Original Article

Histomorphometric Analysis of Residual Alveolar Ridge Preserved using Collagen Cell Occlusive Membrane Alone and Along with Demineralized Bone Matrix Following Tooth Extraction: A Randomized Control Trial

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Abstract

Context: The changes in the volume and dimensions of the alveolar bone after tooth extraction often lead to challenges in prosthetic rehabilitation of the same necessitating ridge preservation procedures (RPP). **Aim:** The aim of this randomized clinical trial was to evaluate and compare the dimensional and histomorphometric changes of the sites preserved using the collagen membrane with and without demineralized bone matrix (DMBM). **Settings and Design:** Interventional, parallel-design, double blinded, randomized controlled trail. **Materials and Methods:** A randomized controlled trial was designed with 45 participants having at least 2 teeth indicated for were enrolled in this study. The sites were randomly assigned to the control group (RPP using collagen membrane) and the test group (RPP using collagen membrane with DMBM). The clinical parameters assessed were alveolar bone width and alveolar bone height. Histomorphometric analysis was carried out on tissue trephined from the preserved sites to evaluate the percentage of bone and connective tissue (CT %) formed 8 months postRPP. **Statistical Analysis Used:** Shapiro − Wilk test and paired and unpaired *t*-test. **Results:** Horizontal resorption was significantly less in the test group (7.375 ± 1.64). Histomorphometry of these sites revealed a complete absence of residual graft particles, presence of trabecular bone, and a more mineralized matrix (63.256%) as compared to the control sites (46.833%). **Conclusions:** The use of DMBM along with the collagen membrane for RPP yielded better results both clinically and histomorphometically.

Keywords: *Bone graft, guided bone regeneration, periodontal surgery*

Introduction

The goal of dental treatment is to maintain the teeth in optimum health, reflected in its function and aesthetics. However, sometimes due to severely compromised support or endodontic architecture, tooth extraction is inevitable where the objective of the dental therapy becomes restoration of the lost structure.[1] Several treatment options available range from a removable prosthesis to implant therapy. Irrespective of the treatment we choose, availability of adequate osseous architecture is essential for its stability, retention, and support.[2] On the other hand, tooth extraction sets off a series of biological changes, such as resorption of the residual alveolar bone and shrinkage of the overlying mucosa leading to undesirable esthetics.[3] Moreover, for implant therapy, the absence of adequate bone volume may necessitate additional surgeries such as ridge augmentation and sinus lift associated with considerable patient morbidity.[4]

Alveolar ridge preservation refers to a practice of minimizing the bone resorption that follows tooth extraction and preparing the same for future restorations with better esthetics while minimizing the number of surgical interventions.[1] It is achieved by grafting the socket with a biomaterial to overbuild the facial bone wall,[5] occluding the access to the socket using a barrier membrane,[6] or a combination of both.[7] A considerable amount of evidence suggests varying degree of success in the above mentioned procedures,[7-12] but no conclusion yet regarding the superiority of one as compared to others.

Thus, the present study was done to evaluate and compare the quantitative and qualitative effect of alveolar ridge preservation technique using bone graft

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and collagen membrane with collagen membrane alone, 8 months postextraction. Further, this study provides compelling evidence and data regarding the use of biomaterials in ridge preservation techniques.

Materials and Methods

This study was approved by our Institutional Ethical Committee (Institutional Ethics Committee, No: IEC/SCBDCH/010/2018, dated: December 28, 2018) before its commencement and was conducted in accordance with the Declaration of Helsinki of 1975, as revised in 2000. This was an interventional, parallel-design, double-blinded, randomized controlled trail performed from May 2018 to May 2019 in our department. A written informed consent was obtained from all the participants after they received a written and oral explanation of the study's objectives, risks, and benefits.

Patient selection

As determined in a sample of patients attending the outpatient department, at least 30 sites in each study group were necessary to detect a variation of 1 mm in alveolar bone height (ABH) and width with a 5% significance level and a power of 80%. Anticipating an attrition of 20%, 45 subjects, aged 18–45 years with a good oral hygiene (plaque scores <1),[13] were enrolled in the study from May 2018 to October 2018 [Figure 1] on the basis of a predecided criteria. Inclusion criteria: (1) At least two teeth in different arch, indicated for extraction due to endodontic reasons or root fracture, confirmed by clinical and radiographic evaluations, (2) the area adjacent to the said tooth should be dentate, and (3) presence of at least 2 mm of keratinized tissue to allow easy flap management during the procedure.

