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COMPARATIVE ANALYSIS OF TWO METHODS OF SOCKET PRESERVATION: A PILOT STUDY

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КОМПАРАТИВНА АНАЛИЗА ДВЕ МЕТОДЕ ПРЕЗЕРВАЦИЈЕ ПОСТЕКСТРАКЦИОНЕ АЛВЕОЛЕ: ПИЛОТ-СТУДИЈА

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ABSTRACT

Objective. Volumetric changes of the residual alveolar ridge begin after tooth extraction. They are more pronounced in the vestibule-oral aspect than in the coronary-apical aspect. In order to preserve the volume of hard and soft tissues, several types of bone grafts, bone substitutes and biomaterials have been used. PRF (Platelet Rich Fibrin) as an autologous blood derivative has been used in recent years as a solo graft material or in combination with other graft materials. The aim of this study was clinical and radiological evaluation of two different methods of socket preservation.

Methods. Two study groups of 10 subjects each, one with socket preservation with solo PRF and the other with PRF+xenograft. Dimensional changes after 4 and 6 months, density of the newly formed bone after 4 months with CBCT 3D (cone beam computed tomography) imaging technique, postoperative morbidity during the first 7 days after intervention were evaluated.

Results. Statistical analysis confirmed lower bone resorption in the PRF+GRAFT test group compared to the PRF group. Better density of the newly formed bone was found in the PRF+GRAFT group and better ratio between the density in the socket and the density in the periapical region. Postoperative morbidity decreased in both groups.

Conclusion. Recommendation for the use of PRF as an adjuvant with other grafts and substitutes, as well as a solo graft material.

Key words: *bone regeneration; tooth socket; platelet-rich fibrin.*

САЖЕТАК

Циљ. Волуметријске промене резидуалног алвеоларног гребена почињу након екстракције зуба. Оне су израженије у вестибуло-оралном аспекту него у коронарно-апикалном аспекту. Ради очувања волумена тврдих и меких ткива коришћено је неколико врста коштаних графтова, коштаних супституената и биоматеријала. PRF (Platelet Rich Fibrin), као аутологни крвни дериват, употребљава се последњих година као самостални графт материјал или у комбинацији с другим графт материјалима. Циљ студије био је да се обави клиничка и радиолошка евалуација две различите методе презервације постекстракционе алвеоле.

Методе. Испитиване су две групе, са по 10 испитаника у свакој групи, с презервираном постекстракционом алвеолом са соло PRF и PRF + ксенографт. Евалуиране су димензионалне промене после четири месеца и шест месеци, густина новоформиране кости после четири месеца и постоперативни морбидитет током првих седам дана након интервенције.

Резултати. Статистичке анализе потврђују мању коштану ресорпцију у PRF + ксенографт тест групи у поређењу с PRF групом. Боља је густина новоформиране кости у PRF + ксенографт групи, као и однос између густине кости у алвеоли и густине у периапикалној регији. Постоперативни морбидитет смањен је у обе групе.

Закључак. Препоручује се примена PRF-а као додатка другим графтовима или супституентима и као самосталног графт материјал.

Кључне речи: *регенерација костију; зубна алвеола; фибрин богат тромбоцитима.*

INTRODUCTION

Post-extraction wound healing processes and volume changes of hard and soft tissues begin immediately after tooth extraction, as the most commonly performed oral-surgical intervention. They end with the stages of bone modeling and remodeling, or bone apposition and resorption (1). The resorption of the residual alveolar ridge is a time-dependent process that is most pronounced in the first year, especially in the first six months, when two thirds of the total volume is resorbed. It is more pronounced in the vestibule-oral aspect than in the coronary-apical aspect (2, 3).

The preservation, as well as the creation of the biological foundation, or maintaining the quantity and quality of the hard and soft tissues of the residual alveolar ridge, are the basis for successful further implant-prosthetic or prosthetic rehabilitation. All this is aimed at satisfying the aesthetic and functional needs of the patient. In this direction, the methods of guided bone regeneration (GBR) and guided tissue regeneration (GTR) are being developed. GBR methods, on the other hand, are divided into residual alveolar ridge augmentation (ARA), which involves restoration the lost volume of the residual alveolar ridge, and residual alveolar ridge preservation

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(ARP), which also includes preservation of the post-extraction socket (SP). and is recommended as the most predictable, economical, and the simplest method of GBR (4, 5). In GBR methods, several types of bone grafts, bone substitutes and biomaterials are used, and, depending on their origin, they are grouped into autografts, allografts, xenografts and alloplastic materials. Autografts are considered the gold standard in GBR as well as GTR (6, 7).

