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Doi: 10.7126/cumudj. 471947 *RESEARCH ARTICLES*

THE EFFECTS OF DIFFERENT PLATELET-RICH CONCENTRATES ON EXTRACTION SITE HEALING

Farklı Plateletten Zengin Konsantrelerin Çekim Alanı İyileşmesi Üzerine Etkileri

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ABSTRACT

Objective: Some physiological changes may occur following tooth extraction, and symptoms during the post-extraction period may affect the patient's quality of life. Many techniques have been developed to promote soft/hard tissue healing. Accordingly, this study compared the early soft tissue healing characteristics of extraction sites treated with leukocyte-and-platelet-rich fibrin (L-PRF), titanium-prepared platelet-rich fibrin (T-PRF), and untreated control sites.

Materials and Methods: This study included 42 single-rooted teeth. The extraction sites were treated with L- or T-PRF. Extraction sockets left to heal spontaneously were defined as control sites. The Landry Wound Healing Index (LWHI) and H_2O_2 bubbling test results for the complete wound epithelization (CWE) rates were recorded 1 and 2 weeks postoperatively. All patients were asked to record a visual analogue scale (VAS) value for pain and the number of analgesics taken during the 2 days after extraction.

Results: The LWHI improved significantly in all groups 2 weeks postoperatively compared with 1 week (p<0.05). However, there was no difference among the three groups in each week. The CWE ratios were 7.1%, 53.3%, and 69.2% in the control, L-PRF, and T-PRF groups at 1 week, respectively. The CWE rate of the control group was significantly lower than in both test groups. (p<0.05) At 2nd weeks, both test groups showed 100% CWE compared with 35.7% in the controls. The VAS score 1 day postoperatively was significantly higher in the controls than in both test groups. (p<0.05) There was no significant difference among the groups at day 2. There was also no significant difference among the groups in the number of analgesics taken.

Conclusion: Within the limitations of this study, both T-PRF and L-PRF, which are completely autologous biomaterials, similarly enhanced wound epithelization and reduced postoperative discomfort at extraction sockets.

Key Words: tooth extraction, platelet-rich fibrin, wound healing

ÖZ

Amaç: Diş çekimi sonrası, yara iyileşmesi döneminde görülen bazı durumlar hastaların yaşam kalitesini olumsuz etkileyebilmektedir. Hem diş çekimi sonrası yara iyileşmesini desteklemek, hem de hastaların yaşam kalitesini artırmak amacı ile birçok teknik geliştirilmiştir. Bu nedenle bu çalışmanın amacı, lökosit-trombositten açısından zengin fibrin (L-TZF), titanyumla hazırlanan trombositten zengin fibrin (T-TZF) ile tedavi edilmiş çekim soketleri ile ve tedavi edilmemiş kontrol bölgelerinin erken yumuşak doku iyileşmesini karşılaştırmaktır.

Gereç ve Yöntem: Çalışmaya toplam 42 tek köklü diş dahil edildi. Rastgele olarak belirlenen, L-TZF (n=15) ve T-TZF (n=13) uygulanan alanlar test bölgeleri olarak belirlenirken, kendiliğinden iyileşmeye bırakılan çekim soketleri kontrol grubu (n=14) olarak değerlendirmeye alınmıştır. Landry Yara İyileşme İndeksi (LYİİ) skorları ve yaranın tamamen epitelizasyonun (YTE) için H_2O_2 kabarcık testi sonuçları işlem sonrası 1 ve 2. haftalarda kaydedildi. Ayrıca hastadan, çekimden sonraki 2 gün boyunca VAS skalasını işaretlemesi ve aldığı analjeziklerin sayısını kaydetmesi istendi.

Bulgular: İkinci haftada 1. haftaya göre tüm gruplarda LYİİ skorları istatistiksel olarak anlamlı derecede yüksekti. (p *<0,05*) Ancak üç grup arasında anlamlı fark yoktu. H_2O_2 kabarcık testi sonuçlarına göre, 1. haftadaki YTE oranı kontrol, L-TZF ve T-TZF grupları için sırasıyla %7,1, %53.3 ve %69.2 idi. Kontrol grubunun oranı, her iki test grubuna göre istatistiksel olarak anlamlı derecede düşüktü (p *<0,05*). 2. haftadaki test gruplarının her ikisi de %100 YTE göstermişti, ancak bu oran kontrol grubunda sadece %35,7 idi. VAS skoru, 1. günde, kontrol grubunda her iki gruptan da istatistiksel olarak anlamlı derecede yüksekti (p *<0,05*). 2. günde gruplar arasında anlamlı fark yoktu. Alınan analjezik sayısı bakımından gruplar arasında anlamlı bir fark yoktu.

