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ORIGINAL ARTICLE

Effectiveness of a polycaprolactone scaffold combined with platelet-rich fibrin as guided tissue regeneration materials for preserving an implant-supported overdenture

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KEYWORDS

Socket;
Implant;

Abstract *Objectives:* This study aimed to assess the effectiveness of ridge preservation using a polycaprolactone (PCL) scaffold combined with platelet-rich fibrin (PRF) to promote bone regeneration before implantation.

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Polycaprolactone;
Platelet-rich fibrin

Materials and Methods: This prospective study was conducted at Al-Azhar University in Egypt. It included 30 participants requiring the extraction of their last mandibular premolar before constructing an implant-supported overdenture. The participants were divided into three groups: Group A was treated with a PCL scaffold and PRF as ridge preservative materials, Group B was treated with PRF alone, and Group C (control) was treated with no preservative material. Bone samples were collected for histomorphometric analysis at implant placement.

Results: The participants' mean age was 65.3 ± 4.27 years, and 18 (60%) were male. Postoperative alveolar bone lengths differed significantly between Groups A and B ($P = 0.001$). However, alveolar bone width changes did not differ significantly among groups. In contrast, the postoperative bone density and loss differed significantly among groups ($P = 0.001$).

Conclusion: Combining two ridge preservation techniques (PCL and PRF) enhanced participants' alveolar bone remodelling by decreasing its resorption and maintaining its width.

1. Introduction

After tooth extraction, irreversible bone loss and alveolar ridge atrophy can compromise the aesthetics and limit additional prosthetic options (Abdelqader Altaweel et al., 2021; Pagni et al., 2012). Song et al. (2020) found that approximately 50% of the alveolar bone width is lost within 12 months after tooth extraction. The primary goal of tissue engineering is the augmentation of bone deficiencies throughout the body, particularly in the craniofacial region (Lopez et al., 2021; Mossaad et al., 2021). Bone regeneration replacement materials must be biocompatible, biodegradable, easy to apply, effective for bone repair, and highly adaptable to bone defects (Helal et al., 2016; Veljanovski et al., 2021; Wang et al., 2002). Various scaffold types and natural or synthetic materials, such as metals, ceramics, and polymers, have been used to stimulate and enhance bone regeneration (Kim et al., 2021; Lim et al., 2021). Each option has different osteoinductive, osteoconductive, biocompatibility, biodegradability, and chemical properties, necessitating various techniques for their design and application (Zimmerling et al., 2021, Eldeeb et al., 2022).

Polycaprolactone (PCL) is a synthetic biodegradable polymer approved by the United States Food and Drug Administration due to its biocompatibility, stability, ease of manipulation, and suitable price for use in low- and middle-income countries (Dwivedi et al., 2020; Sousa et al., 2022a). Its mechanical strength makes PCL an excellent choice for scaffold and tissue-engineering development studies. Moreover, it is degraded into non-toxic byproducts and metabolised through the tricarboxylic acid cycle (Eftekhari et al., 2018). Previous studies have shown that the roughness of the nanofiber surface created on PCL nanoparticles promotes cell adhesion, proliferation, and differentiation (Asadian et al., 2020; Patel and Gray, 2021; Simonpieri et al., 2009).

This study aimed to assess the effectiveness of ridge preservation using a PCL nanofiber scaffold combined with a platelet-rich fibrin (PRF) membrane in improving bone socket regeneration. Its null hypothesis was that bone socket regeneration improvements would not differ significantly between a PCL scaffold combined with a PRF membrane and a PRF membrane alone.

2. Materials and methods

2.1. Study design and setting

This study recruited participants from outpatient clinics in the Faculty of Dental Medicine at Al-Azhar University in Cairo, Egypt. It was conducted between September 2021 and August 2022. All participants received written and verbal information about the study methodology and any risks associated with the surgery and the study before they gave written consent to participate. The study protocol was approved by the Ethical Committee at Al-Azhar University.

2.2. Participant eligibility criteria

This study's participants were all completely edentulous patients (except for their bilateral premolars, which required extraction) who were non-smokers, free of neuromuscular and/or temporomandibular disorder (TMD) signs and symptoms, and had a Class I angle classification according to the American College of Prosthodontists. Patients with a history of autoimmune disease, radiotherapy or chemotherapy in the past five years, metabolic bone diseases, and/or other conditions, such as long-term steroid or antibiotic use, TMD, bleeding problems, or anticoagulant medication-uncontrolled diabetes, were excluded from this study.