The PRF protocol is a physiological method based on using centrifugal force to fractionate blood elements from platelet-enriched fibrin in specially designed tubes, glass-coated on the inside, opposite to the complicated procedure of obtaining PRP, and using bovine fibrin and an anticoagulant of the calcium chloride type. After the centrifugation procedure in the A-PRF tubes, three separate fractions are obtained in the test tube, namely: a layer of supernatant or platelet-poor plasma (PPP), fibrin coagulum (Fibrin cloth) and erythrocyte sediment (ES) (8). The mechanism of action of PRF is complex and it includes the structure and the composition which enables its application in several indications in oral and maxillofacial surgery (9-10).

The aim of this comparative prospective study is the clinical and radiological evaluation of two different methods of socket preservation (PRF+graft and solo PRF).

PATIENTS AND METHODS

In this clinical study, 20 patients were included, who were all older than 18 years of age, of both sexes, fulfilling inclusion and exclusion criteria, and having previously signed an informed consent (Informed Consent Form-ICF) according to the Helsinki Declaration of 1975, revised in 2013 to perform the interventions.

Inclusion criteria: patients aged 18-65 years and health status of patients, classified as ASA I and ASA II, according to the ASA (American Society of Anesthesiologists) classification of diseases.

Exclusion criteria: patients with a medical condition classified from ASA III-ASA V, according to the ASA classification, pregnant and lactating women, patients with metabolic and other bone diseases (osteoporosis, osteopetrosis, Paget's disease, benign and malignant tumors, etc.), patients who received systemic bisphosphonate therapy, due to compromised bone metabolism during its use.

The clinical study was performed at the Clinic for Oral Surgery and Implantology at the University Dental Clinic "St. Panteleimon" - Skopje. The patients were divided into two groups of 10 patients. PRF was used as a sole graft material in the first group, and in the second group the new bone matrix of a combination of PRF with xenograft (Sticky bone) was used for socket preservation.

The selection of patients included in the study, began with setting an indication for the extraction of a particular tooth. It was established after taking a detailed history of the patient, as well as clinical and paraclinical examinations.

Figure 1. Vacutainer Venipuncture

Figure 2. A-PRF Centrifugation

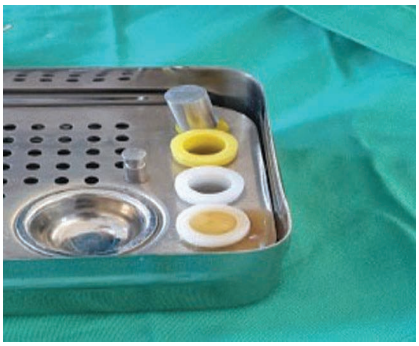

Figure 3. PRF Plug.

Figure 4. PRF membrane

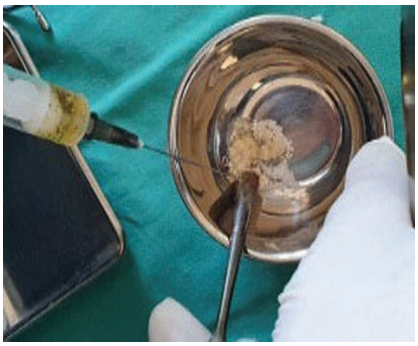

Figure 5. Sticky bone

Figure 6. Stabilization suture

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Subjects were further included or excluded from the study according to the strictly determined criteria.

All oral surgical interventions were performed respecting the principles of asepsis and antisepsis and surgical protocols, as well as surgical debridement of the post-extraction wound.

After the extraction of the indicated teeth, in the first group, the preparation of PRF for the socket preservation was started, with venipuncture of blood in specially designed A-PRF tubes of 10 ml according to the Vacutainer method (Figure 1), and centrifugation according to the Choukroun modification method to obtain A-PRF (Figure 2). PRF plugs and PRF membranes were formed in a specially designed PRF-box (Figure 3, 4). The plugs were applied in the post-extraction alveoli, they were covered with the membranes and stabilization sutures were placed.