Sonuç: Tamamen otolog biyomateryaller olan T-TZF ve L-TZF, çekim soketlerinde yara epitelizasyonu arttırarak ameliyat sonrası hisedilen rahatsızlığı azaltır.

Anahtar Kelimeler: diş çekimi, trombositten zengin fibrin, yara iyileşmesi

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INTRODUCTION

The alveolar process is a tooth dependent tissue that develops in conjunction with the eruption of the teeth.[1] After tooth extraction, physiological changes start in the soft and hard tissues. The resorption process is responsible for the dimensional changes that occur after tooth extraction. The amount of hard tissue resorption differs considerably between subjects. Therefore, a reduction of up to 50% of the original bone width can occur after tooth extraction. This decrease is greater in the buccal area than in the lingual/palatal areas, partly because the buccal bone is thinner.[2,3] Tooth extraction and implant placement in aesthetic areas are of particular importance in such cases. The dimensional change is most common in the first 3 months, but may continue until the end of the first year after extraction.[4] Symptoms such as pain, bleeding, and swelling may affect soft tissue healing and the patient's quality of life after tooth extraction.[5] Many techniques and materials have been proposed to promote soft and hard tissue healing and preserve tissue volume after extraction.[6-10] With our increased knowledge of bone regeneration and advances in biotechnology, new biologically active biomaterials have been developed to overcome the disadvantages of autogenous and non-autogenous materials, such as first- and second-generation platelet concentrates.[11] In the first-generation platelet concentrate, platelet-rich plasma (PRP) is obtained by adding chemical additives (e.g., bovine thrombin and calcium chloride) to manipulate the clotting process, resulting in a product with an unnaturally short life, quick resorption, and poor regenerative properties. Leukocyte- and platelet-rich fibrin (L-PRF) is obtained from the patient's own blood, without adding any anticoagulant, during natural clot formation. L-PRF membranes consist of high-density cross-linked fibrin networks and viable platelets and leukocytes. This bioskeleton releases growth factors, adhesion molecules, and pro- and anti-inflammatory cytokines for up to 7 days.[12, 13] This modulates the inflammatory process, increasing angiogenesis and tissue regeneration.[14] It is a preferred active biological product because it is inexpensive, easy to obtain, completely autogenous, and has beneficial biological properties in post-extraction socket protection. Titanium-based PRF (T-PRF) is promising, especially in soft and hard tissue augmentation, due to its fibrin structure, which is tighter than that of L-PRF, and it is prepared in Grade IV titanium tubes.[15,16] When T-PRF was applied to secondary wound areas in the mouth, it produced faster epithelization, less postoperative bleeding, and better wound healing than spontaneous healing.[17] T-PRF also has osteoinductive properties similar to those of bone and preserves tissue volume.[17,18] Rapid, complete soft tissue healing after tooth extraction minimizes surgical complications and enables subsequent implant placement. Therefore, this study compared the soft tissue healing of human tooth extraction sites using L-PRF, T-PRF, and a non-grafted control after 2 weeks.

MATERIALS AND METHODS

This study was done in accordance with the Helsinki Declaration of 1975 (revised in 2000). The study protocol was approved by the Clinical Research Ethics Commitee of Kanuni Education and Research Hospital. (protocol number: 2018/03)

The participants were over 18 years of age, in good general health, and required a single tooth extraction and subsequent replacement with an implant in anterior or premolar sites. Patients were excluded if they had any systemic disease that affected wound healing (e.g., diabetes or scleroderma); had undergone radiotherapy, chemotherapy, or bisphosphonate therapy; were pregnant; were current smokers; or had poor oral hygiene and motivation.

The study included 42 teeth, which were divided into three study groups: the control

group (n=14) underwent natural socket healing after tooth extraction without applying any material; the L-PRF group (n=15) had L-PRF added to the socket following tooth extraction; and the T-PRF group (n=13) had T-PRF added to the socket following tooth extraction.

Exclusion criteria for the extraction sockets were the presence of a tooth or an oro-antral connection, or a radiographically diagnosed endodontic lesion larger than 5 mm.