Exclusion criteria: (1) Pregnancy or lactation, (2) history of systemic illness or condition that contraindicates any elective surgical procedures (i.e., diabetes, autoimmune dysfunction, prolonged cortisone therapy, or chemotherapy, history of cardiovascular accidents), (3) use of tobacco in any form, (4) history of long-term nonsteroidal anti-inflammatory drug therapy, and (5) antibiotic prophylaxis within 6 months of the study.

Randomization and allocation

The sites were randomly allocated into test and control group by a computer-generated sequence performed by an author Silicon controlled rectifier unaware of the clinical parameters. The codes generated were placed in an envelope and opened by the operator Statutory Sick Pay at the time of surgery. In sites included in the test group, sockets were preserved using a bone graft along with the barrier membrane, and in the control site, only barrier membrane was placed.

Preoperative protocol

After enrolment, all the participants underwent an initial nonsurgical therapy including full mouth supra and subgingival scaling and root planing (SRP) using ultrasonic scalers (NSK) and hand instruments (Gracey curettes 7/8, 9/10, 11/12, 13/14, Hu Friedy, India) to ensure a healthy periodontium before the onset of surgical phase. Each of them was then given a standardized set of oral hygiene instruction both verbally and in the written format. Alginate impressions were taken 4 weeks after SRP, and study casts were poured. An acrylic template [Figure 2] was fabricated on the study cast extending one tooth mesial and distal to the tooth indicated for extraction. This template was used as a reference for the vertical measurements during the course of the study.

