The Benefits of Platelet-Rich Fibrin in Promoting Post-Extraction Healing

CHERANA GIOGA[1], EDWIN SEVER BECHIR[2]*, FARAH CURT MOLA[2], CARMEN LILIANA DEFTA[3], ANAMARIA BECHIR[1], CARMEN BIRIS[2], ADINA MAGDALENA BUNGET[5]

[1] Titu Maiorescu University of Bucharest, Faculty of Dental Medicine, 67A Gheorghe Petrascu Str., 031593, Bucharest, Romania

[2] Medicine and Pharmacy University of Tirgu Mures, Faculty of Dental Medicine, 38 Gheorghe Marinescu Str., 540142, Tirgu Mures, Romania

[3] Carol Davila Medicine and Pharmacy University of Bucharest, Faculty of Dental Medicine, 37 Dionisie Lupus Street, 020021 Bucharest, Romania

[4] Medicine and Pharmacy University of Craiova, Faculty of Dental Medicine, 2-4 Petru Rares Str., 200349, Craiova, Romania

The aim of this study was to evaluate pain intensity and wound healing of the post-extraction sites after the use of Platelet-Rich Fibrin (PRF). 240 patients which needed difficult or multiple extractions were included in the study. The extractions were realized under local anesthesia, with piezotome and pliers. The patients were divided in two groups, the first group of 120 patients which benefited the application of PRF in the post-extraction alveoli, and the second group of 120 patients represented the control group (without application of PRF). A questionnaire was realized after a VAS analog scale and was used to quantify the post-intervention pain intensity in the postoperative four days. The assessment of the post-extraction sites healing period was performed clinically. According to the obtained results, the healing period of the post-extraction sites was shorter in the patients of first group (PRF), compared to the sites of control group patients. No postextractional healing complications occurred in the patients of first group/PRF. The study demonstrated the benefits of PRF insertion in post-intervention healing.

Keywords: difficult or multiple extractions, PRF insertion, pain intensity, healing period

Dental biomaterials are defined as substances or combinations of substances, of natural or synthetic origin, which are in intimate contact with the living tissues of the human body. A material is biocompatible when it does not produce any physiological, cellular and immunological, local or systemic disorder [1]. Besides biomechanical properties, biocompatibility represented by the host response to a biomaterial is one of the most important parameter taken into account [2,3]. In generally, the biocompatible materials are represented by scaffolds with microporous structures, within the cells are able to grow and to generating new tissue [4,5].

A scaffold should acts as a temporary basis for various cell populations, for tissue regeneration/repair [6]. By modulating cellular proliferation, by accelerating extracellular matrix synthesis and by promoting angiogenesis, growth factors play a role in the evolution of undifferentiated mesenchymal cells to specialized cell lines or tissue healing. They are initially deposited in the extracellular matrix and they are released during matrix degradation [7]. Platelet-Rich Fibrin (PRF) is defined as an autologous platelet and growth factors rich fibrin matrix with roles in wound healing and tissue repair [8]. The three-dimensional fibrin network inserted into the treated area determines effective neovascularization of the area, accelerated wound healing, and rapid scar tissue remodeling [9]. PRF is obtained from the patient's blood extracted during the surgical procedure and processed by specific protocols and special equipment by a procedure that does not require the biochemical influence of harvested blood [10].

VAS is one-dimensional analog scale used for measuring the pain intensity in adult populations. VAS scale have the advantage of easy and quick use, as well as the amount of time required to fill in the questionnaire, and also the low cost [11,12].

* email: bechir.edwin@gmail.com; Phone: (+40)723396969

The purpose of this study was to evaluate the effects of PRF in the densification of the maxillary bones, applied for the improvement / healing of the post-extraction wound.

Experimental part

Material and method

In order to perform this study, we selected 240 patients, divided them into two groups of 120 patients. The patients of first group (60 females and 60 males, aged 29-58, mean age 43.5 years, ± 14.5 years), benefited PRF biomaterial insertion after difficult/multiple dental extractions. The second group of patients was represented by the control group and included 120 patients too (60 females and 60 males, aged 29-58, mean age 43.5 years, ± 14.5 years), without application of PRF in the post-extraction alveoli.

Chart 1 shows the distribution of patients by age in the two studied groups.