Protocols used during and after tooth extraction

Eligible teeth were extracted gently under local anesthesia without elevating a flap. Granulation tissue was removed and the socket was washed with sterile saline after tooth extraction. In the test groups, L-PRF or T-PRF membranes obtained from the patient's own blood were firmly placed in the extraction socket and sutured with a polypropylene 4-0 horizontal mattress suture. In the control group, no additional material was placed, and the socket was sutured similarly. The suture was removed after 1 week. Patients were advised to record their pain level using a visual analogue scale (VAS) and the number of analgesics taken for 2 days after tooth extraction. The Landry wound healing index (LWHI) and H_2O_2 epithelization test were performed after 1 and 2 weeks.

Landry Wound Healing Index

The LWHI evaluates the extraction region based on tissue color, response to touch, marginality of the incision line, and extent of the area. The rating is from 1=very poor to 5=excellent.

1. **Very poor**: ≥50% of the gingiva is red; touch causes bleeding; granulation tissue is present; the incision margin is not epithelialized, with loss of epithelium beyond the incision margin; and suppuration is present.
2. **Poor**: ≥50% of the gingiva is red; touch causes bleeding; granulation tissue is present; the incision margin is not epithelialized; and connective tissue is exposed.
3. **Good**: ≥25 to <50% of the gingiva is red; there is no bleeding on palpation; there is no granulation tissue; and no connective tissue is exposed at the incision margin.
4. **Very good**: <25% of the gingiva is red; there is no bleeding on palpation; there is no granulation tissue; and no connective tissue is exposed at the incision margin.
5. **Excellent**: All tissues are pink; there is no bleeding on palpation; there is no granulation tissue; and no connective tissue is exposed at the incision margin.

Wound epithelization

Complete wound epithelization (CWE) was evaluated clinically using the H_2O_2 bubbling test, which is based on the principle that if the epithelium is discontinuous, H_2O_2 will diffuse into the connective tissue and catalase will act on the H_2O_2 to release water and oxygen, producing bubbles in the wound. The area to be evaluated was dried and 3% H_2O_2 was sprinkled on the wound using a syringe. The appearance of bubbles suggested that the surgical site was not completely epithelialized. If there were no bubbles, it was assumed that CWE had occurred. The rate of CWE was calculated as follows:

CWE (%) = number of sites with CWE (+) × 100 / total number of sockets.

L-PRF and T-PRF Preparation Procedures

Venous blood from the patient was rapidly transferred to tubes that did not contain an anticoagulant to trigger platelet activation and fibrin polymerization. The tube was then centrifuged at 2700 rpm for 12 min (Nuve NF 200; Ankara, Turkey). This resulted in three layers in the tube: serum at the top, PRF in the middle, and erythrocytes at the bottom. The PRF in the middle layer was squeezed between sterile moistened sponges and the membrane was separated from the serum. A glass tube was used to prepare L-PRF and a Grade IV

titanium tube to prepare T-PRF. Two L-PRF or T-PRF membranes were used for each socket.

Statistical analysis

The data were analyzed using IBM SPSS Statistics for Windows 22.0 (IBM Corp., Armonk, NY, USA). Qualitative data are presented as numbers, percentages, and the mean and standard deviation. The conformity of the measured data to the normal distribution was evaluated with the Kolmogorov-Smirnov/Shapiro-Wilk test. Numerical variables were compared among the three independent groups using the Kruskal-Wallis test when the distribution was not normal. Numerical variables were compared between two dependent groups with Wilcoxon's test when the distribution was not normal. The chi-square test was used to analyze the differences between categorical variables in independent groups. Statistically, $p<0.05$ was considered significant.

RESULTS

The study enrolled 32 non-smoking patients (mean age 43.74±9.36 years) in whom single-rooted teeth were extracted for periodontal reasons (57.1%), caries (21.4%), endodontic reasons (14.3%), or trauma (7.1%).

Table 1 shows the LWHI. The values were significantly better for all groups at 2 weeks compared with 1 week ($p<0.05$). However, there was no difference among the three groups in each week, despite better results with T-PRF.

Table 1. Landry Wound Healing Indexes

Groups	1st Week	2nd Week	*p*
Control	3.21±0.69	4.36±0.49	*<0.05*
L-PRF	3.53±0.64	4.53±0.52	*<0.05*
T-PRF	3.69±0.48	4.69±0.48	*<0.05*
p	*NS*	*NS*	

Values are presented as mean±standard deviation.
Statistically significantly different between first and second week (p<0.05). (Wilcoxon's test)
Statistically non- significant among groups NS (p>0.05). (Kruskal-Wallis test)

Table 2 shows the results of CWE using the H_2O_2 test. Wound epithelization was completed in 7.1%, 53.3%, and 69.2% of the control, L-PRF, and T-PRF groups, respectively. The rate was significantly lower in the controls than in both test groups ($p<0.05$). At 2 weeks, both of the test groups showed 100% CWE compared with only 35.7% in the control group ($p<0.05$).