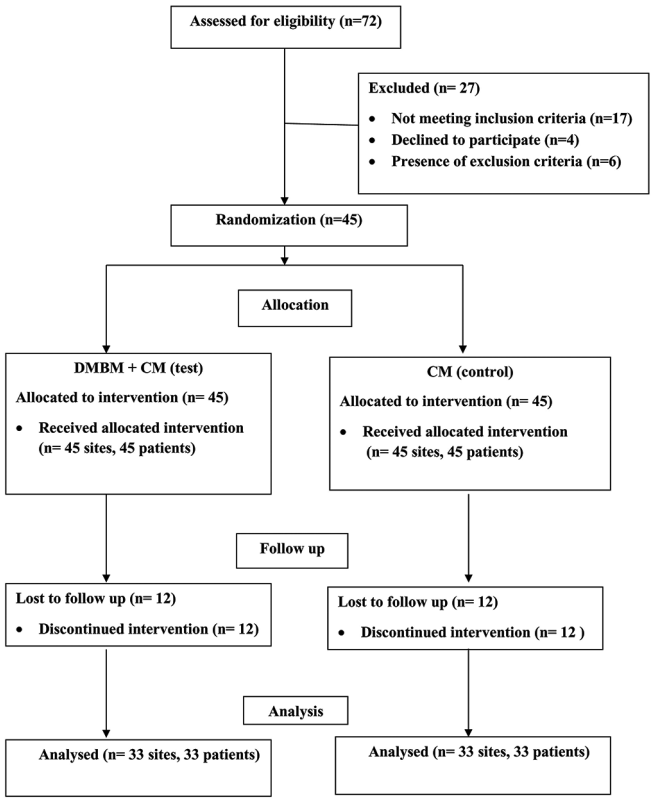

Figure 1: Consort flowchart showing enrolment of participants

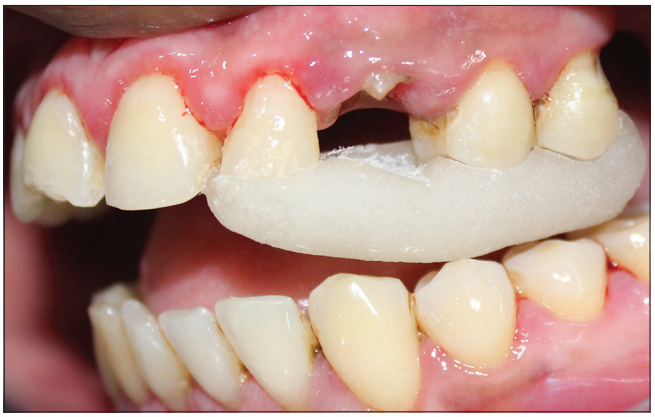

Figure 2: Acrylic stent used for measurement of alveolar bone height

Surgical protocol

The surgical treatment phase was initiated 5 weeks after oral prophylaxis only if full mouth plaque index (FMPI) is <1. After ensuring adequate sterilization, the operative area was anesthetized by suitable nerve block and local infiltration using 2% lignocaine Hydrochloride (HCL) with adrenaline (1:100,000). Using no. 15 BP blade, a sulcular incision was given followed by two slightly diverging vertical incisions at mesiobuccal and distobuccal line angles of the tooth indicated for extraction. A full-thickness periodontal flap was elevated on the buccal aspect using a mucoperiosteal elevator and the tooth was extracted as atraumatically as possible [Figure 3] with the use of periotomes (Periotome # 3 and Periotome # 4GDC, India). The socket was then thoroughly curetted, followed by saline irrigation. In the test site, the extraction socket is filled with hydrated demineralized bone matrix particles, size 250 µm (Osseograft demineralized bone matrix [DMBM], Advanced Biotech Products, India) and covered with a hydrated collagen membrane, size 15 mm × 20 mm (HEALIGUIDE Bio Resorbable Guided bone regeneration (GBR) Membrane, Advanced Biotech Products, India) trimmed to fit the extraction socket and extended to 3 mm on intact alveolar bone [Figure 4]. In the control site, the freshly curetted extraction socket was covered with the trimmed collagen membrane [Figure 5].

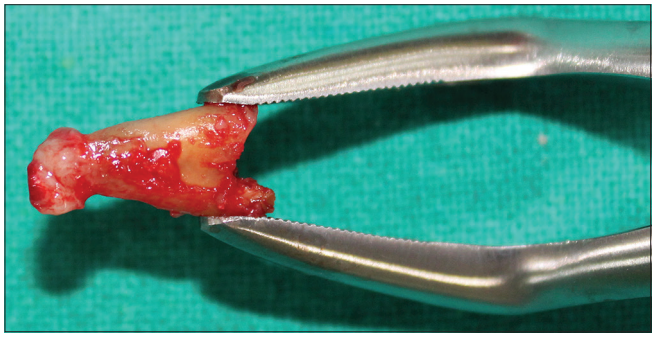

Figure 3: Atraumatic extraction using Periotome #3 and #4

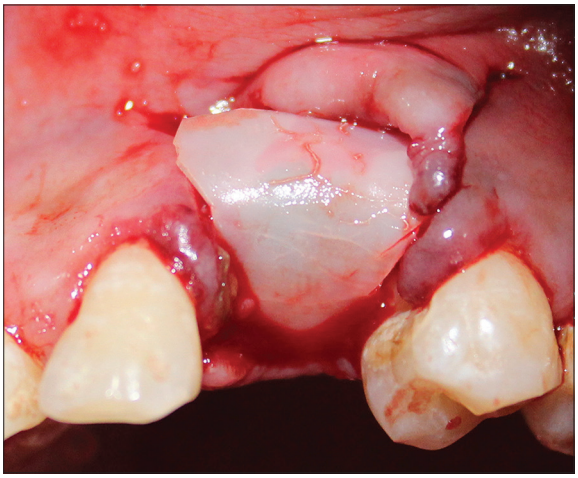

Figure 5: Placement of collagen membrane at control site

Primary closure of flaps was ensured and secured using 4-0 black silk suture (Mersilk, Ethicon, Johnson and Johnson Private Limited).

Cone-beam computed tomography (CT) images were taken for planning the implant surgery 8 months (35 weeks) postextraction in the experimental sites. As described previously, under aseptic conditions, a full-thickness mucoperiosteal flap was elevated after giving a crestal incision with Bard Parker blade No. 15 under adequate local anesthesia. A Surgical trephine (Dental Implant Trephine Drill Bur Ø 3 mm, SS White, Gurgaon, India) with external and internal diameter 3 mm and 2 mm was used to harvest tissue from the core of all the extraction sites to a depth of 6 mm [Figure 6]. Suitable sized endosseous implants (Aktiv Implant System, Implant Genesis, Kerela, India) were placed in accordance to the manufacturers' guidelines. The flap was then repositioned and sutured with 4.0 black silk sutures.