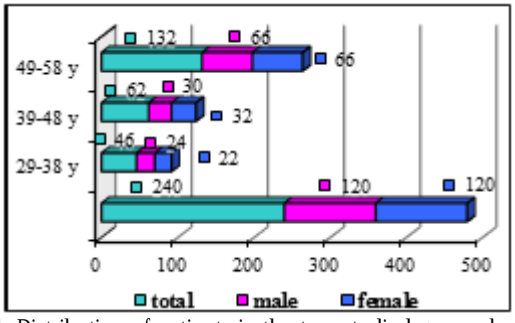

Chart 1. Distribution of patients in the two studied groups by age

The study was conducted in the Dental Medicine Faculties of Bucharest, Tirgu Mures, and Craiova.

The criteria for inclusion in the study were represented by systemic factors (no chronic diseases, to not influence the healing of post-extraction sites), behavioral factors (non-smoking patients), dental and periodontal factors (Silness and Loe dental index ranging from 0 to 1 and

interdental papillary index-PBI index score 1 at the time of surgery), patients who previously had postoperative pains of varying degrees of intensity in dental area. Exclusion criteria were represented by patients with chronic diseases, dental and periodontal factors (Silness and Loe 2-3 dental index, respectively 2-3 PBI index previous surgery on interventional sites), patients who previously did not experience extractions in the oral cavity, pregnant/lactating patients, those are used contraceptives, and the smokers.

The examination and selection of the patients was conducted by the researchers who efectuated subsequently the surgical procedure. The postoperative determinations were realized by the other researchers, which were not informed about the patient's belongin in the study group.

The used protocol in PRF preparation consisted in venous blood collection (without anticoagulants), centrifugation (1500 rpm, 12 min), for obtaining the three fractions of blood (fig. 1).

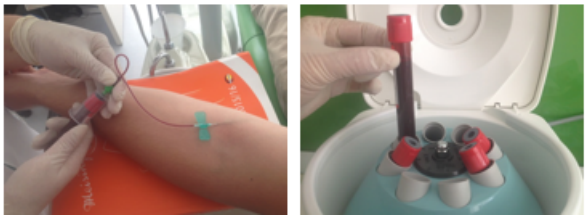

Fig. 1. Collecting venous blood and inserting vacutainers into the centrifuge

Removal of the centrifugation mass from vacutainers, collecting the fraction for application in the surgical site and obtaining the PRF for use are presented in figure 2.

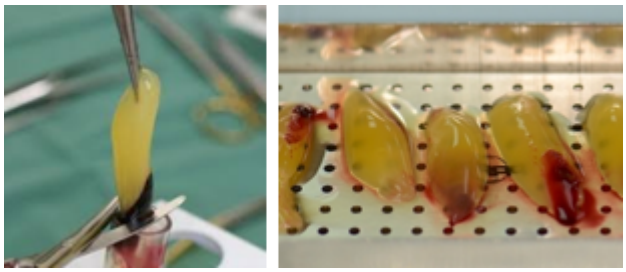

Fig. 2. Appearance of the obtained and ready for use PRF

The clinical, interventional and postoperative protocol applied to all patients, were: specialized consultation; complementary imaging examinations (retroalveolar/ OPG/CBCT); diagnosis of the oral cavity and general health status; establishing the treatment plan; signing the agreement for the treatment plan and of the informed consent; professional cleaning; the rinse of the oral cavity with sodium bicarbonate solution (to increase oral pH, two days before surgery and twice a day for one week after intervention); performing difficult/multiple extractions, as atraumatic as possible, preferably by surgery with piezotome, under local anesthesia. In the first group (PRF) of this study, the post-interventional addition of PRF was performed directly as a *filler* in post-extraction site and at the end of the surgery, the resulting blood plasma was used to hydrate the operated surface. All the sutures were realized with teflon thread (to avoid microbial overload at the perilesional soft parts). All patients used Gengigel spray with hyaluronic acid (20 mL, Ricerfarm), 2 sprays per day on the intervention area of oral tissue. Non-steroidal anti-inflammatory medication (Ibuprofen 200 mg film-coated tablets, 3x2 daily for five days) was indicated. We explained to each patient in part how to complete the post-operative pain evaluation questionnaire. Removal of teflon threads were performed at 7 days after the intervention.

