Platelet-Rich Fibrin as Palatal Wound Dressing Post-Free Gingival Graft: A Review

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Abstract

The gold standard procedure for gingival recession is the free gingival graft (FGG), although it leaves an open wound in the donor area that is prone to problems. Platelet-rich Fibrin (PRF) has been shown to aid in the healing of palatal wounds. Nonetheless, there hasn't been much debate about the PRF's mechanism. The purpose of this narrative review was to discuss about the effects and mechanisms of PRF components on palatal wound healing following FGG.

In vivo and in vitro experiments revealed that PRF reduces delayed bleeding because of its mechanical qualities, which act as mechanical protection and restore destroyed tissue components. PRF's high platelet content stimulates platelet aggregation when it comes into contact with injured blood vessel collagen, which helps to maintain hemostasis. Platelet activation also promotes cell migration and proliferation within the fibrin matrix. Platelets also regulate the release of growth factors such as PDGF, IGF-1, EGF, VEGF, and TGF-β, which activate macrophages, fibroblasts, and endothelial cells in blood vessels. The presence of leukocytes impacts healing by commencing the neoangiogenesis process. By analyzing the patient's pain level, clinical trials discovered lower inflammation in palatal wounds treated with PRF. Furthermore, PRF has been demonstrated to considerably accelerate palatal wound epithelialization.

PRF is preferable when used as a wound dressing for the palate following FGG. Platelets, leukocytes, growth factors, fibrin matrix, and anti-inflammatory cytokines can all see increased expression as a result of this factor's involvement.

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Introduction

Free gingival graft (FGG) is one of the mucogingival surgical therapies used to improve the width of the attached gingiva and root coverage.[1] The palatal mucosa is often used as donor tissue.[2] Despite its gold-standard designation, FGG has the drawback of producing open wounds, interfering with wound healing, and increasing patient morbidity.[3,4] One of the problems of palatal wounds is prolonged inflammation, which presents as discomfort and dietary changes. Moreover, disruption to the epithelial barrier in palatal wounds results in infection, delayed bleeding, and chronic wound progression.[5,6] Following FGG, adequate wound management is required to promote palatal wound healing. PRF (Platelet-Rich Fibrin) is a platelet concentration of the second generation utilized extensively in regenerative dentistry.[7-9] PRF comprises fibrin clots, platelets, and leukocytes, which can produce growth factor and cytokine-like molecules.[7,8] PRF features fibrin clumps that are more flexible and useful as scaffolding.[10] The fibrin clot can extend the half-life of released compounds such as growth factors and cytokines. The combination of these elements is crucial for wound healing to proceed without incident.[11]

The expression of pro-inflammatory cytokines can be suppressed by growth factors and anti-inflammatory cytokines, hence lowering inflammation and accelerating wound healing.[12,13] By influencing epithelial cell proliferation and migration and limiting delayed bleeding, growth factors expedite wound healing.[6,14,15] It affects the metabolism of epithelial cells and fibroblasts and protects the wound from the environment.[16] Well-adapted

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fibrin reduces delayed bleeding.[6] All of these benefits make PRF a superior palatal wound dressing for expediting palatal wound healing after FGG surgery.

There are no adverse effects associated with the usage of autologous PRF membranes in patients.[17] In contrast to amniotic membranes, PRF membranes can be used as a biological dressing with a simpler and less expensive preparation technique.[18] Although research has demonstrated that PRF can accelerate palatal wound healing and reduce morbidity in patients who have undergone FGG, studies of the function of each PRF component remain limited. The purpose of this review is to discuss the role and mechanism of PRF components in palatal wound healing following FGG.

Materials and methods

A search of the databases produced 962 literatures. The screening of titles and abstracts was followed by the removal of duplicates, which resulted in the collection of 30 items of literature. From Quartile 1 through Quartile 4, there are five works of literature that are absent. We looked at a total of 25 pieces of research, including 13 randomized controlled trials (RCTs), 3 case series, 1 *in vivo* study, and 8 *in vitro* studies. Figure 1 shows a chart that displays the results of the literature search.