Postoperative care

All the participants were prescribed to use 0.2% Chlorhexidine Gluconate (Clohex ADS, Dr. Reddy's Laboratories Ltd, INDIA) 10 ml, twice daily as oral rinse, systemic antibiotics, i.e., amoxicillin 500 mg (Almox 500,

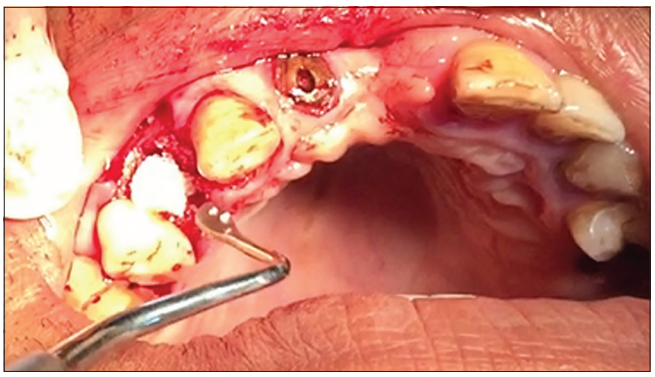

Figure 4: Placement of Demineralized bone matrix graft at test site

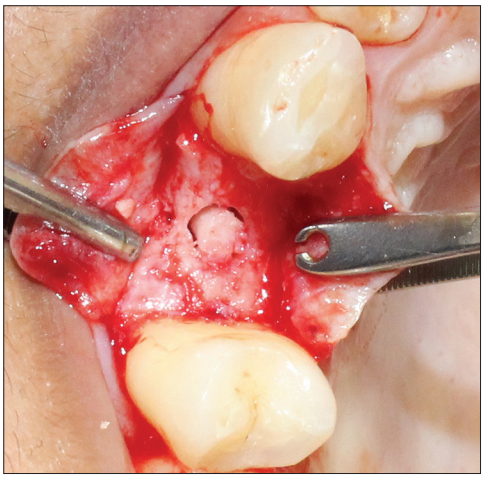

Figure 6: Osseous tissue core harvested from prepared site using Trephine Drill Bur

Alkem Laboratories, India) and analgesics, i.e., ibuprofen 400 mg (Brufen-400, abbott, India) once every 8 h for 5 days. The sutures were removed after 10 days.

Histologic preparation

The core samples were fixed with 10% formalin and decalcified within 3 days using 100 cc of decalcifying fluid made of a standard solution of 5% nitric acid and distilled water at 18°C–30°C. The blocks were washed with 90% alcohol, dehydrated in benzene and embedded in paraffin. Longitudinal sections of 6 µm were obtained using a diamond saw microtome and stained in hematoxylin and eosin. Three consecutive sections were randomly selected for the histological analysis under an optical microscope (Lawrence and Mayo Pvt. Ltd, India) with a digital video camera attached to it with a computer back up.

Clinical and histomorphometric examination

FMPI was recorded on the day of surgery using a periodontal probe (University of North Carolina-15 periodontal probe, Hu-friedy, Chicago, IL, USA). An examiner unaware of the randomization or treatment allocation measures the alveolar bone width (ABW: Distance of the buccal cortical plate to the alveolar ridge from the mid-crestal region located using the acrylic stent as a guide) using a calliper device (Bone Caliper Castroviejo CLC20 L, GDC, India) of 0.5 mm calibration [Figure 7] and ABH buccal and lingual (ABHB, ABHL: Distance from the edge of the acrylic stent to the alveolar ridge crest at mid-buccal and mid-lingual aspect, respectively) using a periodontal probe (University of North Carolina-15 periodontal probe, Hu-friedy, Chicago, IL, USA) on two occasions: Immediately after extraction and after 8 months and just before implant placement [Figures 8 and 9]. Histomorphometric analysis was done using a software, Image J–National Institutes of Health (Java 8) to evaluate the percentages of bone formed, connective tissue formed (CT %) and residual graft material in all the images at a magnification of ×400 [Figures 10 and 11]. Intraoral periapical radiographs were taken 8 months postplacement of bone graft and membrane and were compared with the postextraction socket for bone fill [Figures 12-14].

Statistical analysis

The statistical analysis was done using the statistical software (SPSS version 25) IBM Corp, Armonk (NY, USA).