To assess the post-interventional pain intensity, we distributed a questionnaire to each patient included in the study. Patients noted the pain intensity at the end of the first, second, third and fourth day after the surgery intervention. The questions, according to the analogical visual scale VAS, presented as extreme reference points 0 = no pain and 10 = extreme pain. Patients scored the reference for the most severe pain experienced during the days studied (days 1, 2, 3 and 4) (fig. 3).

	Group	On the day of surgery	The first day after surgery	The second day after surgery	The third day after surgery
The average of pain intensity after cessation of the anesthetic effect	1	VAS 0	VAS 0	VAS 0	VAS 0
		VAS 1-3	VAS 1-3	VAS 1-3	VAS 1-3
		VAS 4-6	VAS 4-6	VAS 4-6	VAS 4-6
		VAS 7-9	VAS 7-9	VAS 7-9	VAS 7-9
		VAS 10	VAS 10	VAS 10	VAS 10
	2	VAS 0	VAS 0	VAS 0	VAS 0
		VAS 1-3	VAS 1-3	VAS 1-3	VAS 1-3
		VAS 4-6	VAS 4-6	VAS 4-6	VAS 4-6
		VAS 7-9	VAS 7-9	VAS 7-9	VAS 7-9
		VAS 10	VAS 10	VAS 10	VAS 10
		VAS 0	VAS 0	VAS 0	VAS 0

Fig. 3. Pain intensity questionnaire (VAS) used in this research

The second part of questionnaire recorded the responses of the patients to the other four questions: administration of anti-inflammatory drugs in higher dose than prescribed; taking other drugs or other medications than prescribed; addressability to another dentist, due to post-surgical pain; the incapacity to work.

In figure 4 is presented the case of a patient with a radicular rest at level of tooth 4.6. The extraction was performed conservatively with the dental piezoelectric instrument and the dental alveolus was immediately filled with PRF.

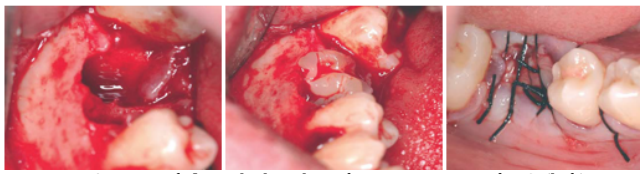

Fig. 4. Aspect of dental alveolar after extraction of 4.6 (left), PRF completion in the alveolus (center) and sutured postexractional wound (right)

Table 1 present the reported answers of pain intensity in the patients, according to the analogical visual scale for pain. The reference points used in our study were: VAS 0 = no pain; VAS 1-3 = mild/moderate pain; VAS 4-6 = moderate/severe pain; VAS 7-9 = very severe pain; VAS 10 = the most intense pain possible.

Regarding the pain intensity reported by patients participating in the study, according to the analog scale, we observed that the pain was more acute the first day, then decreased linearly. The most acute levels of pain intensity were recorded during the first 36 hours after the disappearance of the anesthetic effect, and the reported pain level at the end of the first and second day after surgery was significantly higher, compared to days 3 and 4.

During the first and second evenings, the noted pain intensity was even more pronounced in those who underwent lower jaw surgery compared to those performed at the upper jaw.

We also noticed that all patients aged less than 38 years (46 patients, 24 female and 22 males) experienced higher post-intervention pains, with an average by one VAS unit.

