ORIGINAL RESEARCH

Evaluation of Effectiveness of Nanocrystalline Hydroxyapatite and Demineralized Bone Matrix Combined with Titanium-platelet Rich Fibrin for Ridge Preservation: A Randomized Controlled Clinical Trial

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Abstract

Aim: Preservation of ridge dimensions is the important aspect after tooth extraction for prosthetic and implant rehabilitation. Titanium-platelet rich fibrin (T-PRF) is an autologous biomaterial, and when used with bone graft it could enhance the bone regeneration. Hence, the aim of this study was to evaluate the combined effect of T-PRF with nanocrystalline hydroxyapatite (Nano-HA) and T-PRF with demineralized bone matrix (DMBM).

Materials and methods: Twenty systemically healthy patients were included in the study and were randomly assigned into two groups. Ten patients were treated with atraumatic extraction followed by ridge preservation using Nano-HA bone graft and T-PRF. In another group of ten patients, ridge preservation was done using a xenograft-DMBM. Preoperative cone beam computed tomography (CBCT) and postoperative CBCT after 3 months were evaluated for bone fill. The clinical parameters of ridge width (RW) and ridge height were measured clinically, with the help of UNC 15 probe, after 3 months.

Results: The treatment modality resulted in significant bone fill in CBCT and adequate RW clinically in both the groups. The mean bone density in the Nano-HA + T-PRF group was recorded as 776.72 ± 223.94, and 854.72 ± 183.57 was observed in the DMBM + T-PRF group, after 14–16 weeks.

Conclusion: The study's findings indicate that ridge preservation performed at the time of extraction is a reliable and predictable approach for minimizing alveolar bone resorption. Additionally, the combination of T-PRF with bone grafts yields effective results in a relatively short timeframe.

Clinical significance: This technique involves combining osteoconductive material from Nano-HA and DMBM and the growth factor-rich matrix of T PRF for quicker healing and better esthetic and functional results. It reduces morbidity in patients, does not require an autogenous graft, is biocompatible, and is economical; therefore, both clinical practice and regenerative research in the field of dentistry are advanced. Hence, it is one of the important evidences through this original study.

Keywords: Augmentation, Bone grafts, Extraction socket, Platelet concentrate, Remodeling, Ridge deformity.

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Introduction

Localized ridge deformities of varying severity often arise in cases of tooth extraction, particularly in patients with advanced bone loss. This deformity can occur due to the removal of the four-walled socket that initially protects the blood clot, or as a result of extensive carious or periapical lesions, or fractures of the root or labial bone. In cases with progressive bone loss, the likelihood of substantial carious or periapical lesions increases, contributing to the formation of localized ridge deformities. While implant placement is generally regarded as the preferred treatment for tooth replacement, it may not be feasible in every case, especially when considering bone shape and density.[1]

Poorly managed tooth extraction sockets further exacerbate typical bone changes expected in the 1st year postextraction, particularly within the initial 3 months when approximately two-thirds of alveolar bone loss occurs. The primary therapeutic strategy for facilitating future implant placement and achieving esthetically acceptable fixed or removable prostheses is to preserve the bone during tooth extraction.[2]

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Ridge preservation techniques are crucial for maintaining both soft and hard tissues. Massive alveolar bone resorption is seen in the 1st year of extraction, and can reach up to 50% loss in height and width. Therefore, it can cause inconvenient placement of dental implants later or esthetic shortcoming. It also reduces the requirement for complicated bone grafting procedures, streamlines future treatment, and prevents further oral health complications, thereby bettering long-term rehabilitation that could be functional or esthetic in nature.[1,2]

Various graft materials have been utilized to maintain the dimensions of the alveolar ridge postextraction, including autogenous bone grafts and allografts. Autogenous bone grafts are highly prized because of their biological advantages, but they have several disadvantages, including the donor site might cause some adverse complications, such as pain and infection and nerve damage or scarring at the second surgical site, and recovery may take longer because of healing at both the donor and recipient sites. There are also allografts, using human donors. Healing with allografts is generally slower than healing achieved with autografts because the body has to rely on its own inherent capabilities for bone incorporation. While some of these materials can partially preserve alveolar ridge proportions, they may also interfere with normal healing processes, leading to variable outcomes in bone tissue growth within the socket.[3]

