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Key Findings

The sockets that received type I bovine Achilles tendon collagen plug with bioactive resorbable calcium apatite crystal showed statistically significant wound closure surface when compared to the group that received cortico-cancellous allograft covered by adense polytetrafluoroethylene membrane at 3- and 4-weeks post-operatively.

Abstract

Background: The aim of this prospective observational randomized clinical study was to compare the percentage of wound closure surface area after using two different ridge preservation procedures. In addition, patient pain levels were registered using the Visual Analog Scale (VAS).

Materials & Methods: Twenty extraction sites were randomly allocated to either group using computer-generated randomization assignment software. The groups were: group 1, received type I bovine Achilles tendon Collagen Plug with Bioactive Resorbable Calcium Apatite Crystals (CPCAC); and, group II, received Cortico-Cancellous Bone Chips (CCBC) mix and a Dense Polytetrafluoroethylene (dPTFE) barrier membrane. The patients received a VAS pain rating scale to report their pain levels at 1-, 3-, 5- and 7-days post-operatively (PO). Digital planimetry was used to calculate (mm²) the wound closure surface area at baseline, 1-, 2-, 3-, 4-, 6- and 8-week PO. Paired ‘t’ and student ‘t’ statistical tests were employed to compare the data from both groups. Statistical significance was evaluated at p<0.05.

Results: There was no statistical significance when comparing groups, I and II for 1- and 2-week time periods. However, there was statistical significance for group I which showed higher closure rate when compared to group II at the 3-week (p=0.015) and 4-week (p=0.027) PO visits. The patient pain levels evaluated by the VAS pain rating scale showed no statistical significance between the two groups.

Conclusion: The sockets that received CPCAC showed higher wound surface closure when compared to the group that received CCBC with dPTFE at 3-, and 4-weeks post-operatively.

Keywords: Ridge Preservation; Type I Bovine Achilles Tendon Collagen Membrane; Dense Polytetrafluoroethylene; Wound Closure; Visual Analog Scale.

Introduction

Tooth loss is accompanied by three-dimensional bone remodeling and ridge atrophy[1]. The cellular remodeling processes that occur 1 year after tooth loss result in up to 50% loss of the alveolar bony ridge width, especially in the anterior maxilla [2]. A high percentage of the alveolar bone resorption occurs within the first 3 to 6 months post-extraction[3]. If ridge preservation is not conducted at the time of extraction, 40%-60% of the total alveolar bone volume is lost during the first 2–3 months post extraction, and this phenomenon has shown to continue to occur at a rate of 0.25%–0.5% loss per year[4]. The effectiveness of alveolar ridge preservation techniques has been confirmed by many studies. A systematic review by Avila-Ortiz et al[5], which evaluated the clinical effects of tooth extraction with and without ridge preservation of non-molar teeth, found that ridge preserved sites had a mean of 1.89 mm less loss in the buccolingual ridge dimension and 2.07 mm less loss in the vertical ridge dimension. Thus, ridge preservation increases the possibility of the clinician to place the implant in a restoratively driven position. Alveolar ridge preservation can be achieved by utilizing a variety of materials and techniques. Autogenous bone
has been considered the gold standard of bone grafts due to its inability to induce an immunologic reaction and to having the three main properties of the ideal bone graft (osteocconductivity, osteogenicity, and osteoinduction) [6]. Due to the associated patient morbidity and clinical time to harvest autogenous bone, dental research has focused on developing substitutes to autogenous bone grafts which resulted in the production of allografts, xenografts and alloplasts [7].

One of the early classical techniques in ridge preservation involved the use of particulate bone graft with a non-resorbable barrier membrane[8]. From a clinical efficiency standpoint, mixing and packing the particulate bone graft can be time consuming, and there is high potential for the site to become infected due to membrane exposure and for the graft to wash out[9]. In addition, the use of non-resorbable membranes for ridge preservation has the clinical disadvantage of needing a second procedure for its removal during the healing phase[6]. The need to facilitate the clinical bone delivery techniques by replacing the particulate structure with a plug device is clinically appealing to both the patient and the clinician as it saves procedural time, eliminates the potential for graft washout, and dramatically reduces procedural costs by avoiding use of a barrier membrane.

