The Effect of a Plasma With Platelet-rich Fibrin in Bone Regeneration and on Rate of Orthodontic Tooth Movement in Adolescents

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The aim of this study was to evaluate the effect of platelet-rich fibrin (PRF), placed in extraction sockets, on bone regeneration and orthodontic tooth movement in adolescents. Fourty extraction sockets from twenty patients requiring extraction of first premolars based on their orthodontic treatment plan participated in this split-mouth clinical trial. Immediately, the teeth adjacent to the defects were pulled together by a NiTi closed-coil spring with constant force. The bone regeneration and the amount of orthodontic tooth movement was evaluated.

Keywords: plasma, platelet-rich fibrin, bone regeneration, orthodontic tooth movement, adolescents

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Regenerative oral medicine entails the replacement of tissues lost to disease or injury with physiologically equivalent engineered tissues[1]. Tissues from the oral cavity are of complex nature with bordering mineralized and soft tissue components, both of which harbor unique progenitor populations residing within specialized extracellular matrix frameworks [2, 3]. Mimicking such complex environments by using chemically homogenous scaffolds and uniform stem cell populations is often challenging. Instead, recent approaches favor complex natural scaffolds that allow for repopulation with the patient's own cells, thereby producing an autologous tissue-engineered organ [4].

One such complex natural scaffold ideally suited for autologous tissue regeneration is platelet-rich fibrin (PRF) is a second generation platelet containing biomaterial with potential applications in wound healing. Unlike the first generation of platelet-rich products, such as platelet-rich plasma (PRP), PRF does not require the addition of an anticoagulant (such as ethylenediaminete-traacetic acid [EDTA]) during the initial drawing of blood, nor calcium chloride nor bovine thrombin to induce polymerization [5,6]. PRF traps platelets and platelet cytokines in a fibrin gel. Its multitude of cytokines at concentrations significantly higher than the baseline blood levels stimulates autologous regeneration [7]. Articular cartilage repair [8-10], regeneration after oral and maxillofacial surgery [11-13], and wound healing [14], all depend on the presence of cytokines that stimulate the migration and proliferation of cells within the affected part of the body.

PRF predominantly consists of a fibrin matrix rich in platelet and leukocyte cytokines such as IL-1, -4, -6, and growth factors such as Transforming Growth Factor beta 1 (TGF-β1), Platelet Derived Growth Factor (PDGF), and Vascular Endothelial Growth Factor (VEGF) [1]. Fibrin gels exploit the final stage of the coagulation cascade in which fibrinogen molecules self-assemble into a highly biocompatible three-dimensional fiber network [15]. The combination of fibrins and cytokines within PRF becomes a powerful bioscaffold with an integrated reservoir of growth factors for tissue regeneration [16].

Resorptive remodeling of the alveolar ridge commonly occurs following tooth extraction. This process may be beneficial in fixed orthodontic treatment of patients with severe crowding [17-19]. Adequate volume of alveolar bone is a prerequisite for successful orthodontic tooth movement during space closure.

Considering the simultaneous positive effect of PRF on bone healing, socket preservation, and acceleration of tooth movement, the current study tested the application of PRF in tooth extraction sockets to evaluate its efficacy for acceleration of space closure phase of orthodontic treatment. This study sought to evaluate whether PRF application can accelerate bone regeneration ant orthodontic tooth movement.

Experimental part

Methods and materials

This split-mouth clinical trial evaluated the efficacy of application of PRF in extraction sockets for acceleration of bone regeneration and orthodontic tooth movement in fixed orthodontic patients. A split-mouth design was used to limit the effect of interpersonal variations on response to PRF. The study was conducted in the Department of Oral and MaxilloFacial Surgery of Gr. T. Popa University of Medicine and Pharmacy, Iasi, Romania between January 2018 and November 2018.

Participants selection

Participants were selected from patients referred to the Department of Oral and MaxilloFacial Surgery of Gr. T. Popa University of Medicine and Pharmacy, Iasi, Romania. Girls and boys orthodontic patients between 12 - 20 years with extraction treatment plan who met the following inclusion criteria were included presence of maxillary and mandibular permanent teeth except for third molars, comprehensive orthodontic treatment plan of bilateral symmetric extraction of first maxillary premolar teeth, no medication intake or systemic disease, and full banding/bonding of teeth in both arches. The exclusion criteria were history of previous orthodontic treatment, syndromic patients, systemic diseases, or medication intake such as

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nonsteroidal anti-inflammatory drugs, which would interfere with bone regeneration and orthodontic tooth movement.