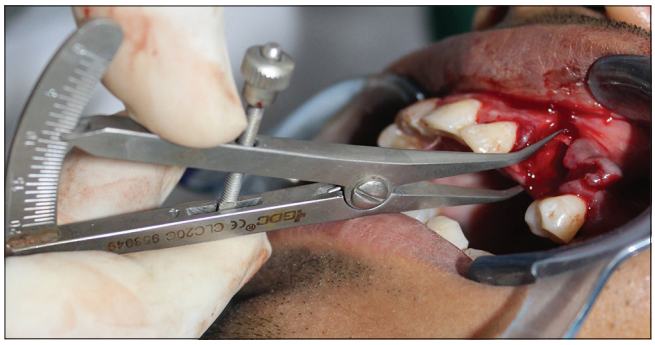

Figure 7: Measurement of alveolar bone width with Bone Calliper

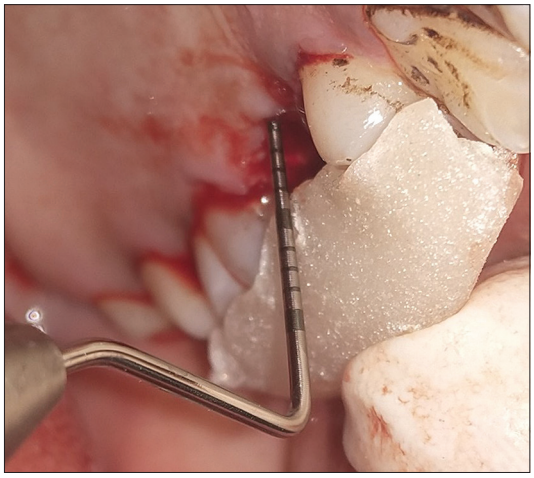

Figure 8: Measurement of lingual alveolar bone height

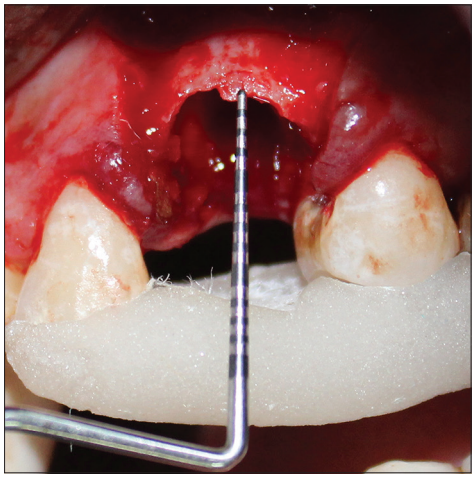

Figure 9: Measurement of buccal alveolar bone height

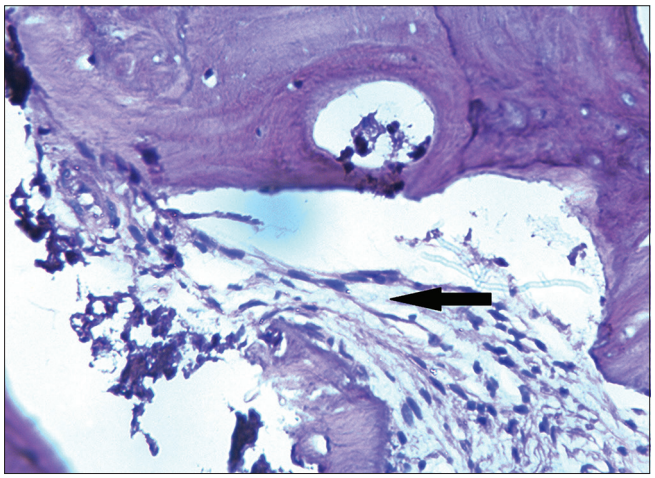

Figure 10: Control Site-Histologic section showing mostly unmineralized connective tissue (hematoxylin and eosin ×400)

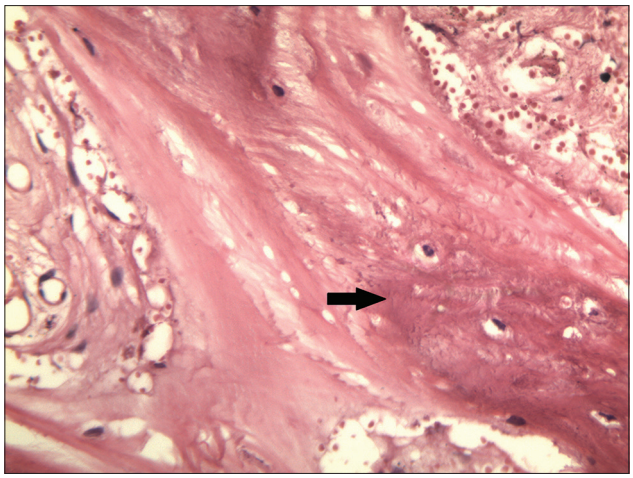

Figure 11: Test Site histologic section showing majority of mineralised osseous matrix (hematoxylin and eosin ×400)