The Osteogen® Bone Grafting Plug (Impladent Ltda., Jamaica, NY, USA) consists of type I bovine Achilles tendon collagen with bioactive resorbable calcium apatite crystals (CPCAC) to create a structure that mimics the organic and inorganic components of physiologic bone. CPCAC was first developed to serve as a one-step grafting solution for ridge preservation without the need for a barrier membrane[10].

Although the CPCAC has been on the dental market for several years, soft tissue healing studies comparing it to the conventional procedures for ridge preservation are limited. Thus, the primary objective of this prospective observational randomized clinical study is to compare the percentage of wound closure surface area in the group that received CPCAC with the group that received bone graft and a non-resorbable (cytoplast) membrane for ridge preservation.

Materials and Methods

Participant Enrollment

This prospective observational randomized clinical study was reviewed and approved by the Institutional Review Board (IRB) of the University of Tennessee Health Science Center (UTHSC) in agreement with the Helsinki Declaration of 1975, as revised in 2013. (IRB approval no. 18-06428-F). The study was reviewed with all participants and written consent was obtained prior to treatment. A Mann-Whitney U test was conducted at the 5% statistical significance level. Power analysis (using Minitab statistical software) determined that 20 extraction sites (10 of each group) were required to detect a mean statistical difference in the percentage of wound closure surface area. Patients were enrolled from July 2019 through January 2020. However, due to the Covid-19 pandemic and subsequently school closure, the last three patients were removed from the study. The inclusion criteria were: 1) UT Clinic subjects; 2) willing to cooperate with the post-operative (PO) instructions; 3) availability of returning for 8 visits for data collection. The exclusion criteria included: 1) uncontrolled diabetes (HbA1C > 7.0); 2) history of use of bisphosphonates; 3) heavy smokers (20 pack years or more). At the consultation appointment, after informed consent was obtained, a standardized intraoral occlusal digital photograph of the tooth to be extracted was taken.

Surgical protocol

The ridge preservation surgical treatment groups were: group 1 (control), the use of cortico-cancellous allograft (MinerOss®, Bio-Horizons, Birmingham, AL, USA) with surgical site coverage using Cytoplast membrane (Ti-250, Deore Materials, Osteohealth, USA); and group 2 (experimental) the use of Osteogen® plug (Osteogen® plug, Impladent Ltda., Jamaica, NY, USA). Randomization was conducted by a computer-generated randomization assignment software (Sealed Envelope, simple randomizer, Ltda. 2017). At the treatment appointment, the patient received local anesthesia and a minimal flap was reflected on the facial and lingual/palatal aspects of the tooth to be extracted. Next, the tooth was extracted in an atraumatic fashion. The socket was curetted to ensure complete removal of any granulation tissue and then irrigated with sterile saline. Ridge preservation using CPCAC was done according to the protocol described by Impladent[10]. The CPCAC comes in 2 sizes, for the anterior or pre-molar extraction sites, the small CPCAC was used. The large CPCAC was only used for molar extraction sites. The CPCAC is placed dry in a profusely bleeding extraction socket and compressed to fill the entire socket up to the soft tissue level.

Ridge preservation using CCBC was achieved by soaking the bone chips in the patient’s blood taken from under the minimal flap. The bone chips were packed into the extraction site to the level of the adjacent bony crests. Next, approximately 2 mm of the Cytoplast® membrane edges were placed beneath the minimally elevated flap circumferentially. The flaps were then passively sutured using one “hidden X” suture. A ruler was then placed adjacent to the extraction site and an intraoral occlusal photograph was taken of the entire circumference of the extraction site, including the ruler, which was used to calibrate the photography for measurement accuracy purposes. Written and verbal postoperative instructions were given to the patient. A prescription was given for chlorhexidine gluconate 0.12% with instructions to rinse twice daily with 15 ml for 30 seconds. In addition, patients were given a standard antibiotic regimen of amoxicillin 500 mg TID for 7 days. If the patient reported a penicillin allergy, the alternative medication prescribed wasclindamycin 300 mg TID for 7 days. The prescribed pain medication was ibuprofen 400mg every 4-6 hours for the first 2 days post-operatively. The patients were given a Visual Analog Scale (VAS) to rate their pain levels. This