In the patients of the second group, after tooth extraction, the preparation of sticky bone was started by mixing the particulate xenograft of bovine origin with

Figure 7. CBCT solo PRF

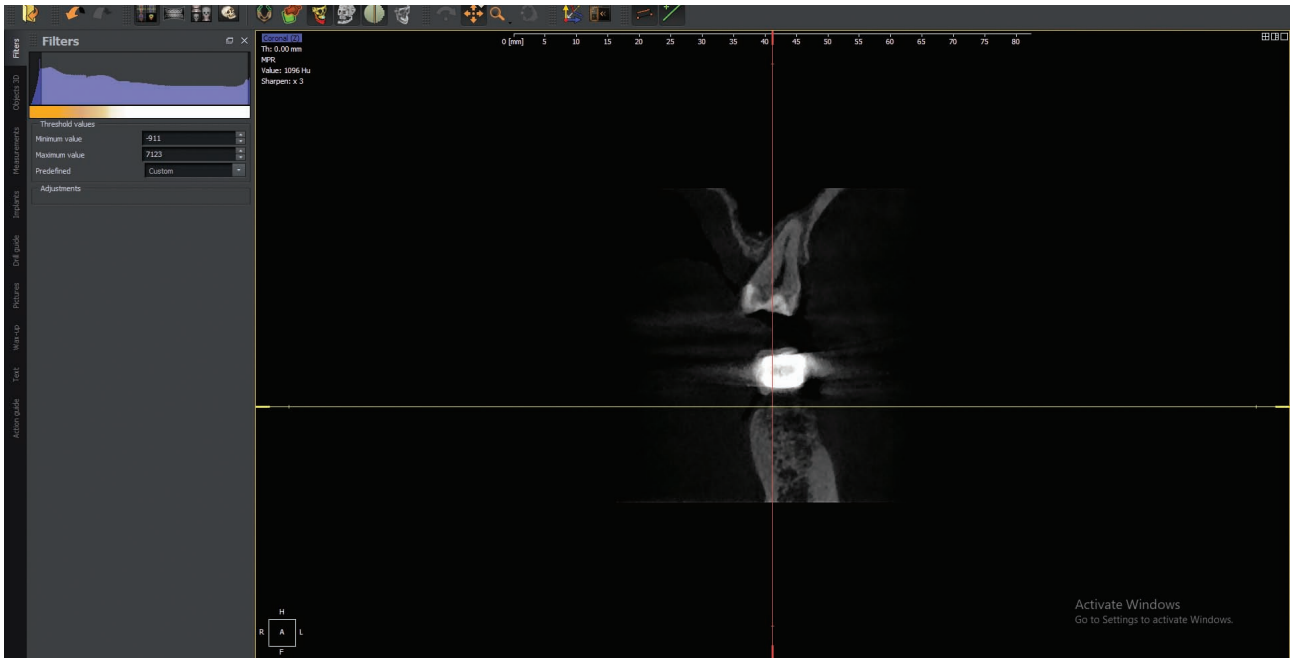

Figure 8. CBCT PRF+GRAFT

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PRF supernatant and chopped pieces of one membrane to the desired consistency (Figure 5). Using the PRF sticky bone instruments, the complex graft (sticky bone) was applied and adapted in the post-extraction sockets by applying gentle pressure for discrete condensation and modeling. Then the complex graft was covered with the second PRF membrane and stabilization sutures were placed (Figure 6).

Immediately after the surgical extractions of the indicated teeth, and preservation of the post-extraction alveoli with the two graft materials in the two studied groups, clinical measurements of the width of the residual alveolar ridge at its most prominent points were performed, using a bone measurement caliper. Measurement of the height of the residual alveolar ridge of the post-extraction alveolus was performed from the cement-enamel junction of the adjacent tooth to the top of the interdental septum with the adjacent tooth, with a graduated periodontal probe. Measurement of the height of the interdental papilla was performed from the cement-enamel junction of the agonist tooth to the tip of the interdental papilla, with a graduated periodontal probe.

Postoperative morbidity was also evaluated in the period immediately after the oral-surgical intervention by noting data on body temperature, presence of pain according to VAS (visual analogue scale), presence of postoperative edema, hematoma, trismus, regional lymphadenitis, function lost and use of analgesic.

Four months postoperatively, the clinical measurements of the width and height parameters of the residual alveolar ridge, as well as the height of the interdental papilla, were performed again, in the same way as before.