Nanocrystalline hydroxyapatite (Nano-HA) has shown promise due to its resorption and remodeling capabilities. Histological studies of NanoBone® have revealed evidence of angiogenesis, resorption, remodeling, osteoinduction, and osteoconduction, with active remodeling observed within 3–5 months. Compared with conventional HA, Nano-HA offers better osteoconductivity because it closely resembles the mineral phase of natural bone. Its interaction with the surrounding bone tissue is facilitated by its nanoscale nature. The nanostructure of Nano-HA enhances the adhesion, proliferation, and differentiation of osteogenic progenitor cells, while also improving sinterability and densification, thereby increasing fracture toughness and mechanical properties.[4]

Osseograft, derived from high-purity type I collagen, is another promising material. Specifically, demineralized bone matrix (DMBM), made from approximately 250 µm-sized particles of bovine cortical bone, is commonly used in implants, sinus lifts, and ridge augmentation procedures, with complete host bone replacement occurring in about 4–6 months. It can act as a template for the formation of new bone and provides a scaffold that resorbs slowly.[5]

Platelet-rich plasma (PRP), a plasma fraction enriched with platelets, offers several regenerative benefits, promoting the repair of bone and connective tissue. However, PRP preparation can be time-consuming and exhibits technique sensitivity. To enhance the characteristics of PRP, titanium platelet-rich fibrin (T-PRF) has been developed as a third-generation platelet concentrate. T-PRF mitigates risks associated with silica contamination from glass vacuum containers typically used for PRP preparation.[6]

Combining Nano-HA with T-PRF may overcome the limited osteoinductive capacity of synthetic materials. Combination of DBBM with T-PRF could provide a bioactive environment that promotes faster and more predictable bone regeneration. Analyzing these combinations can reveal information about long-term results, handling ease, and cost-effectiveness, all of which are important for regular clinical use. This study is novel because it uniquely investigates the synergistic effects of combining T-PRF with Nano-HA and DMBM. It analyzed their combined efficacy in alveolar ridge preservation, focusing on bioactivity,

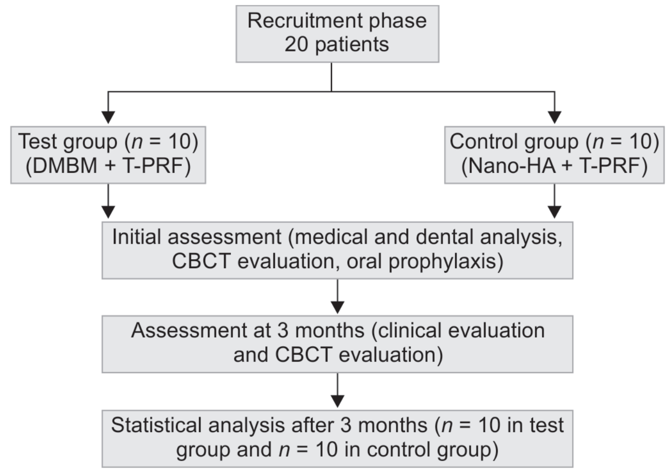

Fig. 1: The consolidated standards of reporting trails flowchart

osteoinduction, and predictability, areas not previously studied in such combinations.

Therefore, the aim of this study was to evaluate the combined effects of T-PRF with Nano-HA and T-PRF with DMBM in the treatment of alveolar ridge preservation following atraumatic extraction.

Materials and Methods

A randomized controlled clinical trial was conducted. Institutional ethical clearance was obtained (DMIHER(DU)/IEC/2023/47), followed by its registration at the Clinical Trial Registry–India (CTRI/2024/03/063461). The participants for this study were selected from the Outpatient Department of Periodontics and Implantology based on specific inclusion and exclusion criteria. Randomization was performed using a computer-generated random number sequence. A single-blind method was used, where the participants were unaware of their group allocation to reduce potential bias in self-reported outcomes. The clinicians conducting the procedures and assessments were not blinded, as they needed to implement specific treatment protocols. The consolidated standards of reporting trails flowchart is shown in Figure 1.

Sample Size

The sample size was estimated using the data from the previous study by Al Qabbani et al.[7] Calculated using Statistical Package for the Social Sciences, 27.0 version, open-source calculator-SS Mean, was determined by taking the pooled standard deviation of 1.21 mm and the mean difference of 1.07 mm. Given a type I error rate of 5% ($Z\alpha = 1.96$) and a power of 80% ($Z\beta = 0.84$), the formula produced 20 participants. This accounts for unpredictability and impact size while guaranteeing enough power to identify notable changes in ridge width (RW). Thus, 20 subjects were randomly distributed in each group. The data were recorded and statistically analyzed.