Table 2. H_2O_2 test results- Complete Wound Epithelization

Groups	1st Week	2nd Week
Control	7.1 %*	35.7%
L-PRF	53.3%	100 %
T-PRF	69.2%	100%
p	*<0.05*	

Values are presented as mean±standard deviation.
Statistically significantly different between first and second week (*p<0.05*) (Wilcoxon's test)
Statistically non- significant among groups NS (*p>0.05*). (Kruskal-Wallis test)

Table 3 gives the mean and standard deviation of the patients' VAS scores for pain.

Table 3. The VAS scores

Groups	1st day	2nd day
Control	5.5±1.5*	1.29±1.49
L-PRF	3.2±2.04	0.47±0.92
T-PRF	3.85±1.82	0.46±0.52
p	*<0.05*	*NS*

Values are presented as mean±standard deviation.
*Statistically significantly different among groups at first day (*p<0.05*) (Kruskal-Wallis test)
NS: Statistically non-significant among groups at second day (*p>0.05*) (Kruskal-Wallis test)

The VAS scores decreased gradually in all groups. On day 1, the score was significantly higher in the control group than in both test groups ($p<0.05$). There was no significant difference among the groups on day 2. The number of analgesics recorded did not differ significantly among the groups at any time (Table 4).

Table 4. The number of analgesics

Groups	1st day	2nd day
Control	1.43±1.09	0.36±0.74
L-PRF	0.87±0.83	0.07±0.29
T-PRF	0.77±0.44	0
p	*NS*	*NS*

Values are presented as mean±standard deviation.
NS: Statistically non-significant among groups ($p>0.05$) (Kruskal-Wallis test)

DISCUSSION

Bone resorption is inevitable after tooth extraction. Socket preservation after tooth extraction is crucial for successful, predictable dental implant treatment. Platelet concentrates stimulate soft and hard tissue healing via various mechanisms.[19] In our study, both test groups exhibited positive outcomes in terms of CWE and the VAS score in the early soft tissue healing period.

Wound epithelization is important in secondary wound healing. In natural socket healing, a secondary wound is formed, which may cause pain and discomfort until the connective tissue is completely covered by epithelium. The cells in platelet concentrates populate the surgical wound area; the fibrin matrix serves as a supporting matrix, and growth factors placed in the socket accelerate healing by stimulating angiogenesis, clot formation, and epithelization.[20,21] We used L-PRF and T-PRF membranes to fill the socket. Consequently, the area of secondary healing covered by the platelet concentrates showed a pattern similar to primary wound healing. Ustaoğlu *et al*.[17] observed the positive effect of these biomaterials on secondary wound healing in free gingival graft donor sites. The T-PRF membranes were used as palatal healing material and were superior to the control condition at 14 days in terms of CWE. Similar to our study, this effect was observed 1 and 2 weeks after tooth extraction.

Our study participants were non-smokers because cigarette smoking affects the normal healing of extraction sockets, especially via nicotine-released catecholamines, which inhibit epithelization.[22] For example, one study used L-PRF to promote healing after an extraction in smokers, but it did not reduce pain or improve socket closure.[23]

T-PRF is a third-generation PRF product. It has a firmer fibrin network and slower resorption time than L-PRF.[16] Ours is the first study to evaluate the effects of T-PRF in the early stage of soft tissue healing after an extraction, and T-PRF was superior to the control in terms of CWE and VAS scores. The CWE rate was nearly 70% for the T-PRF group and 53.3% for the L-PRF group, although the difference was not significant. The high ratio of the T-PRF group was attributed to the dense, stable fibrin matrix, which serves as a scaffold for cell proliferation.

The VAS scores of the patients after extraction were significantly higher in the controls than in both test groups. Following extraction, patients have pain, bleeding, and swelling. The main reported advantages of using autologous platelet concentrates are better soft tissue epithelization and less pain, swelling, and inflammation.[24-26] These may be related to reduced food stagnation in the extraction socket, reduced postoperative bleeding, and the anti-inflammatory and anti-microbial activity of the platelet concentrates.[27-29]

CONCLUSION

Both T-PRF and L-PRF enhanced wound epithelization and reduced postoperative patient discomfort. They served as a stable fibrin matrix. The long-term effects of these biomaterials on soft and hard tissues should be evaluated in split-mouth clinical studies with more participants.

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