Also, four months postoperatively, paraclinical measurements of the density of the newly formed bone within the preserved alveoli, as well as the density of the newly formed bone in the periapical region of the post-extraction alveolus, were performed. These paraclinical examinations were performed using CBCT (cone beam computed tomography) - 3D imaging technique on OWANDY I-MAX 2/3D device, and analyzed on OWANDY Quckvision 2/3D software, expressed in HU (Hounsfield Units) (Figures 7, 8).

Data were described as number and/or percentage, or mean with standard errors of mean (SEM), where appropriate. The differences between groups were explored using the t-test followed by 1-way ANOVA, where appropriate. A p-value of less than 0.05 was considered significant. All analyses were made using the statistical program GraphPad Prism 9 (USA).

RESULTS

Distribution of post-extraction alveoli according to the localization is presented in Figure 9. From the graphic display of the distribution of post-extraction alveoli with subsequent socket preservation in both studied groups, there was a notable representation of surgical interventions in all regions in both jaws, with the exception of upper incisors (Figures 9 and 10).

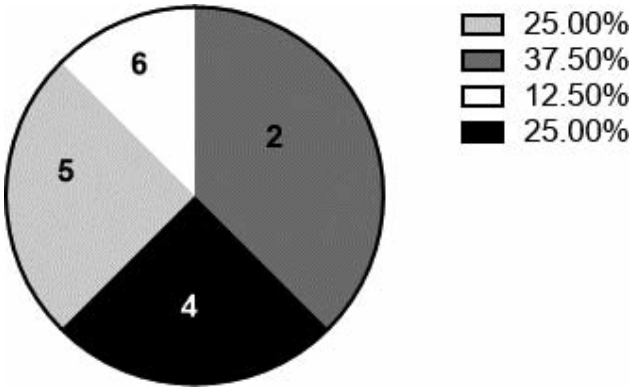

Figure 9. Distribution of the localization of preserved alveoli in the group of patients treated with PRF (1 - upper incisors, 2 - upper premolars, 3 - upper molars, 4 - lower incisors, 5 - lower premolars, 6 - lower molars).

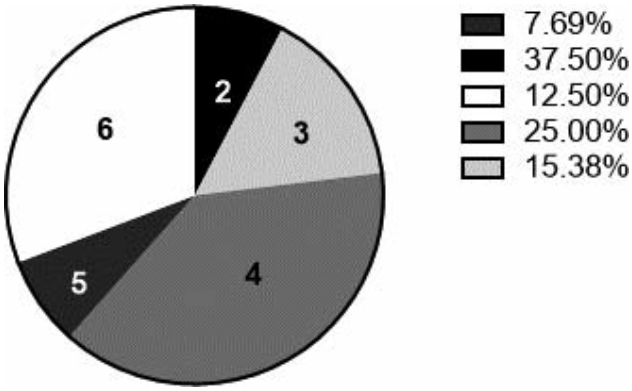

Figure 10. Distribution of the localization of preserved alveoli in the group of patients treated with PRF (1 - upper incisors, 2 - upper premolars, 3 - upper molars, 4 - lower incisors, 5 - lower premolars, 6 - lower molars).

Dimensional changes

Statistical analysis was performed on measurements of residual alveolar ridge width in vestibule-oral aspect, height of residual alveolar ridge in coronal-apical aspect, and height of interdental papillae. The same parameters were analyzed within the studied groups in the three periods (immediately after the intervention, 4 months postoperatively, and 6 months postoperatively), as well as a comparison of the dimensional differences between the two studied groups.

Horizontal changes

The measured mean width of the post-extraction alveoli immediately postoperatively was 11.01 mm±2.61, with a loss of width of 1.44±0.85 after 4 months and consequently 2.30±1.05 after 6 months postoperatively in

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the studied group with PRF as an independent graft material.

In the studied group with PRF+GRAFT, the measured mean width of the post-extraction alveoli immediately postoperatively was 10.51mm±1.94, with a loss of width of 1.39±0.92 after 4 months and consequently 1.47±0.89 after 6 months postoperatively.