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Figure 1: Occlusal view of tooth #30 at 4-week PO for ridge preservation using MinerOss® and a Cytoplast® membrane. Note presence of a ruler for calibration purposes and delineation of the open wound surface (dotted lines) made using the selection tool from Adobe Photoshop CS, providing the surface area (mm²). In this sample, the area is 37.74 mm².

Statistical analysis

The student’s t-test was applied to the results for multiple comparisons. The calculated probability was considered statistical significance at or below 0.05 (p ≤ 0.05). Also, the non-parametrical test, Wilcoxon-Mann-Whitney test, was used for comparing Vas pain levels between the groups.
Results

Seventeen (17) patients were enrolled from the period of July 2019 to January 2020. The patient profile included 10 females and 7 males, with ages ranging from 13 to 82. Two (2) patients were withdrawn due to lack of compliance to the scheduled PO visits. An additional three patients were withdrawn due to the COVID-19 related school closure, leaving a total of 12 patients who completed the study (Figure 3). Of the 12 patients who completed the study, the average age was 55 (range 27 to 82), consisting of 9 females and 3 males (Table 1). One (1) patient was a current light smoker (10 cigarettes/day), 2 patients were previous smokers that quit more than 10 years ago, and 3 patients had type II diabetes Mellitus that was under control (HbA1c < 7%). None of the patients developed any complications and PO infections. A total of 17 extraction sites were evaluated, of which 4 patients had 9 extraction sites in group 1, the remaining extraction sites were for group 2. By the end of the 8-week PO visit, all extraction sites were completely keratinized. Group 2 showed an earlier complete epithelialization and keratinization of the extraction sights in comparison to group 1.

In this study, the calculations of wound closure surface area for groups 1 and 2 were compared to the baseline (immediately post-surgery). The mean wound surface area difference between the two groups was not significant for the 1-, and 2-week PO visits. At the 3-, and 4-week PO visits, group 2 showed higher closure rate when compared to group 1. This difference was statistically significant [3-week (p=0.015) and 4-week (p=0.027) (Table 2). The patient’s pain level, as evaluated by the VAS pain rating scale, revealed no significant difference between the two groups for the 4 evaluated time periods.

Discussion

The primary purpose of ridge preservation is to maintain the ridge dimensions to allow for restoratively driven implant placement [11,12]. Second, ridge preservation procedures may provide adequate vital bone for dental implant placement [11,12]. Xenografts and allografts are the two most commonly used bone graft materials in dentistry today. CPCAC is a unique product in that it is a synergy between both bovine type I bovine Achilles tendon collagen and non-ceramic resorbable calcium apatite bone graft crystals. The collagen serves as a carrier of the bone graft, hence the ease of handling the product. According to the product guidelines (Impladent Ltd.®, Jamaica, NY, USA), the bovine type I collagen serves as a scaffold for keratinized tissue to develop over the grafted site. This may explain why the sites in group 2 had faster epithelialization and keratinization in comparison to group 1. Furthermore, collagen is a key component of a healing wound. Type I collagen is the most abundant

Figure 3: Flow chart of patient enrolment, allocation, follow up and analysis

Table 1) Patient profile demonstrating the gender, any significant medical conditions and number of teeth in each group.