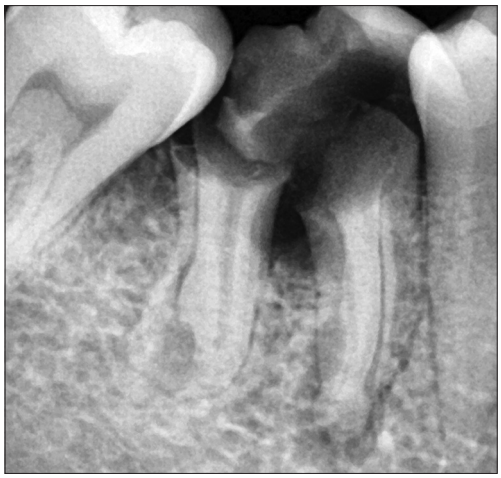

Figure 12: Intraoral periapical radiograph showing root stump

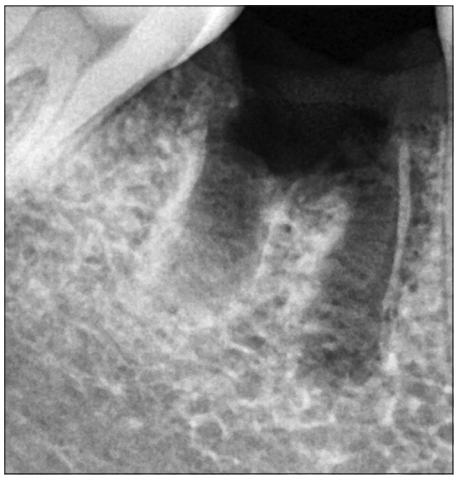

Figure 13: Intraoral periapical radiograph of test site postextraction

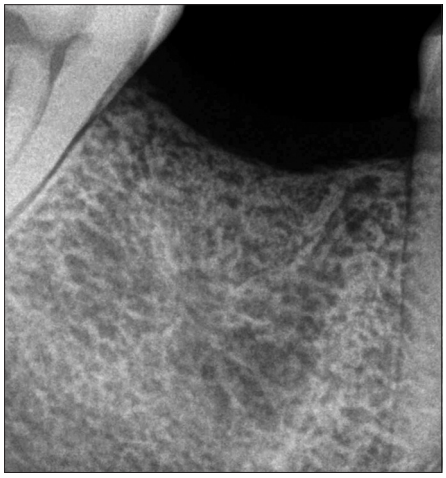

Figure 14: Intraoral periapical radiograph showing considerable bone fill 8 months postextraction at the test site

The normality of the data was tested using Shapiro − Wilk test. Paired *t*-test was used to compare the change in plaque scores, hard tissue parameters (ABW, ABHB, and ABHL), and histomorphometric parameters for intergroup comparison. Unpaired *t*-test was used for intragroup comparisons. The level of significance was set at $P < 0.05$.

Results

Table 1 shows demographic characteristic of the study population, with a well-matched sex ratio (M:22, F:23) having a mean age of 37 ± 10 years and 37.7 ± 7.8 years, respectively.

Tables 1 and 2 compare the mean and change in mean values, respectively, for full mouth plaque scores, alveolar ridge width, buccal bone height, lingual bone height. Mean plaque scores at baseline and during implant placement were 0.875 ± 0.135 and 1.008 ± 0.156 among the study population. The plaque scores showed slight statistically nonsignificant increase during implant placement, indicating adequate plaque control among study participants. ABW showed slight decrease during implant placement in both the sites. Control sites showed statistically significant decrease in mean ABW as compared to test sites ($P = 0.03$). Buccal bone height and lingual bone height were increased in both control and test sites during implant placement; however, the change in the mean values was not statistically significant.

Histomorphometric evaluation

Table 3 reports the results of the histomorphometry. The amount of trabecular bone for the test group was 63.256 ± 8.024, and for the control group, it was 46.833 ± 7.271. On the other hand, the CT % was 36.754 ± 8.024 for the test and 53.087 ± 7.141 for the control group. The percentage of bone formed was significantly more in the test group as compared to the control group ($P = 0.0001$). Inflammatory cells were sparsely distributed. There was no residual graft particle in any of the specimen.