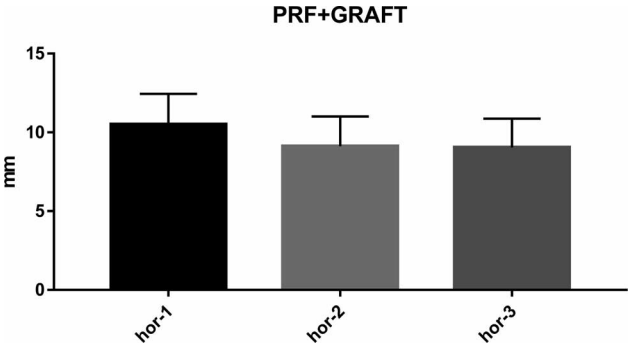

Figure 11. Presentation of the horizontal dimensions in the group of patients treated with PRF+GRAFT (1 - immediately before intervention, 2 - 4 months after intervention, 3 - 6 months after intervention).

A statistically significant difference ($p<0.05$) was determined between the measurements of the horizontal dimension of the post-extraction alveoli taken immediately before the intervention and after 6 months of the intervention in the study group in which PRF was used as a solo graft material for the socket preservation (Figure 11).

Vertical changes

Dimensional changes in the coronary-apical direction ranged with the mean value of 3.75 mm±1.04 immediately postoperatively, with a loss of 0.50±1.31 during the first 4 months and consequently 1.00±1.07 after 6 months for the studied group with PRF as an independent graft material.

The vertical dimension of the post extraction alveolus in the studied group with PRF+GRAFT ranged from the mean value of 4.81 mm±2.08 immediately postoperatively, with reduced dimensions of 0.27±1.45 in the first 4 months and 0.19±1.49 in the first six months.

The statistical analysis did not show statistical significance of the dimensional changes for vertical loss in the two studied groups (Figures 12, 13).

Dimensional changes of interdental papilla height

The height of the interdental papillae ranged from the mean value of 0.94 mm±0.56 immediately postoperatively to a loss of 0.50±0.96 after 4 months and consequently 0.88±0.79 in the first six months in the study group with PRF as the sole graft material.

The dimensional differences of the interdental papillae in the studied group with PRF+GRAFT ranged from the mean value of 1.69 mm±1.03 immediately postoperatively, through a loss of 0.62±0.96 after 4 months to 0.85±0.88 after the first six months.

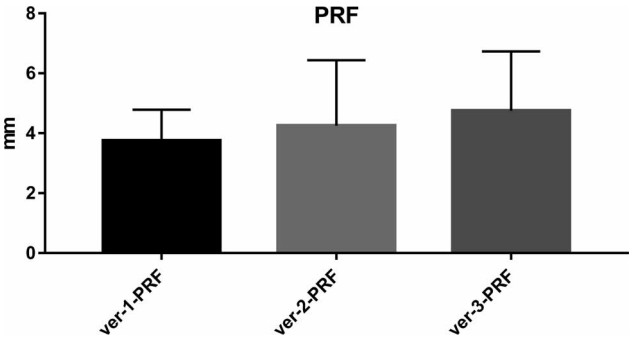

Figure 12. Display of vertical dimensions in the group of patients treated with PRF (1 - immediately before intervention, 2 - 4 months after intervention, 3 - 6 months after intervention).

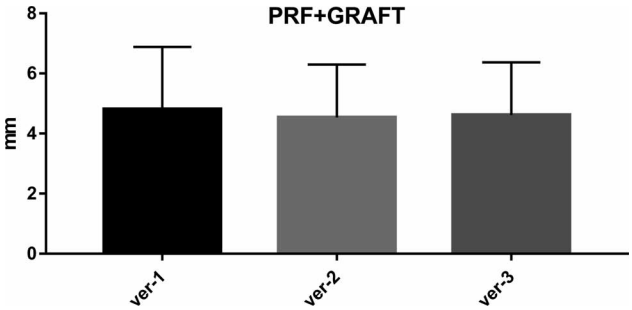

Figure 13. Display of vertical dimensions in the group of patients treated with PRF+GRAFT (1 - immediately before intervention, 2 - 4 months after intervention, 3 - 6 months after intervention).

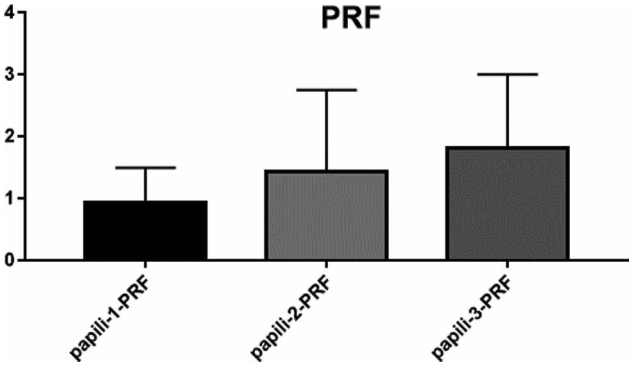

Figure 14. Presentation of the height of the interdental papillae in the group of patients treated with PRF (1 - immediately before intervention, 2 - 4 months after intervention, 3 - 6 months after intervention).