Each patient or each parent of patients under 18 years old signed an informed consent form after receiving a thorough explanation regarding the study. In one-quadrant of each superior jaw, the extraction socket was preserved by immediate placement of PRF as the experimental group, while the other side served as the control group for secondary healing.

Sample size was calculated to be forty extraction sockets (n = 20 in each group). In each patient there were 2 extraction sockets.

Preparation of plasma with platelet-rich fibrin

The protocol for PRF preparation was simple and included the collection of whole venous blood from the brachial vein using a 10 mL syringe. The collected blood was transferred into two sterile vacutainer tubes (9 mL) without anticoagulant and were placed symmetrically into the centrifuge device. The intraspin tubes were immediately centrifuged at 2700 rpm for 12 min, after which, three layers were formed: red blood cells at the bottom, upper straw-colored cellular plasma, and the middle fraction containing the fibrin clot and platelets. The upper straw-colored layer was discarded, and the middle fraction was collected, 2 mm below the lower dividing line, which was PRF (fig.1).

Treatment protocol

Each patient received an orthodontic treatment with fixed appliances (MBT prescription, 0.22 slot), requiring extraction of their first maxillary premolars according to their orthodontic treatment plan and then was performed the augmentation of extraction socket with PRF unilaterally. Extraction of first maxillary premolars was performed on both sides in the same day. On one side of each jaw, the extraction socket was preserved by immediate placement of PRF in the extraction socket as the experimental group and the other sides served as the control for secondary healing, without any grafting (fig.2).

The PRF plugs were placed gently into the socket, and the sockets were sutured using 4-0 Vicryl sutures (Ethicon). The teeth adjacent to the defect were then pulled together by a NiTi closed-coil spring (Ormco®, Orange, California, USA) with constant level of force. A piece of 0.016 × 0.022-inch stainless steel wire was used as the main archwire. The sites were examined weekly for any appliance dislodgment.

Bone regeneration and orthodontic tooth movement evaluation

Bone regeneration was evaluated by cone beam computed tomography (CBCT) examination at two month after extraction of each first maxillary premolar. Qualitative evaluation of bone regeneration was made using paraaxial reconstructions for each region of interest (ROI) (fig.3). The measurements were performed bilaterally in the region of first maxillary premolar.

The CBCT device used was the PlanmecaPromax 3D Mid (Planmeca OY, Helsinki, Finland). The scans were carried out under the following exposure conditions: 90 kV, 12 mA, and exposure time of 18.3 s. Initial and final reconstructions were carried out by Romexis 2.3.1 software (Planmeca, Helsinki, Finland).

The healing process was evaluated by measuring the density of bone in the region of each firs maxillary premolar (fig.3), which was classified in to four groups: D1, D2, D3

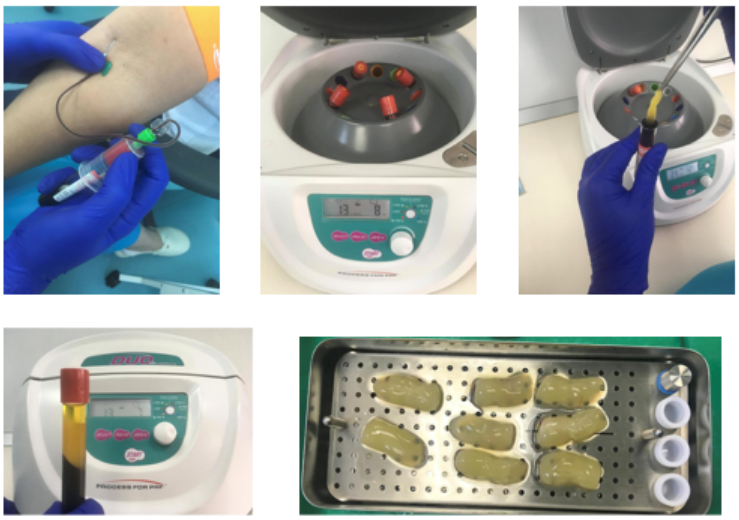

Fig. 1 Preparation of platelet-rich fibrin from the blood of each patient.