Radiographic evaluation shows considerable bone fill in the 8 months postextraction socket at the test site.

Table 1: Demographic characteristics and comparison of mean plaque score, alveolar bone width, alveolar bone height buccal, and alveolar bone height lingual at baseline and 6 months interval within study groups

	n		Mean age	
Males	22		37±10	
Females	23		37.7±7.8	
Group	**Plaque score**	**ABW**	**ABHB**	**ABHL**
Bone graft+collagen membrane				
Baseline	0.875±0.135	9.75±1.4	9.958±0.987	10.125±0.907
6 months	1.008±0.156	7.375±1.639	11.167±0.866	10.916±1.018
P	0.288	0.874	0.866	0.987
Collagen membrane				
Baseline	0.875±0.135	9.7917±1.075	10.042±1.287	10.916±1.018
6 months	1.008±0.156	6.916±0.996	11.292±1.322	11.125±1.002
P	0.288	0.211	0.798	0.558

Unpaired *t*-test, Significant at $P<0.05$. Values are presented as mean±SD. ABW: Alveolar bone width; ABHB: Alveolar bone height buccal; ABHL: Alveolar bone height lingual; SD: Standard deviation

Table 2: Comparison of change in mean plaque score, alveolar bone width, alveolar bone height buccal and alveolar bone height lingual from baseline to 6 months between study groups

Group	ABW	ABHB	ABHL
Bone graft+collagen membrane	−2.375±0.711	1.208±0.334	0.792±0.334
Collagen membrane	−2.875±0.482	1.25±0.5	1±0.738
P	0.03*	0.813	0.383

*Significant at $P<0.05$, Paired *t*-test. Values are presented as mean±SD. ABW: Alveolar bone width; ABHB: Alveolar bone height buccal; ABHL: Alveolar bone height lingual; SD: Standard deviation

Discussion

In this split-mouth study, we aimed to compare the residual alveolar ridge profile clinically and histologically, 8 months postextraction in sites preserved with collagen membrane with and without DMBM. We observed that there was a reduction in both height and width in spite of the ridge preservation procedures. Since alveolar bone is a tooth-dependent structure, dimensional changes postexodontia is inevitable.[14] In a study conducted on beagle dogs, it was reported that maximum ridge resorption occurred in the first 6 months after tooth loss.[15] Tan *et al*.[16] reported that, 6 months after tooth extraction, alveolar bone resorption ranged from 29%–63% to 11%–22% in buccolingual and apicocoronal direction and the rate of resorption maximum in the first 3 months after extraction. Alveolar ridge preservation refers to minimizing this bone loss so that it can be rehabilitated without any functional or esthetic deficit.[17] In our study, the mean bone loss was 2.37–2.87 mm bucco-lingually and 1.2–1.25 mm apico-coronally which is very minimal as compared to the bone loss that occurs in a naturally healing extraction socket. In a study comparing the alveolar bone loss 9 months postextraction, Barone *et al*.[14] reported 2.5–2.9 mm decrease in ABW in sites preserved with a xenograft and collagen membrane as compared to 4.5–6.2 mm in the naturally healing sockets. Thus, a naturally healing extraction socket often leads to decrease in alveolar bone volume and often calls for soft-tissue and hard-tissue augmentation procedures during subsequent prosthetic rehabilitation.[3] There was no such incidence in our trail and all the sites were successfully rehabilitated with implants without any additional surgical procedures.

We evaluated the reduction in bone height on the lingual and buccal aspect of the sites and observed similar levels of bone loss in test (ABHB = 1.2 ± 0.33, ABHL = 0.79 ± 0.73) and the control group (ABHB = 1.25 ± 0.33, ABHL = 1 ± 0.73). The soft and hard tissue on the lingual side being thicker exhibited reduced rate of resorption which reflected in significantly less reduction in lingual bone height as compared to the buccal alveolar bone.[18] In the bucco-lingual aspect; however, the bone loss was significantly less in the test group (2.37 ± 0.71) as compared to the control group (2.87 ± 0.48) indicating the clinical superiority of using DMBM along with occlusive membrane. Lekovic *et al*.,[6] in 1998 reported that use of a bioabsorbable membrane made of glycolide and lactide polymers for preserving alveolar ridges significantly reduced horizontal and vertical bone loss and led to greater extraction socket bone fill. The use of bio-membrane is based on the principle of guided tissue regeneration.[6,19] It prevents migration of the faster forming epithelial cells into the socket while the slowly forming osteoblasts can replace the granulation tissue with bone cells. The use of bone graft in addition to the membrane is a derivation of principle of GBR.[3] It helps in regeneration by osteogenesis, oseoconduction, or osteoinduction with the membrane serving as a barrier.[19] In this trail, we used DMBM having osteoconductive properties along with collagen membrane in the test site. It provides a scaffold to conduct the formation of blood vessels, stabilizes blood clot, and supports the soft-tissue flap thus improving the quality and quantity of the new formed bone.[3,20,21] The barrier membrane occludes the epithelial cells and promotes