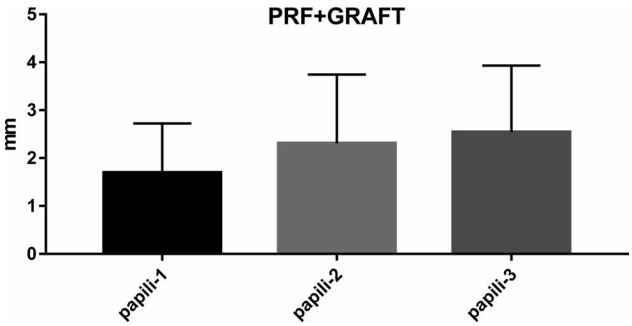

Figure 15. Presentation of the height of the interdental papillae in the group of patients treated with PRF+GRAFT (1 - immediately before intervention, 2 - 4 months after intervention, 3 - 6 months after intervention)

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Comparison between the studied groups

Horizontal dimension

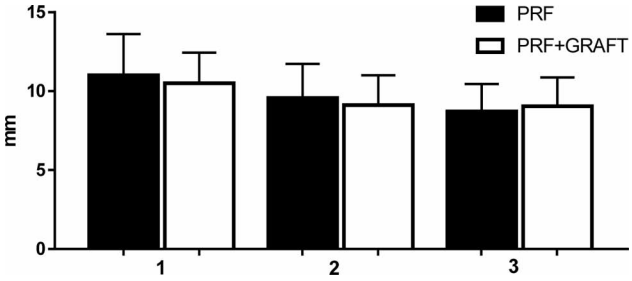

Figure 16. 8. Comparison of the horizontal dimensions between the two studied groups (1 - immediately before the intervention, 2 - 4 months after the intervention, 3 - 6 months after the intervention)

Vertical dimension

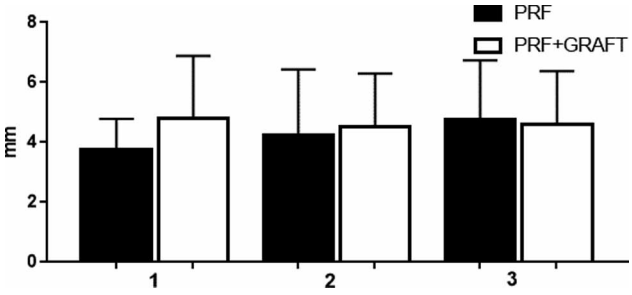

Figure 17. Comparison of the vertical dimensions between the two studied groups (1 - immediately before the intervention, 2 - 4 months after the intervention, 3 - 6 months after the intervention).

Dimension of interdental papillae height

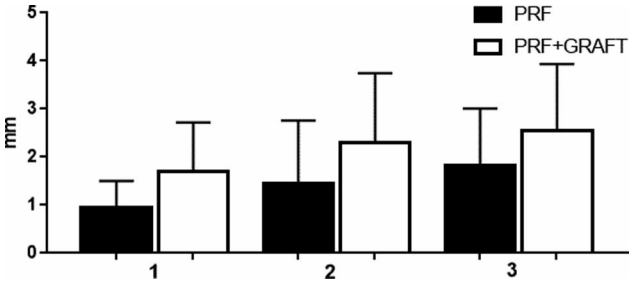

Figure 18. Comparison of the height of the interdental papillae between the two studied groups (1 - immediately before intervention, 2 - 4 months after intervention, 3 - 6 months after intervention).

From the comparative statistical analyzes of the dimensional changes of the residual alveolar ridge width and height and the interdental papilla height between the two studied groups, no statistical significance was observed (Figures 16-18).