2.3. Sample size calculation

The G*Power statistical power analysis tool (version 3.1.9.7) was used to calculate the appropriate number of patients in each treatment group, considering a type 1 (alpha) error rate of 0.05 and 80% power to detect a change in the ridge diameter of 1.0 mm. It was determined that each group should contain at least 10 patients.

2.4. Patient grouping and randomisation

Each participant was randomly assigned to one of three treatment groups at the time of surgery using computerised software: Group A (test group) was treated with PCL nanofiber and PRF as socket preservation materials after extraction, Group B (positive control) was treated with PRF alone, and Group C (negative control) was treated using the standard procedure. A single surgeon performed all procedures. Before the surgery, the radiographic parameters on cone-beam computed tomography (CBCT) were assessed twice, and the clinical parameters were assessed by a third examiner blind to the study groups and study protocol. The premolar tooth extraction was traumatically performed using a periotome under local anaesthesia. The height of the buccal and lingual bone plate was clinically inspected at the mid-buccal site using a periodontal probe.

2.5. PRF preparation and PCL membrane application

Ten millilitres of intravenous blood was drawn and placed into two glass-coated plastic tubes without anticoagulants, which were immediately centrifuged at 3000 rpm for 10 min. The centrifugation created three layers that were collected: a bottom layer comprising red blood cells (RBCs), a middle layer comprising fibrin clots (PRF), and a top layer comprising platelet-rich plasma (Mijiritsky et al., 2021a).

For participants in Groups A and B, the PRF with a thin layer of RBCs was divided into small segments and backed into the socket to fill the socket. For participants in Group A, a membrane comprised of electrospun PCL nanofibres about 1 cm long was applied, created from 5 g of PCL powder purchased from Sigma-Aldrich (molecular weight = 70,000–90,000).

The first surgery outcomes were: (1) postoperative pain assessed using a Visual Analogue Scale at 24 and 48 h after preservative surgery; (2) a CBCT radiograph obtained immediately after surgery to measure bone height and width; and (3) another CBCT radiograph obtained six months after socket preservation surgery to measure bone loss, height, and density and for implant planning.

2.6. Second surgery

Six months after the first surgery, a surgical guide and a delayed flapless dental implant were applied. The surgical guide was fixed in its site with fixing pins. Next, 5 mm of bone was harvested from the implant site for histological examination. Then, the implant site was prepared by sequential drilling at a low speed (2000 rpm) until the desired dimensions were reached while being thoroughly irrigated with normal saline. Finally, the implant was inserted using a manual ratchet Torque handle. All participants received a conventional complete denture fabricated from polymethyl methacrylate. The denture was loaded three months after implant placement.

2.7. Histological analyses

Bone biopsies were preserved in 10% phosphate-buffered formalin before decalcifying in a 5% hydrochloric acid solution, dehydrating in a graded alcohol solution series, and embedding in paraffin. Hematoxylin and eosin were used to stain 5-m thick histological sections before they were digitally scanned at various magnifications.

2.8. Statistical data analysis

Statistical analyses were conducted using SPSS software (version 23.0; IBM, USA). The intra-class coefficient was used to assess the repeatability of intra-examiner (test–retest) results. An analysis of variance (ANOVA) F-test was used to assess inter-group differences. Significant ANOVA tests were further examined using pairwise post hoc Bonferroni tests. Non-parametric Chi-square tests were used to investigate relationships between categorical variables (e.g. sex). A $P < 0.05$ was considered statistically significant.

3. Results

3.1. Population characteristics

This study included 30 participants, 10 in each group, comprising 18 males (60%) and 12 females (40%) with a mean age of 65.30 ± 4.27 years (range: 59–71). Preoperatively, their mean alveolar bone length was 10.37 mm, width was 5.78 mm, and density was 630. Postoperatively, their mean alveolar bone length was 10.77 mm, width was 6.06 mm, bone loss was 1.44 mm, and bone density was 723.7 (Table 1).

The post hoc test comparisons showed that postoperative alveolar bone lengths differed significantly between Groups A and B ($P \leq 0.0001$) but not between Groups A and C or between Groups B and C. While postoperative changes in alveolar bone widths were significantly greater in Groups A and B than in Group C, they did not differ significantly between Groups A and B ($P > 0.001$). Postoperative bone density and loss differed significantly between groups ($P = 0.001$; Table 2). Postoperative alveolar bone length, width, or loss did not differ significantly by age or sex across groups (Table 3).

