.5772% ± 5.86% in the mandible at six months post-extraction. No differences were observed between the maxilla and mandible ($p>0.05$).

Discussion

ARP procedures are used to reduce bone loss and maintain gingival tissue shape after tooth extraction. Furthermore, the width of the alveolar socket is very important for later implant placement without any complication (i.e. bone fenestration), and excellent esthetics and function. This study has reported that the clinical protocol of using a bovine bone graft associated with a *Tseal* was effective in maintaining up to 86% of the alveolar width in both the maxilla and mandible.

Some clinical studies (Lekovic *et al.,* 1998; Barone *et al.,* 2008; Cardaropoli *et al.,* 2012; Jung *et al.,* 2013; Fernandes *et al.,* 2016) have observed a mean horizontal

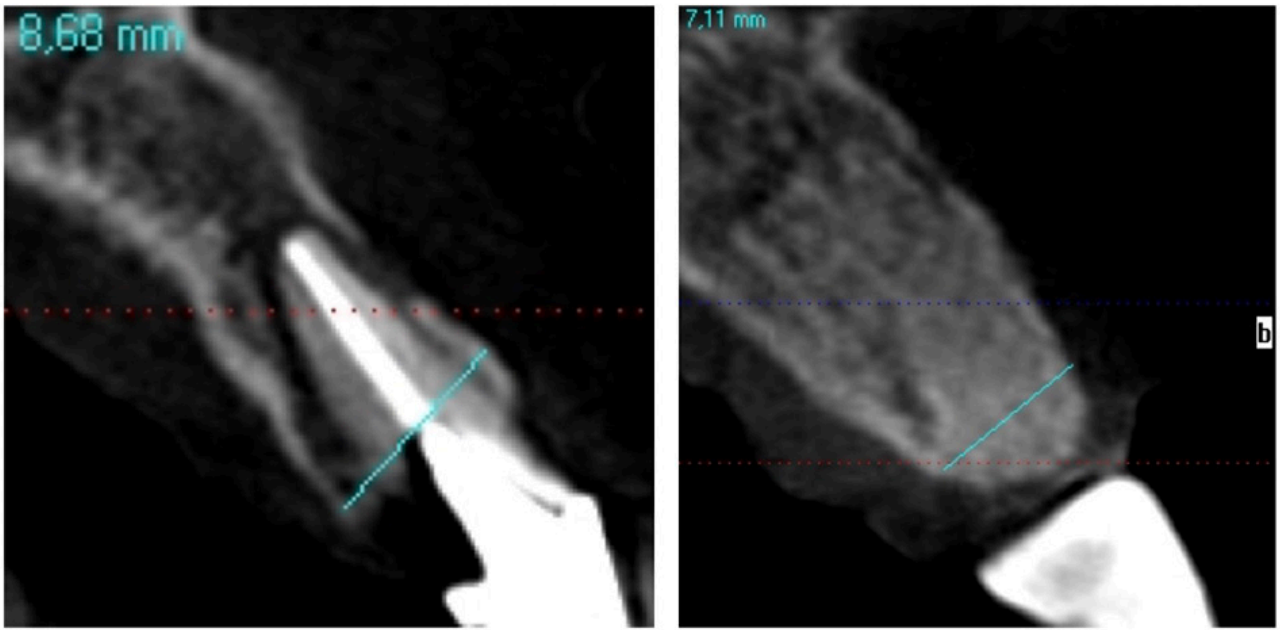

Figure 3. Cone-beam computed tomography (CBCT) slice section at baseline (left) and at 6 months post-extraction (right).

Table 1. Values of individuals' HW measurements at baseline and at 6 months post-extraction, and the change in millimeters and the percentage of change between time-points.

Subject	Teeth	Baseline	6-months	Change	% Change
#1	8	6.92	5.69	1.23	82.23
#2	8	8.68	7.11	1.57	81.91
#3	9	8.91	8.23	0.68	92.36
#4	5	7.5	6.73	0.77	89.73
#5	4	9.0	8.0	1.0	88.89
#6	11	10.0	8.0	2.0	80.00
#7	14	9.06	7.94	1.12	87.64
#8	14	13.0	11.0	2.0	84.62
#9	15	11.0	10.0	1.0	90.91
#10	24	8.5	8.4	0.1	96.91
#11	23	9.1	9.0	0.1	99.69
#12	19	7.85	7.45	0.4	94.90
#13	30	10.0	9.00	1.0	90.00
#14	30	12.6	11.2	1.4	88.89
#15	30	12.97	13.00	0.03	100.00
#16	31	13.0	11.0	2.0	84.62
Mean (±SD)		9.88± 2.04[a]	8.85 ± 1.92[b]	1.02 ± 0.66	89.55 ± 6.11