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Gender</th>
<th>Medical conditions</th>
<th>Teeth in each group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Group I</td>
</tr>
<tr>
<td>1</td>
<td>F</td>
<td>none</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>Diabetes, HTN</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>HTN, hypothyroidism</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>none</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>Diabetes, HTN</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>Hepatitis</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>none</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>Hepatitis</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>none</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>Hepatitis</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>Asthma, joint replacement</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>9</td>
</tr>
</tbody>
</table>
Table 2) Table showing mean values, and standard deviation (SD) for surface area (mm²) of wound closure for group I (CPCAC method) and group II (CCAC method) for each evaluated time period: baseline, 1-week, 2-weeks, 3-weeks, and 4-weeks post-operatively (PO). Student t statistical analysis showed statistical significance for standard values at 3-weeks and 4-weeks PO.

<table>
<thead>
<tr>
<th>Surface area closure change compare to the surgery day</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean values for group I</td>
<td>21.25</td>
<td>27.6</td>
<td>14.4*</td>
<td>-28.54†</td>
</tr>
<tr>
<td>(SD = 107.3)</td>
<td>(SD = 70.5)</td>
<td>(SD = 49.6)</td>
<td>(SD = 47.4)</td>
<td></td>
</tr>
<tr>
<td>Mean values for group II</td>
<td>-31.38</td>
<td>-22.73</td>
<td>-49.59*</td>
<td>-73.28†</td>
</tr>
<tr>
<td>(SD = 83.9)</td>
<td>(SD = 111.5)</td>
<td>(SD = 45.4)</td>
<td>(SD = 23.5)</td>
<td></td>
</tr>
</tbody>
</table>

* Statistical significance p=0.014. † Statistical significance p=0.028

structural component of the dermal matrix. The collagen in CPCAC (Osteogen® plug, Impladent Ltda., Jamaica, NY, USA); and other collagen-type dressings, have properties which help create a favorable wound environment to the migration of cells from the epithelial margin across the granulation tissue, encouraging wound closure. Collagen-type dressings produce a significant increase in the fibroblast production and permeation. When migrating cells, such as keratinocytes, contact Type I collagen in collagen-based dressings, the cell releases MMP-1 to breakdown the Type 1 collagen to gelatin, which makes attachment sites more accessible to the cells and thereby enhancing the signaling to the cells responsible for creating granulation tissue [13].

During the proliferation phase of wound healing, fibroblasts change into their myofibroblast phenotype. At this stage wound contraction begins by virtue of the myofibroblasts extending their pseudopodia to attach to fibronectin and collagen in the extracellular matrix [14].

In addition, the graft’s unique combination avoids the need to use a barrier membrane which offers a significant and financial advantage over the conventional technique. The sites in group II experienced delayed epithelialization and keratinization. When the membrane was removed at the 6-week PO, the extraction sites were always erythematous with evident areas of granulation tissue. This is explained by the ability of the non-resorbable barrier membrane to exclude the rapidly proliferating epithelial cells and allow the slower proliferating bone producing cells to infiltrate into the socket [7]. In addition, the use of d-PTFE membranes doesn’t require primary closure [13]. This allows the preservation of existing keratinized tissue width and regeneration of keratinized tissue over the extraction site. The preservation of the keratinized tissue occurs by virtue of secondary epithelialization of the dense connective tissue at the surgical site [8]. The importance of a band of keratinized tissue around implants cannot be underestimated as it has been shown in several studies and systematic reviews that implants with a band of at least 2 mm of keratinized attached tissue have less plaque accumulation, tissue inflammation, mucosal recession and attachment loss in comparison to implants without a band of keratinized tissue [15].

The purpose of this study was to verify how long it took to have a full closure and evaluate other interoccurrence due to each technique (infection and pain). It is well known that the most common complication with ridge preservation procedures is wound dehiscence, which often is attributed to using a non-resorbable membrane[16]. In a socket preservation study by Lekovic[17], the patients with membrane exposure ended with similar results to control sockets which didn't receive bone grafts. Membrane exposure may result in microbial contamination of the membrane and subjacent bone, causing bone resorption, which compromises bone regeneration. It was reported by Nowzari et al[18], that barrier membranes are at risk of becoming populated with putative periodontal pathogens in as early as 3 minutes of intraoral membrane manipulation. In theory, having a faster closure could result in a reduced chance of infection. However, in our study we did not experience infection of the membrane or graft during the 4 weeks the membrane was maintained in the oral cavity prior to its removal.