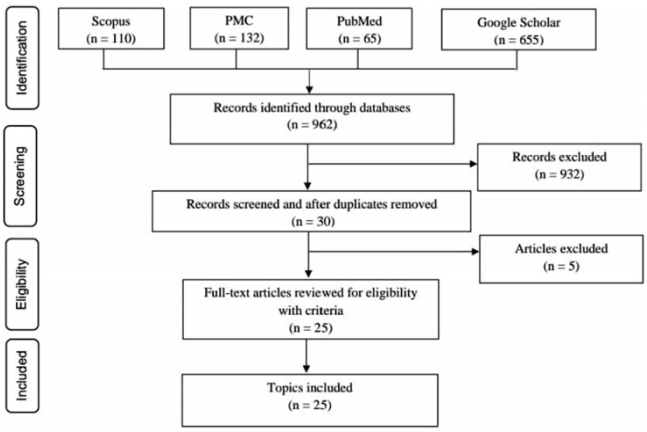

Figure 1. Study workflow and finding.

Discussion

In all investigations, the size of soft tissue grafts in the control and treatment groups was comparable. Several research employed the Sullivan and Atkins approach for soft tissue grafting, although others did not. The thickness of soft tissue grafts ranges from 1.5 to 2 mm.[19-22]

Patients who had undergone FGG surgery received supragingival cleaning, strengthening of oral hygiene, and evaluation of palatal wound healing parameters.[23-25] PRF appropriately causes hemostasis and reduces the incidence of postoperative follow-up bleeding, according to 8 clinical research papers. Due to the physical features of PRF, which operate as mechanical protection and restore damaged tissue structures, an *in vivo* study and *in vitro* investigations revealed that PRF inhibits delayed bleeding.[19,22,26] Suture placement that presses against the wound's edges also promotes blood vessel constriction.[19] Platelet content in PRF is 4-14 times higher than in whole blood when compared to natural blood clots.[27,28] PRF's high platelet content stimulates platelet aggregation when it comes into touch with injured blood vessel collagen, which helps to maintain hemostasis. Platelet activation also promotes cell migration and proliferation within the fibrin matrix. Platelets also regulate the release of growth factors such as PDGF, IGF-1, EGF, VEGF, and TGF-, which activate macrophages, fibroblasts, and endothelial cells in blood vessels. Leukocytes influence healing by starting the process of neoangiogenesis.[28-30] VEGF is a leukocyte-derived angiogenic growth factor that promotes angiogenesis.[30] The PRF fibrin matrix, which is flexible and capable of trapping platelets, regenerative cells, and growth factors with synergistic effects on hemostasis, angiogenesis, and secondary bleeding prevention, facilitates the entire process.[29.30]

Clinical research found that monitoring the patient's pain level reduced inflammation in palatal wounds treated by PRF, and *in vitro* studies examined the mechanism of PRF components in the inflammatory process. The Visual Analogue Scale (VAS) and the Wong-Baker Faces Scale were used to assess pain (WBFS). According to Bahammam's findings, the PRF group had a lower VAS score with a peak value of 2.10, while the control group had a score of 5.46.[21] Similar findings were discovered in the study of Sharma et al., who reported that the PRF group's pain levels decreased earlier than the CollaCote group's.[17] According to the research of Sousa et al, the A-PRF group experienced discomfort only until the second day after surgery, whereas the gelatin sponge group

experienced pain until the 14th day with a higher VAS score.[2] The L-PRF group's VAS score declined from the first day after surgery and was lower than the other two groups.[25] According to another study, only two out of every five PRF patients experienced pain, with VAS values ranging from 1-3.5.[24]

Platelet and leukocyte-expressed cytokines affected PRF's anti-inflammatory activity.[12,31] Platelets in PRF can express anti-inflammatory cytokines such interleukin-4 (IL-4) and interleukin-receptor antagonist (IL-RA), which block the expression of pro-inflammatory cytokines by tissues.[32] This decrease in inflammation alleviates pain in palate wounds, resulting in improved eating habits.[12,31] L-PRF expressed 81.6 35.8 pg/ml of IL-4 and 1.2 0 pg/ml of IL-4 after 24 hours after the PRF manufacturing process, with peak levels reaching at the end of the first week.[12] Additionally, after 6 hours, platelets in PRF express Tumor Necrosis Factor-α (TNF-α) at higher amounts and remain stable between 80 and 100 pg/mL. TNF-α is a pro-inflammatory cytokine that enhances normal inflammatory processes and stimulates the generation of anti-inflammatory cytokines.[31]