	Group	On the day of surgery (first day)		The day after surgery (second day)		Second day after surgery (third day)		Third day after surgery (fourth day)	
The average of pain intensity after the cessation of the anesthetic effect	I 120 patients	VAS 0	-	VAS 0	-	VAS 0	-	VAS 0	18 (=15.00%)
		VAS 1-3	8 (=6.66%)	VAS 1-3	22 (=18.33%)	VAS 1-3	35 (=29.16%)	VAS 1-3	42 (=35.00%)
		VAS 4-6	47 (=39.16%)	VAS 4-6	45 (=37.5%)	VAS 4-6	44 (=36.66%)	VAS 4-6	39 (=32.50%)
		VAS 7-9	44 (=36.66%)	VAS 7-9	46 (=38.33%	VAS 7-9	41 (=34.16%	VAS 7-9	21 (=17.50%)
		VAS 10	21 (17.50%)	VAS 10	7 (=5.83%)	VAS 10	-	VAS 10	-
	II 120 patients	VAS 0	-	VAS 0	-	VAS 0	-	VAS 0	2 (=1.66%)
		VAS 1-3	-	VAS 1-3	-	VAS 1-3	8 (=6.66%)	VAS 1-3	26 (=21.66%)
		VAS 4-6	21 (=17.50%)	VAS 4-6	25 (=20.83%	VAS 4-6	33 (=27.5%)	VAS 4-6	35 (=29.16%)
		VAS 7-9	62 (=51.66%)	VAS 7-9	60 (=50.00%	VAS 7-9	57 (=47.50%	VAS 7-9	38 (=31.66%)
		VAS 10	37 (=30.83%)	VAS 10	35 (=29.16%	VAS 10	22 (=18.33%	VAS 10	19 (=15.83%)

Table 1
REPORTED ANSWERS OF PAIN INTENSITY ACCORDING TO THE VISUAL ANALOGUE SCALE (VAS)

	Group	On the day of surgery	The day after surgery (second day)	The second day after surgery (third day)	The third day after surgery (fourth day)
Administration of anti-inflammatory drugs in higher dose than prescribed	I	19 (=15.83%)	19 (=15.83%)	6 (=5%)	-
	II	35 (=29.16%)	35 (=29.16%)	21 (=17.5%)	17 (=14.16%)
Taking additional medication (antibiotics) than prescribed	I	19 (=15.83%)	19 (=15.83%)	6 (=5%)	-
	II	35 (=29.16%)	35 (=29.16%)	21 (=17.5%)	17 (=14.16%)
Addressable to another dentist due to post-surgical pain	I	-	-	-	-
	II	-	-	-	-
Incapacity to work	I	15 (=12.5)	15 (=12.5)	-	-
	II	33 (=27.5)	33 (=27.5)	26 (=21.66%)	17 (=14.16%)

Table 2
THE RESPONSES OF THE PATIENTS TO THE OTHER QUESTIONS

We have also found that in interventions that lasted more than 60 min, the noted pain of patients was higher, on average by two VAS units, compared to those patients who had surgery within a shorter time interval than 60 min.

The anatomical position of the teeth on the posterior or anterior area of the dental arches also influenced the recorded scores in pain intensity, those in the distal area showing higher scores on average by a VAS unit.

Table 2 lists the responses of the patients to the other four questions (administration of anti-inflammatory drugs in higher dose than prescribed; taking other drugs or other medications than prescribed; addressability to another dentist, due to post-surgical pain; the incapacity to work).

19 patients of the first group (PRF) and 35 patients in the second/control group required the administration of anti-inflammatory drugs in higher dose than prescribed and additional (antibiotic) medication on the day of surgery and the day after surgery. In the second day after surgery, 6 patients of PRF group and 21 patients of control group required the administration of anti-inflammatory drugs in higher dose than prescribed and antibiotic medication. In the third day after surgery, no patient of PRF group and 17 patients of control group required the administration of anti-inflammatory drugs in higher dose than prescribed and antibiotic medication. None of the patients participating in the study addressed another dentist due to post-surgical pain. 17 patients in the first group (PRF) and 33 patients in the second/control group reported the inability to work on the day and the day after surgical intervention. On the third and fourth day, no patient in the first group (PRF) reported the incapacity to work. In the control group, 26 patients reported the incapacity to work on the third day and 17 patients on the fourth day after the intervention.

The evaluations of healing time period of surgical wound was compared by clinical examinations between the two studied groups, performed monthly, for 10 months after teeth extractions. We considered that the wound are clinically healed if not present any indentation (depthless) in the area of edentulous ridges that corresponds with the original alveoli of teeth's. The obtained results are presented in table III, which show the number of cases that, according to the clinical examination, have full healing of the surgical wounds.

The results of the study revealed that the wounds of the patients in group I (which had PRF insertion) healed, on average, twice as fast compared to control group patients. According to these results, it can be noted that the time interval required for post-surgical wound healing was favored by PRF insertion.

We should underline the absence of alveolitis after teeth extraction in PRF grup comparatively with the control group, where appeared 15 cases of alveolitis (12.5% of cases).