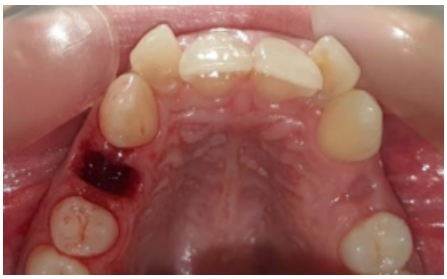

Fig. 2 The right extraction socket was preserved by immediate placement of PRF as the experimental group and the left side served as the control group for secondary healing

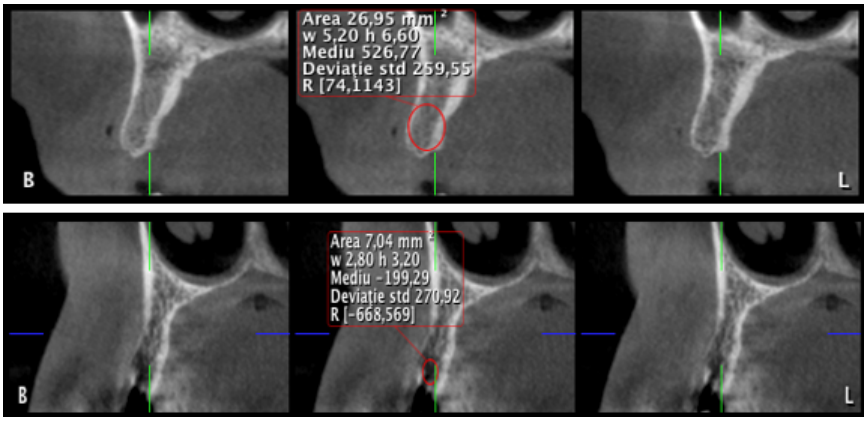

Fig. 3 The measurement of bone density on paraaxial sections on each site of premolar extraction after two months.

and D4. D1 represent homogeneous cortical bone with bone density more than 1250 Hounsfield Unit (HU), D2 represent thick cortical bone with marrow cavity with 850-1250 HU, D3 represent thin cortical bone with dense trabecular bone of good strength with 350-850 HU and D4 represent very thin cortical bone with low density trabecular bone of poor strength with less than 350 HU.

The amount of orthodontic tooth movement was measured by comparing the change in horizontal linear distance between the mid-marginal ridges of the adjacent teeth on a regular basis every 4 weeks for 6 months: before placement of PRF (A) and 4 weeks (B), 8 weeks (B), 12 weeks (C), 16 weeks (D), 20 weeks (E), 24 weeks (E) after placement of PRF. This parameter was evaluated on model cast by measuring with a rule the distance between the adjacent teeth (fig.4).

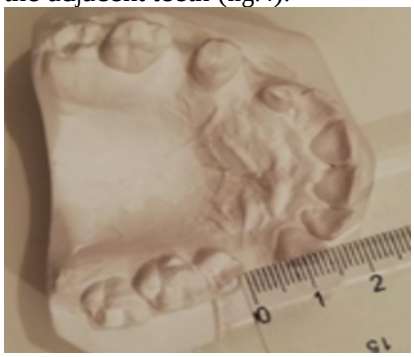

Fig. 4 Measuring the linear distance between the mid-marginal ridges of the adjacent teeth on model cast.

Statistics

Variation analysis was performed using SPSS 19.0 for Windows (SPSS Inc, Chicago, IL, United States of America) and identified the significant differences for average and SD.

Then the average and SD of these values were calculated for each variable for both groups. A significant difference of the compared data was assumed if the probability was less than .05. Individual differences were not considered significant.

Results and discussions

Fourty extraction sockets of twenty patients (9 males, 11 females, mean age of 16.43 years and range 12–20 years) were assessed in this study. All patients completed the follow-up period.

The mean value for the distance between the adjacent teeth to the extraction site started at 5 mm, immediately after extraction and ended after 6 months at 1.9 mm for the experimental group that received PRF graft. For the control group, which have not received the PRF graft, the mean value started at 4.8 mm and ended at 2.9 mm (fig.5).