Platelet and leukocyte growth factors are also involved in PRF's anti-inflammatory mechanism.[31] One of the growth factors secreted by PRF is transforming growth factor beta-1 (TGF-β1). Throughout the experiment, TGF-β1 was identified, with the maximum concentration recorded after one hour. PRF released PDGF-BB in addition to TGF-β1 at all time points, with PDGF-BB concentration increasing considerably after 240g/8 minutes centrifugation.[32] According to Mudalal et al research, L-PRF might express up to 80 pg/mL of PDGF-AA in the first hour, then drop to roughly 50% in the second hour. These growth factors serve as anti-inflammatories, inhibiting the expression of pro-inflammatory cytokines such IL-1, IL-6, and TNF-.[31] Fibrin also has a role in anti-inflammatory processes. PRF has a more flexible fibrin framework than other platelet concentrations.[7] The framework has the ability to extend the release of molecules like growth factors and cytokines.[10]

Feeding patterns are another aspect evaluated during the inflammatory process. There was no change in feeding patterns after FGG. While the patients were advised to chew on the opposite side and eat a soft and cold diet, no examination of feeding habits was undertaken on the day of operation. Ozcan et al. discovered that normal eating habits were better in the PRF group supplemented with butyl cyanoacrylate than in the butyl cyanoacrylate and moist gauze groups in the first and second postoperative weeks. By the third postoperative week, all groups had established normal eating patterns.[25]

The PRF group was shown to have better eating habits than the other groups in general. Feeding patterns were assessed using a VAS score. From the first to third week postoperatively, the VAS score of the PRF group was lower than that of the gelatin sponge group. In the fourth week, there was no significant difference between the two groups, and neither group had experienced changes in eating habits.[19] A numerical rating scale (NRS) score, in addition to the VAS score, can be used to examine feeding habits. In the first and second postoperative weeks, the food behaviors of the PRF and gelatin sponge groups were similar, but the gelatin sponge group only experienced alterations in eating habits in the second week.[22] Because the thickness of the residual soft tissue covering the palate in the study by Balkhede et al. is 2 mm[22], the low feeding habits score of the gelatin sponge group in the study by Balkhede et al. contradicts with the findings of Feminella et al.[19]

The third criteria for measuring wound healing is the wound healing percentage. TGF-β1, PDGF, VEGF, EGF, and IGF-1 are the growth factors found in PRF. It is continually released from a stable fibrin matrix[15] and is associated with the healing of palatal lesions in the PRF group. PRF growth factors promote the proliferation and development of oral epithelial cells.[33] EGF stimulates epithelial cell proliferation and migration, which promotes epithelialization.[15] TGF-β1 promotes MMPs, which aid in epithelial cell migration and proliferation.[34] PDGF promotes epithelialization by boosting the synthesis of other growth factors including IGF-1 and TSP-1. TSP-1 can block PDGF proteolytic and enzymatic breakdown, whilst IGF-1 can enhance epithelial cell motility.[35] Because it is more stable than other platelet concentrate fibrin matrices and does not breakdown quickly when used as a palatal wound dressing following FGG surgery, the PRF fibrin matrix promotes to quicker wound healing. PRF improves the mechanical stability of blood clots and shields the wound surface from denudation during the early stages of wound

healing.[24] Photographing the palatal wound with a digital camera immediately after FGG surgery (baseline value), 1, 2, 3, and 4 weeks later, or until complete epithelialization was accomplished, the percentage of wound healing was measured. To calculate the percentage value of wound healing, divide the healed area by the baseline value and multiply the result by 100.[24] Another study estimated the proportion of wound healing by measuring the area of wound healing with a periodontal probe.[2,17] In the second week, the PRF group had a wound reduction percentage of 98.95%, while the control group had a wound reduction percentage of 97.51%.[36] Because both membranes emit cytokines, glycoproteins, and glycan chains that work synergistically to drive angiogenesis, immunity, and epithelialization, the wound healing rate following PRF membrane application was comparable to collagen dressings.[17]