Study Population

This randomized controlled clinical and radiographic trial was conducted over a 6-month period (from January 5, 2024 to April 1, 2024). Patients meeting the inclusion criteria were randomly assigned to one of the two groups: DMBM + T-PRF (test) or Nano HA + T-PRF (control). A total of 20 patients, each requiring at least one tooth extraction, were recruited. Randomization was performed by one of the authors (RTP) using a coin toss, ensuring an equal distribution of 10 patients per group.

Inclusion Criteria

- Participants must be systemically healthy.
- Only nonsmokers are eligible.
- Participants must be at least 18 years old.
- Must have one or more grossly decayed teeth or root remnants without signs of purulent exudate or cellulitis.
- Sufficient soft tissue health and quantity are required to achieve complete crestal primary wound closure.

Exclusion Criteria

- Individuals unwilling to commit to periodontal maintenance.
- Those with prior periodontal regeneration at the study site.
- Pregnant or nursing women.
- Individuals with a history of systemic illness.

Clinical Parameters

The width of the ridge was measured buccolingually, using an UNC-15 calibrated periodontal probe (Hu-Friedy, University of North Carolina).

Radiographic Measurements

All the patients underwent cone beam computed tomography (CBCT) scanning before and at 14–16 weeks after ridge preservation. Bone density was measured in the socket configuration area before extraction of the teeth and again after 14–16 weeks when defect fill was anticipated.

Presurgical Procedure

After a comprehensive evaluation and diagnosis, full-mouth ultrasonic scaling was conducted. Initial therapy then included oral hygiene instructions, along with guidance on plaque control. Patients continued to receive plaque control instructions until they achieved a plaque score below 25%.

Surgical Procedure

Before surgery, patients were instructed to rinse with a 0.2% chlorhexidine gluconate solution for 1 minute. The procedure was performed under strict aseptic conditions. Local anesthesia was administered through nerve block and infiltration, using 2% lignocaine with 1:80,000 epinephrine (Ligno-Ad, Proxim Remedies, India).

Preparation of T-PRF Membrane

A 10-mL blood sample was collected from the antecubital vein via venipuncture within 1 minute. The sample was immediately transferred into titanium tubes and placed in a centrifuge, which spun at 2,700 rpm for 13 minutes. After centrifugation, the T-PRF clot was retrieved from the tube, discarding the red blood cell residue to yield a reduced platelet concentrate.

Surgical Procedure

Crevicular incision was given around the tooth to be extracted, using No. 15 surgical blade. Atraumatic extraction of the tooth by preservation of cortical bone plate was done. Extraction socket was debrided using curettes, and granulation tissues were removed. Presuturing was done, and the placement of the DMBM was done

Fig. 2: Preoperative photograph

Fig. 3: Demineralized bone matrix bone graft

in clean socket. The T-PRF clot was placed over the bone graft. The surgical site was sutured using 3-0 nonabsorbable silk suture (case 1—ridge preservation using DMBM and T-PRF; Figs 2 to 6).

Similar surgical procedure was done for another group in which Nano-HA was placed in socket followed by T-PRF clot placement (case 2—ridge preservation using Nano-HA and T-PRF; Figs 7 to 11).

Results

A total of 25 patients were initially screened for the study, of which 20 underwent tooth extraction. However, five of these patients were excluded due to noncompliance. Ultimately, 20 patients met the inclusion criteria for the study. The test group comprised 10 participants, including seven females and three males, while the control group also had 10 participants, consisting of six females and four males. Participants ranged in age from 20 to 60 years. Data analysis was conducted using Statistical Package for the Social Sciences version 27.0 and the open-source SS mean calculator. Paired and unpaired *t*-tests were used to assess changes from baseline to the 3rd month for each group. A *p*-value above 0.05 indicated nonsignificant results, while a *p*-value below 0.05 was deemed significant.