The dentist is responsible for the prevention, diagnosis, and treatment of diseases and disorders of the oral cavity and related structures, respectively to the well-being of patients under their care [13]. Biomaterials of different origins are essential for new many biomedical applications such as implants and prosthetics, pharmaceutical

Clinical examination of postextractional area	Group I (PRF)	Group II (Control group)
At 4 months	2 (=1.66%)	-
At 5 months	26 (=21.66%)	8 (=6.66%)
At 6 months	87 (=72.5%)	33 (=27.5%)
At 7 months	12 (=100%)	62 (=51.66%)
At 8 months	12 (=100%)	92 (=76.66%)
At 9 months	120 (=100%)	111 (=92.5%)
At 10 months	120 (=100%)	120 (= 00%)

Table 3
NUMBER OF CASES THAT SHOW COMPLETE HEALING OF SURGICAL WOUNDS

formulations, protein microarrays, drug and gene-delivery agents, or tissue engineering [14]. The history of using PRF in dental medicine and oral and maxillofacial surgery shows the way that materials, biomaterials and dental techniques evolve and sometimes even promote the definition of new clinical therapeutic concepts and protocols in regenerative medicine [15-17]. The use of recombinant growth factors are actually used for the augmentation and regeneration of oral tissues [18]. Recent techniques of local distribution of growth factors to improve the healing phase, the completion of substitutes graft induced a decrease of the healing time [19]. According to data from the literature, the conducted studies show that the use of PRF has a beneficial impact in oral surgery, periodontology and other disciplines of dentistry [20-23]. Using PRF brings significant benefits to dental surgeries because is a platelet concentrate of high immunological value that incorporates, in the form of a fibrin membrane, all the elements that are involved in the immune and healing response [15]. The fibrin matrix has bone-inductive properties and osteoblasts show increased sensitivity to PRF, supported by increased proliferation and differentiation [24]. In scanning electron microscopy images, PRF show highly condensed fibrin bundles with platelet aggregates embedded within the fibrin network (fig. 5) [25].

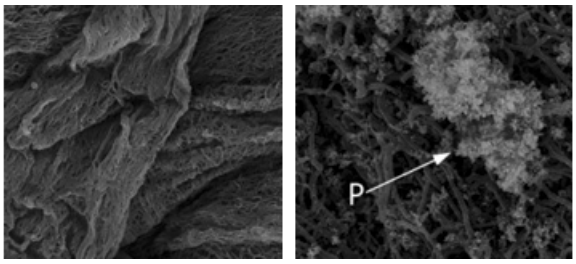

Fig. 5. Scanning electron microscopy images of PRF: left - ×3000; right - ×10,000 [25]

According to Tatullo and all [26], histological results demonstrated that in the samples collected at 106 days after the addition of PRF, lamellar bone tissue with acellular osteocytes, intense eosinophilic bone matrix, also lamellar bone fragments osteocytes and light eosinophilic bone matrix were constituted, probably due to newly-formed bone tissue (fig. 6).

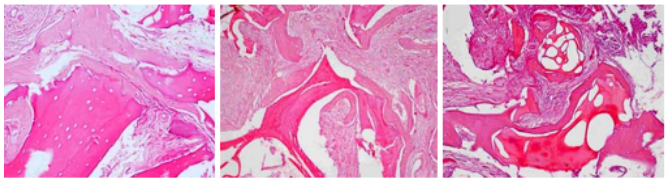

Fig. 6. Histological aspects of the healing process with PRF [26]

PRF is currently used in various surgical procedures such as apical resections, cystectomies, bone marrow tumor extirpation, alveolar bone defects, odontectomies of included third molars and canines, pre-prosthetic surgery, stabilization and protection of implants, a.s. [27-29].

Conclusions

Patients included in the study which benefited the using of PRF autologous biomaterial reported lower post-interventional pain, significantly less discomfort, and significantly lower analgesic doses than the patients of control group.

Based on the results of the study we found that by inserting PRF, the tissue healing process was reduced on average to half of the time period, comparatively with them of control group patients.

The absence of alveolitis after teeth extraction and the minimal dehiscence of wound in the PRF group of patients suggests that PRF biomaterial may support the healing of post-extraction wound.

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