There were no apparent signs of postoperative complications after all procedures, and all participants accepted the technique without complaint. All patients could afford the financial cost of the PCL membrane, with each socket costing no more than US$33.

3.2. Histological results

Participants in Group A showed newly formed bone trabeculae with different stainability, Haversian canals with different sizes and shapes, osteoblast cells lining bone trabeculae, and randomly distributed osteocytes inside the newly formed bone matrix. Reversal lines and irregularly immature bone were also evident. Fibro-cellular marrow cavities, variable large vacuolated osteocytes widely entrapped in lamellar bone, and grafting material remnants were also apparent (Fig. 1).

4. Discussion

Modern bone tissue engineering (BTE) is considered to be in its third generation, using more biocompatible osteoinductive, osteoconductive, and bony-like materials made from various cells, scaffolds, and growth factors, either alone or in combination (Poomprakobsri et al., 2022; Sousa et al., 2022b; Sriputtha

Table 1 Descriptive statistics of preoperative and postoperative ridge preservation protocol measurements using received PCL mixed with PRF in group A, PRF only in group (B) and the control group(C).

Group	Category	Preoperative study variables			Postoperative study variables			
		Alveolar bone Length	Alveolar bone Width	Socket Density	Alveolar bone Length	Alveolar bone Width	Socket Density	Alveolar bone Loss
A	Mean/ SD	8.68 ± 0.22	4.66 ± 0.65	697.40 ± 118.7	10.17 ± 0.51	6.50 ± 0.45	934.1 ± 37.85	0.945 ± 0.20
B	Mean/ SD	11.28 ± 1.56	6.29 ± 0.53	745.5 ± 16.87	12.06 ± 0.80	6.37 ± 0.39	833.1 ± 37.38	1.41 ± 0.21
C	Mean/ SD	11.18 ± 0.47	6.39 ± 0.50	447.1 ± 69.35	10.08 ± 0.46	5.16 ± 0.34	405.80 ± 72.16	1.98 ± 0.05
Total	Mean/ SD	10.73 ± 1.54	5.78 ± 0.97	630 ± 153.8	10.77 ± 1.10	6.06 ± 0.75	724.3 ± 38.1	1.44 ± 0.46
	Min	8.41	4.20	385	9.42	4.74	320	0.70
	Max	13.56	6.92	867	13.25	7.22	973	2.10
P-Value		0.001	0.001	0.001	0.001	0.001	0.001	0.001

*Min = Minimum; ‡Max = maximum; ∞.

Table 2 Intergroup comparison of different postoperative study variables mean values with different RP techniques by Bonferroni Method.

variable	Category Comparisons	*P value*
Alveolar ridge bone length	G II Vs. G I	0.001
	G III Vs. G I	0.944
	G II Vs. G III	0.001
alveolar ridge width	G II Vs. G I	0.890
	G III Vs. G I	0.001
	G II Vs. G III	0.001
Alveolar socket bone density	G II Vs. G I	0.001
	G III Vs. G I	0.001
	G II Vs. G III	0.001
Alveolar bone loss	G II Vs. G I	0.001
	G III Vs. G I	0.001
	G II Vs. G III	0.001

et al., 2022; Tawfik et al., 2022). PCL composite scaffolds are recognised for their significant role in tissue engineering for regenerating bone, ligament, cartilage, skin, nerve, and vascular tissues (Ulery et al., 2011; Zimmerling et al., 2021). PCL is currently more well-known than other synthetic polymers used for BTE, such as polylactic acid, polyglycolic acid, and polylactic glycolic acid (Dwivedi et al., 2020). PCL degrades the slowest, taking 2–3 years. The presence of scaffold remnants was histologically verified during this study's follow-up period. A recent study confirmed the capacity of these nanofiber membranes to promote and guide bone healing in the socket, showing that PCL is a multifunctional biodegradable polymer with exceptional potential in tissue regeneration. It is non-toxic and cytocompatible with diverse human tissues, making it an excellent material for tissue engineering (Abedalwafa et al., 2013).