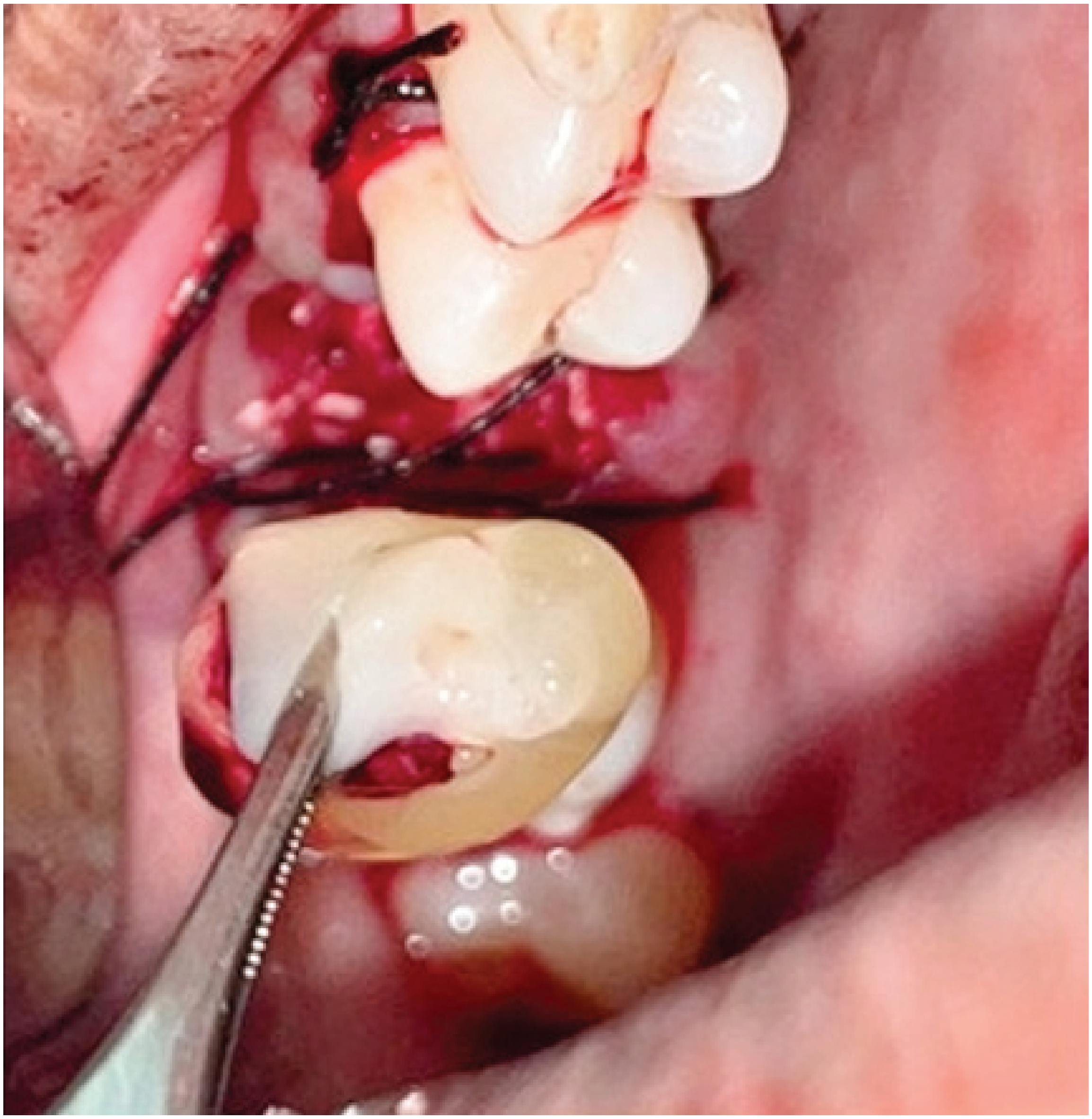

Fig. 4: Placement of T-PRF

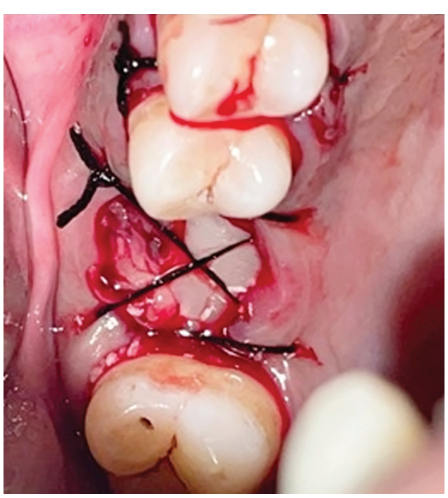

Fig. 5: Suture given

Fig. 6: Postoperative (16 weeks) photograph

Fig. 7: Preoperative photograph

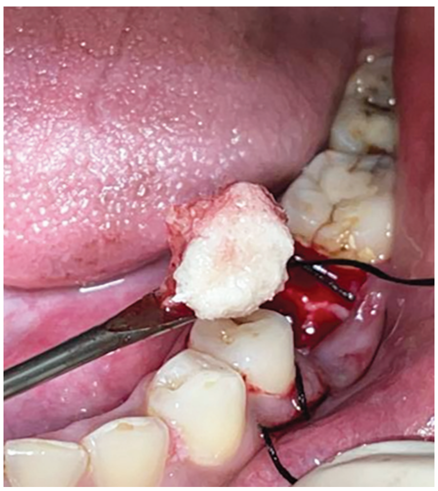

Fig. 8: Nano-HA Bone graft

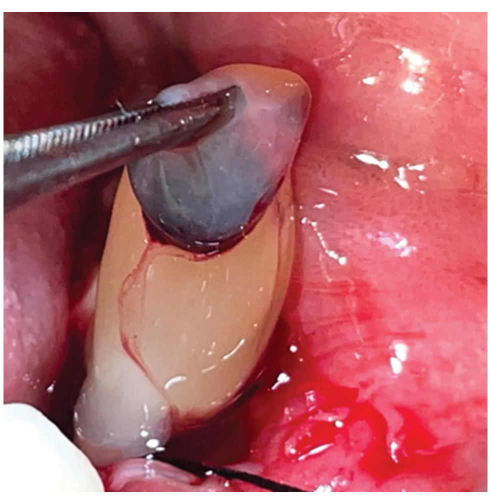

Fig. 9: Placement of T-PRF

Table 1 shows the baseline values of RW and Hounsfield unit (HU) in CBCT. The RW in both the groups was not significant ($p = 0.71$), with mean difference of 0.35 ± 3.12. The mean difference in HU in both the groups was 79.54 ± 313.70 and was not significant ($p = 0.42$).

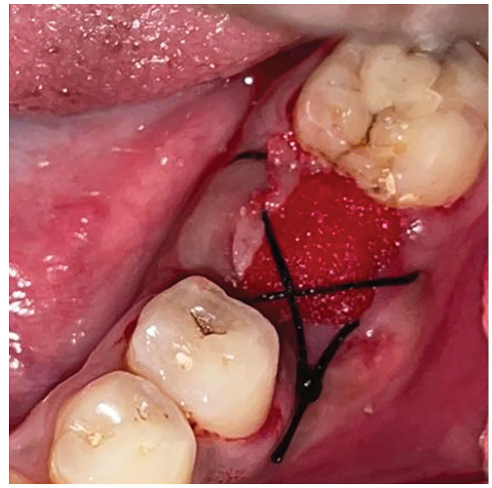

Fig. 10: Suture given

Fig. 11: Postoperative (16 weeks) photograph

In Table 2, the mean RW at baseline in test group was 10.98 ± 2.48 and 9.17 ± 2.14 after 14–16 weeks, with mean difference of 1.81 ± 0.68. The RW was statistically not significant ($p > 0.001$). The mean HU at baseline was 904.36 ± 209.73 and 776.72 ± 223.94 after 3 months, which was not significant ($p > 0.001$) for test group.

In Table 3, in control group, RW at baseline was 10.63 ± 1.99 and 9.46 ± 2.16 after 3 months, with mean difference of 1.17 ± 0.37. It was not significant ($p > 0.001$). HU at baseline was 983.90 ± 191.43 and 854.72 ± 183.57 after 14–16 weeks, with mean difference of 129.12 ± 65.38. HU was not significant ($p > 0.001$).

Table 4 shows that the difference at baseline in RW in both the groups was 1.81 ± 0.68 and 1.17 ± 0.37 after 14–16 weeks, with mean difference of 0.64 ± 0.63. RW was not significant ($p = 0.007$) between two groups. The HU difference in both the groups was 127.63 ± 62.28 at baseline and 129.18 ± 65.39 after 14–16 weeks. The mean difference was 1.54 ± 110.63. HU was statistically not significant ($p = 0.96$). Figure 12 shows the baseline and 14–16 weeks RW values for both the test and control groups, including error bars representing standard deviation (±SD).