CBCT 3D comparison between groups of the density of the newly formed bone in the preserved alveolus and periapical region

With the help of the CBCT 3D imaging technique, 4 months postoperatively, the density of the newly formed bone was measured in the preserved alveoli and in the periapical region, with results for the mean value of 373.88 HU±140.46 within the alveoli and consequently 565.88 HU±195.72 in the periapical region in subjects from the group with PRF used as graft material, and the mean value of 854.62 HU±185.73 in the post-extraction alveoli and 782.46 HU±322.84 in the periapical region in the study group with PRF+GRAFT for preservation of the post-extraction alveoli.

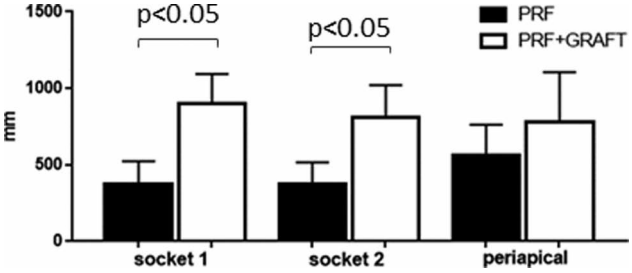

Figure 19. Comparison of the density of the newly created bone in the post-extraction alveolus and periapical region between the two studied groups (socket 1 - coronal projection, socket 2 - sagittal projection, periapical-periapical region).

A statistically significant difference was determined in the density values of the newly formed bone on the CBCT 3D imaging technique in the post-extraction alveoli in the coronal projection ($p<0.05$) and in the sagittal projection ($p<0.05$) between the group of patients treated with PRF alone and the group of patients treated with PRF +GRAFT (Figure 19).

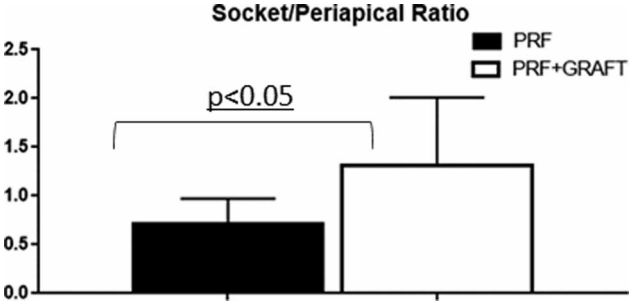

Figure 20. Relationship between the density of the newly created bone in the post-extraction alveolus and the periapical region between the two studied groups (socket - mean value of the dimensions in coronal projection and sagittal projection, periapical-periapical region).

A statistically significant difference was determined in the ratio between the density of the newly created bone in the post-extraction alveolus and the periapical region between the two studied groups ($p<0.05$) (Figure 20).

Postoperative morbidity

Of all the patients included in the study group with PRF as a sole graft material for the socket preservation, postoperative sequelae occurred in two patients, one of whom had moderate pain and postoperative edema that

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occurred on the third day postoperatively, and the second patient had only mild pain. Both patients consumed one analgesic from the group of nonsteroidal anti-inflammatory drugs on the first day after surgery.

In the other study group, where PRF+GRAFT was used for SP, postoperative sequelae occurred in two patients with mild pain and mild postoperative edema, who used one dose of nonsteroidal anti-inflammatory drugs each, in one patient in the immediate postoperative period. Moderate pain, moderate edema and grade II trismus occurred after the extraction of an impacted lower third molar with subsequent SP, and he was prescribed analgesic therapy during the first three days postoperatively.

DISCUSSION

A-PRF as a second generation of autologous blood derivatives is characterized by a specific histomorphometric structure of a tri- and tetra- molecular network of dense fibrin mesh and an incorporated huge of platelets, from which GF I ILs are released, which are of key importance for its properties and mechanism of action. They participate in cell differentiation, proliferation and migration (11).

In a previously performed study by Baca-Gonzalez and associates, the effect of GF and IL on the increased osteoblastic activity and thus on neo-osteogenesis has been proven (12). The effects of PRF-released GF on fibroblast activity have been demonstrated in an in vitro study by Pitzzura and associates, and thus the improved efficacy of PRF in soft tissue healing and increased neocollagenogenesis (13). The positive effects in neoangiogenesis through the released VEGF and PDGF from PRF in combination with xenograft on stem cells from the periodontal ligament have been evaluated in the in vitro study of Nguyen and associates (14).

Dohan and associates described in their study the action of PRF, its influences on defense mechanisms, particularly analyzing the role of cytokines (15). Miron and associates in their study described PRF as a drug delivery system due to its minimally invasive application at the site of tissue rehabilitation, through the slow release of small and large biomolecules from the fibrin matrix in the surrounding tissues until bio resorption of the fibrin network in a period of 10 to 14 days (16).