PRF's efficacy on wound epithelialization has been supported by 12 clinical trials, as well as one in vitro and one in vivo investigation. These studies examine at complete epithelialization, the percentage of palate wound healing, and the thickness of the palatal tissue after FGG surgery. PRF has been proven to greatly expedite palatal wound epithelialization. After two weeks following FGG surgery, the majority of patients in the PRF, I-PRF, A-PRF, and T-PRF groups had complete epithelialization, and all patients had complete epithelialization within three weeks. In patients lacking PRF, postoperative FGG palatal wounds exhibited full epithelialization 4 weeks after surgery.[20-21,23-24] During the second week after FGG surgery, the control group employing a gelatin sponge demonstrated greater complete epithelialization than PRF, according to one case report. That is probable since the wound size was smaller in the gelatin sponge group than in the PRF group.[19,23]

The PRF group, on the other hand, had complete epithelialization two weeks following the FGG procedure. The observation method is the study's limitation. It was discovered through direct viewing, which led to an overestimation of the findings.[20] The width and thickness of the soft tissue graft influenced the duration of epithelialization. The fact that the wound from the single incision method healed faster than the palatal wound following FGG surgery demonstrates this.[19] A thicker PRF membrane degrades more slowly, hastening the process of epithelialization.[2]

The preparatory methods have an effect on PRF ability.[37] Slowing down the centrifugation process in the A-PRF and I-PRF promotes the synthesis of growth factors and neutrophilic granulocytes. Another type of PRF for post-FGG is advanced-PRF (A-PRF), which should be centrifuged at 1.500 rpm for 8 minutes. The A-PRF preparation utilized in this study hastened the closure of palatal wounds after FGG surgery when compared to the control group (gelatin sponge). In the second week, the A-PRF group had a wound healing percentage of 58%, while the control group had 36.6%. This considerable difference could be attributed to the high growth factor concentration of A-high PRF, whereas the gelatin sponge generates a prolonged reaction that promotes inflammation and hinders granulation tissue formation in wounds.[38] PRF membranes outperformed controls in all clinical investigations in terms of wound healing metrics. The results of hydrogen peroxide testing, color photography, and direct clinical evaluation of the palatal mucosa following FGG surgery were used to make this judgment. It was also based on measurements of palatal tissue thickness taken using an endodontic K-file #15, an endodontic spreader, and an endodontic reamer.[15,17,27] Due to the less permanent nature of the autologous fibrin glue, I-PRF revealed the highest tissue thickness values at one month and three months postoperative evaluation (AFG). In the first month, I-PRF tissues produced palatal tissue thickness similar to AFG and sterile tampons when compared to normal PRF preparations.[2,15,17] The adhesive qualities of both AFG and I-PRF are limited. To compensate for these shortcomings, butyl cyanoacrylate, silk, and sutures were used in greater quantities.[15]

Different outcomes were obtained when Titanium PRF was used (T-PRF). Tissue thickness was greater in the T-PRF-treated group than in the control group. The tissue's thickness will diminish in tandem with the T-PRF membrane's resorption. T-PRF contains a thicker, more stable fibrin network, which promotes wound healing. T-PRF also has host conducting characteristics, allowing it to repair palatal tissue thickness. T-PRF also has a longer absorption duration, allowing it to operate as a long-term healing scaffold. It also has antimicrobial capabilities and works as an external stimulant during the healing phase. It

heals as primary wound healing rather than secondary wound healing.[27,39]

The addition of materials such as titanium and butyl-cyanoacrylate (BC) to PRF accelerates hemostasis and reduces delayed bleeding.[25] Titanium's biocompatibility and hemocompatibility are well established. Processing in titanium tubes will increase platelet activation and regeneration in the wound area. Moreover, T-PRF has a thicker fibrin matrix.[33] The addition of BC to PRF enhances the wound's adhesive ability, and hence the hemostatic ability of PRF.[40]

Conclusions

According to research literature, PRF can dramatically minimize delayed bleeding after FGG, reduce pain, improve eating habits, and hasten the healing of the palate wound. The expression of platelets, leukocytes, growth factors, fibrin matrix, and anti-inflammatory cytokines is increased.

Acknowledgments

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Declaration of Interest

There are no competing interests disclosed by the author.

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