All interventions and postoperative healing proceeded well, with no complications observed in either group. The ridge

Table 1: Baseline data between test and control groups: RW and HU

Parameters	*Test*	*Control*	*Difference*	*p-value*
RW	10.98 ± 2.48	10.63 ± 1.99	0.35 ± 3.12	0.71
HU	904.36 ± 209.73	983.90 ± 191.43	79.54 ± 313.70	0.42

Table 2: Clinical RW and CBCT HU in test group (Nano-HA + T-PRF)

Parameters	*Baseline*	*14–16 weeks*	*Difference*	*p-value*
RW	10.98 ± 2.48	9.17 ± 2.14	1.81 ± 0.68	>0.001
HU	904.36 ± 209.73	776.72 ± 223.94	127.63 ± 62.28	>0.001

Table 3: Clinical RW and CBCT HU in control group (DMBM + T-PRF)

Parameters	*Baseline*	*14–16 weeks*	*Difference*	*p-value*
RW	10.63 ± 1.99	9.46 ± 2.16	1.17 ± 0.37	>0.001
HU	983.90 ± 191.43	854.72 ± 183.57	129.12 ± 65.38	>0.001

Table 4: Difference between clinical RW and CBCT HU in test and control groups

Parameters	*Baseline*	*14–16 weeks*	*Difference*	*p-value*
RW	1.81 ± 0.68	1.17 ± 0.37	0.64 ± 0.63	0.007
HU	127.63 ± 62.28	129.18 ± 65.39	1.54 ± 110.63	0.96

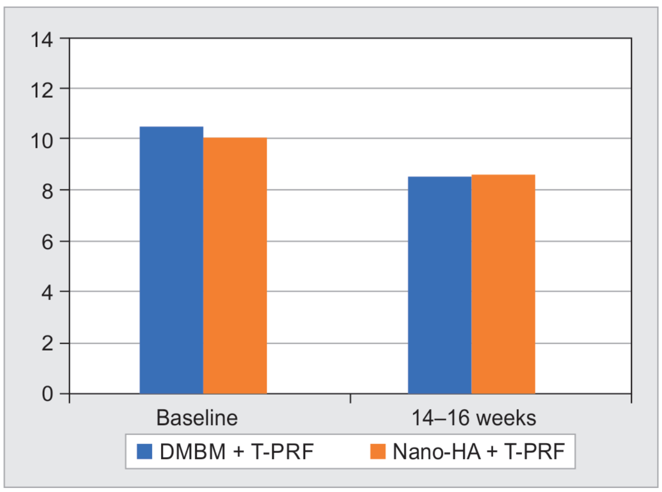

Fig. 12: Bar graph for RW including error bars representing standard deviation (±SD)

architecture remained stable, and clinical parameters were satisfactory in both the control and test groups from baseline to the 3-month follow-up. No significant differences were found in RW and height (HU) between the groups.

Discussion

This study discusses the critical necessity of postextraction maintenance of the alveolar ridge, which is necessary for a successful implant or prosthetic insertion. To improve regeneration, it presents a unique strategy that combines T-PRF with Nano-HA and DMBM. The T-PRF has advantages over traditional platelet concentrates because of its biocompatibility and prolonged growth factor release. The use of standardized outcome measures and a randomized, comparative design further enhance the study's value in verifying these cutting-edge materials. The aim of the study was to evaluate the clinical healing as well as radiographic bone retention after ridge preservation using T-PRF with Nano-HA and with DMBM, after 14–16 weeks of the procedure.

Tunali et al. developed T-PRF using a modified version of the leukocyte-rich platelet fibrin method. This approach is based on the premise that utilizing a titanium tube could be advantageous. Titanium is notable for its exceptional strength-to-weight ratio and corrosion resistance, making it an ideal choice for medical applications. Its biocompatibility is enhanced by its noncorrosive nature, as it forms a protective adhesive oxide layer *in vivo*. Additionally, titanium exhibits a remarkable ability for osseointegration, allowing it to bond structurally and functionally with the surrounding bone. In T-PRF membranes, researchers observed areas of bone tissue and developing connective tissue, indicating that T-PRF may promote the formation of new bone and connective tissue within 30 days in a rabbit wound healing model.[6,7]

Ustaoğlu et al. conducted a randomized controlled trial and found that T-PRF could serve as a viable autogenous alternative to connective tissue grafts for enhancing peri-implant soft tissue thickness and keratinized tissue width, potentially preventing crestal bone resorption during the osseointegration phase.[8] In a year-long study, Oza and Dhadse anticipated improved early bone formation outcomes in healing sockets preserved with T-PRF and demineralized freeze-dried bone allograft in preparation for implant placement.[9] Our study also investigated the effects of T-PRF in both groups, revealing that T-PRF enhances the properties of bone grafts for promoting alveolar bone formation.