Without preservation techniques, patients with an atrophic alveolar ridge may suffer from inadequate bone quality and quantity, necessitating other compromise options, such as mini-implants or single implant-supported overdentures (Abdel Rahim and El Sayed, 2014). Implant-supported overdentures have been widely shown to improve function, speech, comfort, diet, and overall patient satisfaction (Boven et al., 2015; Sharka et al., 2019; Sivaramakrishnan & Sridharan, 2016). Most edentulous patients in this study were men, consistent with earlier findings in our community showing that men in low-income nations are more susceptible to edentulism and undergo more tooth extractions than women (Al-Rafee, 2020; Elsayed et al., 2019; Poomprakobsri et al., 2022).

Table 3 Descriptive statistics of Gender category frequency (%) and mean ± (SD) measurements difference between groups.

Male		Frequency	Alveolar bone length	Alveolar bone width	Bone density	Alveolar bone loss
	A	6	10.16 ± 0.55	6.72 ± 0.53	949.33 ± 30.42	0.912 ± 0.07
	B	7	12.28 ± 0.88	6.64 ± 0.36	851.42 ± 28.11	1.45 ± 0.25
	C	5	9.89 ± 0.52	4.95 ± 0.33	429.80 ± 61.59	1.94 ± 0.04
Total	A + B + C	18	10.77 ± 1.30	6.20 ± 0.88	766.94 ± 22	1.43 ± 0.46
Female	A	4	10.18 ± 0.51	6.29 ± 0.04	911.25 ± 39.93	0.99 ± 0.15
	B	3	11.57 ± 0.02	6.10 ± 0.01	790.33 ± 0.57	1.32 ± 0.01
	C	5	10.28 ± 0.34	5.37 ± 0.22	381.80 ± 80.5	2.02 ± 0.04
Total	A + B + C	12	10.67 ± 0.69	5.92 ± 0.45	660.42 ± 256.04	1.50 ± 0.48
Total (Male and Female)	A	10	10.17 ± 0.51	6.50±/0.45	934.1 ± 37.85	0.95 ± 0.20
	B	10	12.06 ± 0.80	6.47 ± 0.39	833.1 ± 37.88	1.38 ± 0.21
	C	10	10.08 ± 0.46	5.16 ± 0.34	405.8 ± 72.16	1.98 ± 0.05
	P-Value		0.416	0.234	0.237	0.590