Several tools are available to assess wound healing. The wound surface area measured over time is a useful tool to assess the wound healing progress. Wound healing has been measured using estimates, where the wound surface area is an estimate of the length and width of the wound measured by a ruler as an area of a rectangle or an ellipse [19]. Another method is by tracing the wound contour on a transparent film from which the area is measured by counting the number of squares within the contour after the film is placed on a grid [19]. A more advanced, easy to perform and inexpensive method is by using...
a planimetric software and digital photographs. The wound is photographed with a calibrated ruler placed near the wound edge. The photo is then taken to a planimetric software, such as the Adobe Photoshop CS3 used in the present study, where the wound contour is traced. The ruler is used for calibration of the linear dimensions. The software then calculates the delimited area automatically. This wound area measurement technique is utilized by several medical specialties that deal with chronic wound treatment. This was the selected technique to be used in this study and it has shown to yields highly accurate and precise area measurements [20].

The Visual Analog Scale (VAS) is a pain rating scale that subjectively scores pain based on self-reported measures of symptoms. The patient is asked to rate their pain on a 10 cm line that represents a continuum between the two ends of the scale (0 indicating no pain and 10 indicating extreme pain). This scale was first used by Hayes and Patterson in 1921 and is still used today for measurements of pain, mood, appetite etc [21,22]. In this study, we marked every centimeter along the scale to offer the patient the freedom to express themselves because they won’t be tied to a predefined category. This allows more accuracy by detecting minute changes in pain measurement throughout the course of the entire 7 days after surgery. The present study showed no significant difference between the pain levels associated with both groups. Although, the second group shows higher pain levels. This indicates that the grafting technique or material doesn’t have an influence on the pain levels of the patient. To our knowledge, there are no studies that specify whether a particular socket preservation technique causes more pain. The authors noted that the patients that tended to report higher pain scores had a history of reporting pain independent of the procedure conducted. In this study, pain seemed to be patient dependent and not procedure dependent.

There are several limitations in our study. The sample size became limited due to the COVID-19 pandemic which caused three patients to be withdrawn from the study. Even though digital planimetry is an accurate technique to measure wound surface area, such accuracy can only be obtained when the angle between the camera lens and wound plane is 90°. With the camera being handheld, it is difficult to set it at the right angle. The greater the deviation from the camera’s right angle, the greater the measurement error. In a wound photography standardization study, Rennert et al [23] demonstrated that the wound area of 20.1 cm² was underestimated by 7 cm² (34.8%) when the camera was not properly positioned. Another issue is the position of the calibrated ruler. If the angle is not 90°, the ruler may be reproduced as smaller or larger depending on its position in the picture. If the ruler is represented as smaller, the resulting wound surface area will be overestimated in relation to the true surface area. As a result, the measurement can show inaccuracies. To overcome such limitation, two rulers crossed at 90° can be placed over the wound. The resulting wound area would then be calculated as the averaged reproduction of two linear dimensions of two rulers. However, placing two crossed rulers in the mouth over an extraction site may not be physically possible due to the limited space[21]. Therefore, we aimed to keep the camera as close to 90° as possible to the occlusal plane of the adjacent teeth during photographic imaging. A clinical observation in this study was that the ridge width, and consequently keratinization, seemed to be better maintained and broad, respectively, in the group that received cortico-cancellous allograft covered by a dense polytetrafluoroethylene membrane when compared to the type I bovine Achilles tendon collagen plug with bioactive resorbable calcium apatite crystal at the 8-week analysis. Further studies will be conducted in order to verify relationship between initiation and final ridge width and extent of keratinization after ridge preservation.

Conclusion

To our knowledge, this is the first study to utilize digital planimetry to assess the wound closure area in socket preservation procedures using FDBA with d-PTFE and Osteogen. The current findings indicate that there is a significant difference in wound closure at the third and fourth week for the Osteogen group. In addition, there was no significant difference in pain levels between the two techniques.

Acknowledgement

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References