In a histomorphometric study of the residual alveolar ridge utilizing DMBM, Raj et al. observed a complete resorption of graft particles, an increase in trabecular bone, and a more mineralized matrix after 8 months.[10] Mellonig performed a histological evaluation of a bovine-derived bone xenograft used in periodontal osseous defect treatment in humans and reported varying amounts of new bone, cementum, and periodontal ligament formation in three out of four specimens, suggesting that grafting with bovine-derived xenograft may facilitate periodontal regeneration.[11] Similarly, Pascawinata et al. concluded in their study involving rats that the combination of Nano-HA with injectable PRF is a viable option for alveolar bone preservation, as it may reduce resorption and promote new bone formation.[12]

A systematic review by Dewi and Ana found that HA as a bone substitute is a promising candidate for grafting, reducing the risks associated with donor site morbidity and resulting in less pain, although no statistically significant outcomes were observed across studies.[13] A systematic review conducted by Shaikh et al. assessed the efficacy of nanohydroxyapatite (nHA) grafts compared with other bone graft materials in treating periodontal defects. The findings indicated that nHA provides results similar to other graft options in terms of clinical attachment level improvement and reduction in probing depth. The review also emphasized the advantages of nHA, such as its high biocompatibility and structural resemblance to natural bone, which make it a valuable material for periodontal regeneration. This highlights its potential as a reliable alternative for bone grafting applications.[14] The study by Ozzo and Kheirallah investigated nHA and biphasic calcium phosphate. These materials were used to preserve alveolar ridge dimensions following tooth extraction, aiming to determine their relative effectiveness. Both materials showed comparable outcomes in maintaining ridge structure and facilitating bone regeneration, making them effective options for alveolar ridge preservation.[15]

In our investigation, CBCT demonstrated that the bone density and buccolingual dimensions of the alveolar ridge were preserved after 3 months in both groups. The mean bone density in the Nano-HA + T-PRF group was recorded at 776.72 ± 223.94, which was lower than the 854.72 ± 183.57 observed in the DMBM + T-PRF group. The difference in density between the two groups was 1.54 ± 110.63. Although the control group exhibited slightly greater density compared with the test group, this difference was not statistically significant. Clinical assessments indicated that RW was maintained in both groups, and satisfactory healing was observed.

The study has several limitations that affect its generalizability and reliability. A small sample size restricts the ability to extrapolate results to broader populations. Additionally, the follow-up period may be too short to assess long-term bone stability, as bone remodeling can take months or years. Patient heterogeneity, such as age, health conditions, and oral hygiene, could influence outcomes, making it hard to isolate the treatment's effect. The study also lacks direct comparisons with other bioactive materials or grafts, limiting the ability to determine whether the tested treatments are superior. Finally, technique sensitivity in preparing T-PRF could lead to inconsistent results due to variations in preparation methods.

The significance of combining current biomaterials such as DMBM, Nano-HA, and T-PRF to achieve consistent alveolar ridge preservation is emphasized by this study. When ridge stability is needed prior to prosthetic rehabilitation, particularly in areas that are sensitive to esthetics, clinicians should take this combination into account. The T-PRF's synergistic effects improve hard and soft tissue regeneration, which lessens the need for more treatments. To maximize results, practitioners must take into consideration patient-specific elements, including systemic health and compliance. To further validate these findings, larger sample numbers and longer follow-ups are advised in future research.

Conclusion

Within the limitations of this study, it can be concluded that T-PRF combined with bone graft demonstrated improved outcomes in maintaining alveolar ridge dimensions. DMBM with T-PRF has slightly better results compared with Nano-HA with T-PRF. Optimal graft incorporation with T-PRF has proven effective remodeling, as well as uneventful wound healing supports the clinical application of DMBM and Nano-HA with T-PRF to minimize postextraction hard tissue loss. Therefore, combining T-PRF with bone graft can accelerate the healing period of extraction socket.

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