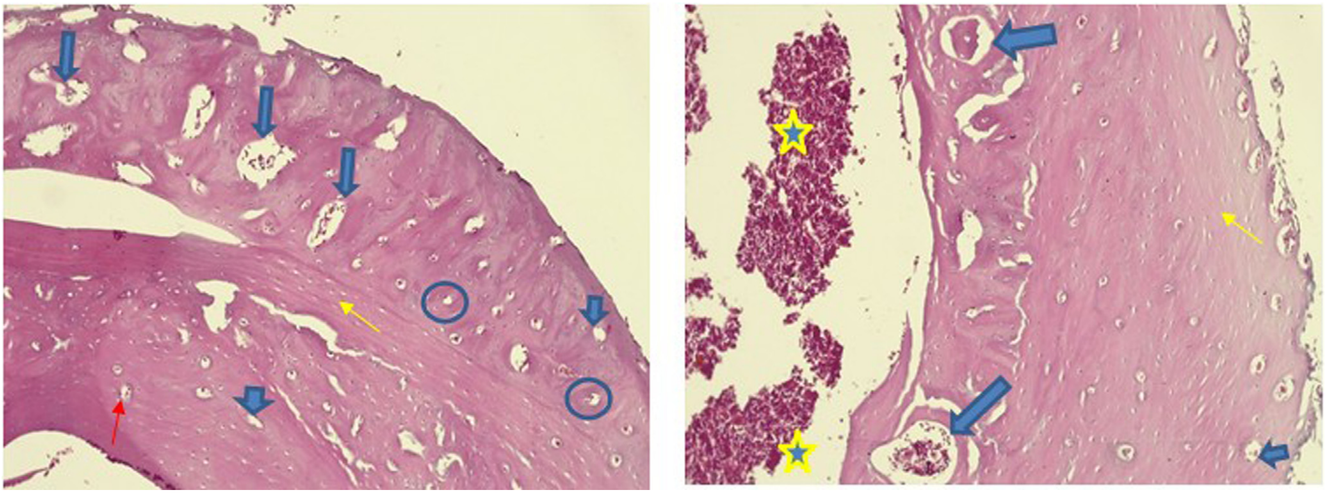

Fig. 1 Photomicrograph of group (I) shows newly formed bone trabeculae with different stainability, Haversian canals with different size and shape (blue arrow), osteoblast cells lining bone trabeculae (yellow arrow), randomly distributed osteocytes inside newly formed bone matrix (red arrow). Reversal lines, irregularly immature bone can also be seen (small circle). Fibro-cellular marrow cavities also noticed. Variable large vacuolated osteocytes and widely enclosed entrapped in lamellar bone (arrow head). Remnant of grafting material (star). H&E (x 200).

This study's superior results with the combined PCL with PRF approach are consistent with other studies recommending coating PCL with fibrin, gelatin, growth factors, or proteoglycan to make its surface more hydrophilic, promoting cell proliferation. This effect may underlie Group A's better ridge height preservation, decreased bone loss, and improved bone densitometric properties (Chuenjitkuntaworn et al., 2016; Mijiritsky et al., 2021b). Numerous studies have examined using PCL membranes in guided tissue regeneration (GTR), showing that visible PCL membranes improve bone growth and bone cell proliferation and attachment (Osathanon et al., 2014). In addition to its use in GTR membranes, PCL has been used to create bone-filling materials to encourage bone regeneration in maxillofacial defects. In many cases, the tailored PCL mesh may be a feasible material for ridge augmentation in the atrophic posterior maxilla, which requires more grafting alternatives than the mandible and additional sinus lifting techniques. The scaffolds are designed to aid the migration and repopulation of alveolar bone and periodontal ligament cells in the affected area, speeding up the healing process (Poomprakobsri et al., 2022; Sousa et al., 2022b).

Group A showed new bone development in this study, possibly because the PCL membrane acts as a physical barrier to stop fibroblast and epithelial cell migration to the target bone region. This outcome was consistent with previous studies showing that PCL membranes have osteoconductivity qualities and immunological compatibility (Chuenjitkuntaworn et al., 2016; Rashad et al., 2018).

Choukroun et al. (2006) created PRF as a second-generation platelet concentrate, a highly concentrated growth factor primarily used for bone defect regeneration. In this study, the PCL nanofibres were covered with a PRF membrane, enhancing the formation of new bone trabeculae in a mature Haversian system (Choukroun et al., 2006; Miron et al., 2017). This result is consistent with other studies showing that PRF membranes can be sliced into minute pieces and put into the graft material, acting as a 'biological matrix' to encourage osteoprogenitor cells to migrate to the centre of the graft and trigger neoangiogenesis (Simonpieri et al., 2009).

PRF improves the efficacy of PCL nanografts by promoting soft tissue repair and bone regeneration. Platelet concentrate technologies include various components, including fibrin matrix and leukocytes, which are sometimes more essential than platelet growth factors. Platelets play an important role in homeostasis and wound healing. They also produce various cytokines and growth factors, giving them antibacterial properties and enabling them to regulate immunological responses (Dohan Ehrenfest et al., 2010; Gandhi et al., 2006). No postoperative infections or severe complications were noticed in our participants, possibly due to the PRF's immunological benefits and high growth factor level. Future studies should compare the long-term effects of these preservation approaches on the alveolar width. The current cases require longer-term monitoring.

5. Conclusions

Combining PCL with PRF enhanced alveolar bone remodelling by decreasing alveolar bone resorption and maintaining its width and height.

Ethical considerations

The present study was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). The study was approved by Research Ethical Committee of Al Azhar University (P-PD-22-07). All patients' personal information was not identified and only the researchers had access to the records.

CrediT authorship contribution statement

Shahenda A. Abdallahb, Shadia Elsayed and Lobna Mohamed contributed to the study concepts. The study design was done by Dr Ebtihal H. Zainalabdeen, Monther Alsharif,. Data acquisition was performed by Lobna Mohamed Abdel-Aziz, Shahenda A. Abdallah, Noura Mohammed bakr, Sara M. Bahaa. Shadia Elsayed, Lobna Mohamed Abdel-Aziz, Shahenda A. Abdallab, and Noura Mohammed bakr contributed to data analyses and interpretation. All authors contributed to the manuscript preparation and manuscript editing and reviewing. All authors read and approved the final manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sdentj.2023.08.012.

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