A key role for the successful rate of long-term survival, as well as the aesthetic and functional outcome of the inserted dental implants, in addition to the bone volume of the residual alveolar ridge, is also its bone density. For that reason, Misch C. made a classification of the alveolar bone according to its density as D1 (> 1250 HU), D2 (850 to 1250 HU), D3 (350 to 850 HU), D4 (150 to 350 HU), and D5 (< 150 HU), expressed in Hounsfield units. Residual alveolar ridge bone with a density of D2 and D3 is recommended as the most recommended for predictable successful implantation (17).

From the results obtained in this clinical study and their statistical analysis, it is noted that the volumetric changes in relation to the width andheight of the residual alveolar ridge as well the interdental papilla height within the studied groups, and the comparison between the studied groups does not give statistically significant differences, except in the study group where PRF was used as the sole graft material and that was in the horizontal dimension measured 6 months postoperatively in relation to the width measured immediately postoperatively.

Regarding the density of the newly created bone in the post-extraction alveoli in the both studied groups, a significant difference is noticeable in favor of the studied group in which PRF+GRAFT was used. A significant difference in the ratio between the density of the newly formed bone in the preserved alveoli and the bone density in the periapical region was also observed in favor of the studied group with PRF+GRAFT.

The evaluation of postoperative morbidity in both studied groups showed reduced postoperative sequelae, and the absence or small number of patients with pain, postoperative edema, hematoma, trismus, infection and increased body temperature, as well as reduced administration of nonsteroidal anti-inflammatory drugs in the postoperative period.

In a similarly designed study by Kollati and associates, volumetric and radiological analyzes were performed on two treated groups. In one, PRF was used as a stand-alone graft material, and in the other, PRF+ CERABONE bovine xenograft was used as graft material. Similar results were observed for horizontal bone loss of 1.28 mm in favor of the xenograft study group. The vertical dimensional difference was 0.62 mm on the mesial, ie 0.38mm on the distal interdental septum. Radiological analysis also showed improved infilling with the newly formed bone in the preserved postextraction alveoli with the combination of PRF with the xenograft material. And the evaluated postoperative morbidity corresponds with our results (18).

The comparative analysis of the two studied groups using alloplastic material alone and in combination with A-PRF indicateed reduced horizontal and vertical resorption, as well as improved neoosteogenesis in the group using A-PRF as an adjuvant, but still no statistically significant difference (19).

In a systematic review study by Jambhekar and associates, in which 32 randomized clinical trials on SP with different types of graft materials were analyzed, information was obtained on horizontal dimensional differences in the first three months, for xenograft - 1.3

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mm, and for physiological resorption without using graft materials - 2.79 mm. The results of our study are superior to graft materials in relation to physiological healing and correspond to data on xenograft as a graft material (20).

In the split-mouth randomized clinical trial of Castro and associates, dimensional, CBCT and histomorphometric analyzes of post-extraction alveoli preserved with A-PRF, L-PRF and with physiological wound healing were performed. It was concluded that there was no significant difference in dimensional changes, but on the other hand, the filling with vital newly formed bone in the alveoli is improved, which is recorded on CBCT, and it was also confirmed on histomorphometric analyzes (21).

In summary, it can be concluded that PRF as a sole autologous graft material has equally good performance and ability to preserve bone quantity (horizontal and vertical dimension) and quality (bone density and architectonics) and provides optimal conditions for later implant-prosthetic rehabilitation. Solo PRF in the socket preservation acts in the direction of maintaining the clinical aspects of the red-white aesthetics (quantity and quality of the soft structures). PRF has a significant impact in reducing postoperative sequelae and reduced overall use of non-steroidal anti-inflammatory drugs. As an autologous, inexpensive and safe graft material, it can be freely recommended in socket preservation techniques.

Herein, authors would like to state that the study had several limitations. First, this was a single-center study at a tertiary public hospital with limited finances that had impact on the sample size. A multi-center study, with a bigger sample size that will include more patients is needed to further clarify the importance of PRF and PRF+xenograft in socket preservation.

CONFLICT OF INTEREST

The authors declare no conflict of interest relating to the manufacturing, distribution, selling and promotion of dental devices and equipment mentioned in the article.

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