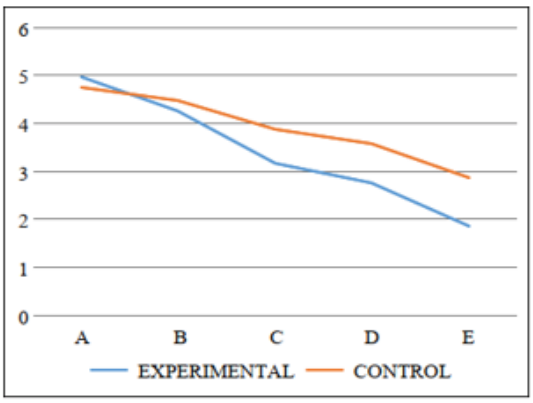

Fig. 5 The mean value of the distance between marginal ridges of the teeth adjacent to sockets in millimeters at different time points

In all evaluation moments, the mean linear measurements between mid-marginal ridges of teeth adjacent to extraction sites were less in experimental groups compared to control. This distance decreased more in experimental side which means that the teeth moved faster than control side.

According to the random effect model, the experimental group which received PRF graft showed higher rate of orthodontic tooth movement (P = 0.006) (fig.5).

The evaluation of bone density after 2 months showed an improvement of bone regeneration in patients who received PRF into the socket. The study revealed the presence of significant correlations between bone quality and socket augmentation with PRF (fig.6).

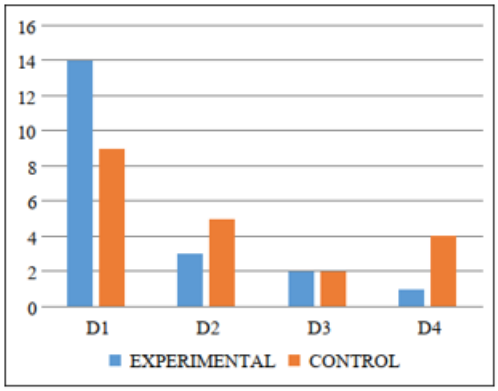

Fig. 6 The distribution of type of bone quality at the site of extraction between the experimental and control group.

The results of this study demonstrated that the distance between mid-marginal ridge points of crowns adjacent to extraction sites was less in experimental groups; therefore, it showed the possible positive efficacy of PRF application in the extraction socket for acceleration of bone regeneration and orthodontic tooth movement. It means that anterior and posterior teeth adjacent to extraction sites moved faster toward each other in experimental groups.

Numerous studies and researcheshave been done on tooth socket healing processes; however, most of these are histological studies with less emphasis on radiographic evaluations [1]. PRF is a platelet concentrate collected on a single fibrin membrane that contains all the constituents favorable for healing.

The scientific rationale behind the use of platelet preparations lies in the fact that the platelet serves as a reservoir of many growth factors that are known to play a crucial role in hard- and soft-tissue healing process. PRF stimulates human osteoblastic proliferation, and histology has shown it to have an effect on neoangiogenesis. PRF is a second-generation platelet concentrate and is a gel-like matrix that contains high concentration of nonactivated, functional, intact platelets contained within a fibrin matrix that releases a relatively constant concentration of growth factors over a period of 7 days [1,22-34].

In filling of a tooth socket by PRF, neovascularization establishes through the PRF clot and an epithelial covering develops [20]. Despite the infectious and inflammatory potential of extraction sockets, rapid healing of the wound occurs without pain, swelling, and other attending signs of inflammation and infectious processes. Similar clinical results were found in the present study in which healing occurred without untoward symptoms. The results of the present study were in accordance with the results of the study conducted by Moya-Villaescusa and Sanchez-Perez [21] which showed PRF to stimulate soft-tissue healing process seen clinically when applied to the fresh extraction sockets. In addition, it seemed to reduce alveolar ridge

resorption following tooth extractions and to positively influence socket healing over a 3-month period.

Conclusions

The present study was designed to evaluate and compare bone regeneration in extraction sockets with and without PRF utilizing the potential of the CBCT in determining the bone density. In the study, appreciable sites where no PRF was used substantiating the use of PRF as an inexpensive autologous material for socket preservation and future rehabilitation.

Also in this study, more decrease horizontal linear measurement between the mid-marginal ridges of teeth in experimental groups than control groups means that application of PRF may accelerate orthodontic tooth movement, particularly in cases with extraction treatment plan.

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