The significance of differences between time points was assessed using the paired Student's t-test (different small letters indicate $p<0.05$); HW; horizontal width, SD; standard deviation

bone resorption of 3.6 to 4.5mm after tooth extraction. In addition, tooth extraction without the use of any ARP procedure have induced percentages of 29% to 63% of horizontal width changes at 6–7 months post-extraction (Tan *et al.,* 2012). In contrast with the data reported in the studies cited above, the Tseal alveolar ridge preservation technique showed a mean horizontal bone resorption value of 1.02 ± 0.66 mm at six months post-surgery; or 9.82% of the baseline horizontal width of the socket. The data from our study confirmed the importance of using a bone graft to fill the alveolar socket after tooth extraction (Barone *et al.,* 2008; Cardaropoli *et al.,* 2012; Jung *et al.,* 2013). Cardaropoli *et al.,* (2012) conducted a clinical study to compare the performance of extraction alone with the use of extraction and an ARP procedure using bovine bone substitute together with a porcine collagen membrane (Bio-Oss + BioGide). The authors reported that the test group showed a significantly lower reduction in the alveolar width from baseline to 4 months (1.04 ± 1.08 mm versus 4.48 ± 0.65 mm), which corresponded to 15% of the initial thickness. In addition, (Jung *et al.,* 2013) showed a horizontal width resorption of approximately 17.4-18.1% by using different ARP approaches, in association with bovine mineralized graft and collagen membranes. Recently, (Avila *et al.,* 2014) reported that the clinical magnitude of the effect of performing the ARP procedure using a bovine bone graft was the buccal width of 1.89 mm, in comparison with tooth extraction only. Therefore, the data from our study are similar or better and indicated that use of the combination of bovine mineral graft and Tseal presented good results when compared with the data of previous studies in the literature.

Our clinical data outcomes could be explained by the fact that xenograft bone has been shown to have good osteoconductive properties and could therefore allow bone growth throughout the bone defect. In addition, non-resorbable membranes are often used in ARP procedures because they help bone healing by separating soft tissues cells from the surgical area and maintaining an adequate shape for bone regeneration (Jung *et al.,* 2013). Therefore, it is important that these graft substitutes allow bone cells to grow around and within the socket. In addition, this ARP technique did not change the mucogingival line since the Tseal could be exposed to the oral cavity. The open-healing approach in cases of ridge preservation was tested before by the use of dense-PTFE membrane (Barber *et al.,* 2007, Hoffmann *et al.,* 2008; Zafiropoulos *et al.,* 2020). These studies (Barber *et al.,* 2007, Hoffmann *et al.,* 2008; Zafiropoulos *et al.,* 2020) reported that because primary closure over the membrane is not required, the surgeon can treat large defects, preserve the interdental papilla, and preserve the full width of keratinized mucosa without

Table 2. Values of individuals' HW measurements at baseline and at 6 months post-extraction and the change in millimeters and the percentage of change between time-points for teeth in the maxilla and mandible.

Subject	Teeth	Baseline	6-months	Change	% Change
Upper jaw					
#1	8	6.92	5.69	1.23	82.23
#2	8	8.68	7.11	1.57	81.91
#3	9	8.91	8.23	0.68	92.36
#4	5	7.5	6.73	0.77	89.73
#5	4	9.0	8.0	1.0	88.89
#6	11	10.0	8.0	2.0	80.00
#7	14	9.06	7.94	1.12	87.64
#8	14	13.0	11.0	2.0	84.62
#9	15	11.0	10.0	1.0	90.91
Mean (±SD)		9.34 ± 1.82[a]	8.08 ± 1.61[b]	1.26 ± 0.49	86.48 ± 4.42
Lower jaw					
#10	24	8.5	8.4	0.1	96.91
#11	23	9.1	9.0	0.1	99.69
#12	19	7.85	7.45	0.4	94.90
#13	30	10.0	9.00	1.0	90.00
#14	30	12.6	11.2	1.4	88.89
#15	30	12.97	13.00	0.03	100.00
#16	31	13.0	11.0	2.0	84.62
Mean (±SD)		10.57 ±2.23[a]	9.86 ±1.93[b]	0.72 ± 0.76	93.57 ± 5.86

The significance of differences between time points was assessed using the paired Student's t-test. The significance of differences between maxilla and mandible was assessed using Student's t test ($p>0.05$) (different small letters indicate $p<0.05$); HW; horizontal width, SD; standard deviation

the concerns of bacterial contamination or infection. In addition, when primary soft tissue coverage over a barrier membrane is not necessary, only minimal flap reflection or dissection is required to place and stabilize the membrane. Thus, vascularization of the graft and surgical site is not compromised and better clinical outcomes could be expected. In addition, Barboza *et al.* (2014) reported that this approach can also result in an increase in the amount of keratinized tissue. The authors showed that post-extraction sites that revived the open-healing approach showed higher keratinized tissue formation than sites that did not receive the membrane. Therefore, better esthetic outcomes are expected during implant therapy.

Despite our good clinical results, this study presented some limitations and they should be interpreted with caution. Our study was a case series analysis made with a convenience sample population, therefore the clinical indication of our findings for all populations needs further confirmatory studies. In addition, a randomized clinical trial with a large number of subjects should be performed in order to confirm our results. It could also be argued that an even larger number of experimental groups should be compared, such as the combination of bovine bone graft and free gingival graft or use of the procedure together with a collagen membrane, as well as the comparison of groups with a control group. However, for the purpose of conducting a good clinical trial we need preliminary data to enable the power size of the clinical trial to be calculated, therefore our study will provide these data in the literature and introduce this clinical approach for future research. Adding, histomorphometric analysis of the repair process will also be important to understand the quality of the bone formed. Thus, despite these limitations, some clinically relevant conclusions could be drawn from this study and the data may be helpful in future studies.

In conclusion, the application of bovine bone graft in an extraction socket, which was then covered with Tseal, resulted in substantial horizontal width preservation of up to 86% of the baseline thickness in the selected population, at 6 months after tooth extraction.

Conflict of Interest Statement

The authors declare that there are no conflicts of interests for any author in the present paper.

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