Table 3: Comparison of mean bone and connective tissue percentage during implant placement for both the groups

Groups	Mean	Minimum	Maximum	*T*	*P*
Bone (%)					
Bone graft+collagen membrane	63.256±8.024	54	79	7.505	0.0001*
Collagen membrane	46.833±7.271	36	52		
CT (%)					
Bone graft+collagen membrane	36.754±8.024	21	46	7.472	0.0001*
Collagen membrane	53.087±7.141	39	63		

*Significant at $P<0.05$, Paired *t*-test. Values are presented as mean±SD. SD: Standard deviation; CT: Connective tissue

the migration of osteoblast cell. Some human studies have reported superior clinical results on using bone grafts along with collagen membrane,[7] but to the best of our knowledge, this is the first split-mouth study to compare the outcome of alveolar ridge preservation using DMBM along with the collagen membrane to that using membrane alone.

Mellonig[22] in 2000 conducted a histologic evaluation of a bovine-derived bone xenograft used in the treatment of periodontal osseous defects in humans and reported formation of varying amounts of new bone, cementum as well as periodontal ligament in 3 out of the 4 specimens, indicating that grafting with a bovine-derived xenograft can possibly lead to periodontal regeneration. Pang *et al*.[3] reported a significantly better bone profile in terms of height, width, and volume, 6 months after extraction when ridge preservation was carried out with deproteinized bovine bone graft and collagen membrane. However, they found no significant difference in primary stability of the implants, osseointegration or bone implant contact (BIC) when the sites were rehabilitated with delayed implants. Such findings raise questions regarding the actual histologic nature of the tissue formed in the extraction sockets. In our study, histomorphometric evaluation of the tissue harvested during implant ostectomy revealed that there were very few inflammatory cells or osteoclasts in both test and control group. The bulk was made up of mainly mineralized and nonmineralized connective tissue. However, the degree of mineralization was higher in the test group. Another important observation was the complete absence of residual graft particles in all the samples from the test group in contrast to previous reports of alveolar ridge preservation using mineralized xenografts. Artzi *et al*.[5] conducted a 9-month histomorphometric evaluation of human extraction socket and reported that the mean bone tissue increased from 15.9% to 63.6% from coronal to apical sections. Further, the new bone tissue formed was adhered to a core of residual graft particles, arranged in cellular woven pattern in the cervical region to lamellar arrangement in the apical region. Pang *et al*.[3] attributed the presence of 15%–30% residual graft materials to the delayed resorption of the graft particles owing to the mineralized matrix.

This increase in mineralized bone matrix in the sockets preserved using DMBM along with collagen membrane would automatically result in better BIC and warrant a better prognosis of implant therapy in terms of primary and secondary stability. Clinically the advantage was assessed by the ease of implant ostectomy, i.e., the alveolar ridge was softer in the control site as compared to the test site rendering the use of DMBM in addition to the barrier membrane a clinical superiority above the use of collagen membrane alone.

Conclusion

Within the limitation of the present study, we can conclude that use of a xenograft with a demineralised matrix along with a barrier membrane for socket preservation is a promising therapeutic approach. Bone graft and collagen membrane resulted in quantitative and qualitative improvement in results for alveolar ridge preservation as compared to the collagen membrane alone. ABH and width were better preserved as well as histologic parameters such as amount of trabecular bone and percentage bone formation was higher with the combination of bone graft and collagen membrane. However, to incorporate the use of bone grafts and collagen membrane as a ridge preservation technique into routine practice, further longitudinal studies evaluating the stability of implants placed at a site preserved must be carried out.

Acknwoledgment

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Conflicts of interest

There are no conflicts of interest.

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