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The Role of Leukocyte and Platelet-Rich Fibrin in Enhancing the Healing of Extraction Sockets: An Overview of the Literature

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Abstract

Introduction: Leukocyte and platelet-rich fibrin (L-PRF) is an emerging material in dentistry, however, there are controversies surrounding its effectiveness. Despite the amount of literature available, debates regarding its effect continue. This review aims to summarize and clarify the data surrounding the use of L-PRF in promoting the healing of extraction sockets, which may offer a better outcome for future treatments. **Purpose:** The purpose of this review is to evaluate the current literature on the use of L-PRF in promoting the healing of extraction sockets, and to provide a comprehensive overview of the available evidence. **Methods:** A comprehensive computer-based search of databases such as PubMed, Medline, and Cochrane Library was conducted. **Results:** The results of this review suggest that L-PRF has shown promise in promoting early healing of extraction sockets, but the evidence for its effectiveness over a longer period is limited. **Conclusion:** Although L-PRF has shown promising results in the early healing periods, its effectiveness over a longer healing period cannot be confirmed based on the available data. More clinical trials with standardized protocols and consistent measurement methods are needed to establish the role of L-PRF in enhancing the healing of extraction sockets.

Keywords

Leukocyte and Platelet Rich Fibrin, Extraction Sockets, Hard Tissue, Soft Tissue

1. Introduction

Dental implants have become a widely accepted solution for restoring missing

teeth, providing a long-lasting and esthetically pleasing option for patients [1] [2]. To increase the success rate of this treatment, it is essential to provide healthy soft and hard tissue for osteointegration around the implant. However, after tooth extraction, the socket undergoes significant changes, including the loss of 50% - 60% of its volume in the first three months [3] [4]. To minimize these changes and preserve the bone volume, immediate implant placement is an ideal solution, but it requires specific conditions such as favorable socket morphology, sufficient initial bone volume, and preservation of the buccal bone [5] [6]. In cases where these conditions are not met, socket preservation is a prophylactic intervention that involves filling the extraction socket with bone substitute materials (BSMs) to maintain the alveolar bone dimension [7] [8]. These BSMs can interfere with the natural healing process, which typically lasts 3 - 6 months, and result in sufficient bone volume for implant placement [9] [10]. They can also be used in conjunction with immediate implant placement when additional socket filling is required [11].

Leukocyte and platelet-rich fibrin (L-PRF) is a promising material in dentistry and has gained attention for its potential in promoting healing in extraction sockets. It is a blood concentrate that is obtained from the patient's own blood through a one-step centrifugation process [12] [13]. Unlike platelet-rich plasma (PRP), which requires a two-step centrifugation process [14], L-PRF contains a high content of platelets and leukocytes in a fibrin matrix along with plasma proteins [15] [16]. The presence of leukocytes in the L-PRF matrix makes it a more complex and dynamic material compared to PRP [17].

L-PRF is considered a biologically active material due to the presence of various growth factors and cytokines that are essential for the healing process. Its fibrin matrix also provides a scaffold for cellular migration and tissue regeneration. In addition, the presence of leukocytes in the L-PRF matrix may also play a role in enhancing the immune response and preventing bacterial infections [15] [16] [17] [18] [19]. These properties of L-PRF make it a potentially useful material in promoting the healing of extraction sockets and improving the outcomes of dental implant placement.

Despite the promising results reported in the literature, the effectiveness of L-PRF in promoting the healing of extraction sockets is still a matter of debate. This review aims to summarize the available evidence and clarify the data surrounding the use of L-PRF in promoting the healing of extraction sockets. The goal is to provide a comprehensive overview of the current state of knowledge regarding L-PRF and its potential as a material in promoting the healing of extraction sockets, with the aim of guiding future clinical and research efforts in this area.

2. Methods

The purpose of this review was to assess the efficacy of leukocyte and platelet-rich fibrin (L-PRF) in promoting healing in extraction sockets. To accom-

plish this, a comprehensive search was performed in databases such as PubMed, Medline, and Cochrane Library. The search was limited to randomized controlled trials (RCTs) and prospective controlled trials (CCTs) that were published in the English language. The studies were selected based on the inclusion criteria of treatment of fresh sockets and treatment using either L-PRF (with or without biomaterials) or spontaneous healing.

A manual review of the abstracts was conducted to identify the 20 articles that met the inclusion criteria. Further analysis was performed on these 20 articles to determine the 12 studies that exclusively used L-PRF. These studies were included in the review to reduce the heterogeneity of the data and provide a clear understanding of the effect of L-PRF on the healing of extraction sockets [18]-[29].

The studies were summarized in **Table 1**, which presented the study design and preparation protocols. The heterogeneity in the protocol used to produce L-PRF was evident, with a range of centrifugation speeds of 2700 - 3000 rounds per minute and centrifugation times of 10 - 12 minutes. The exception was the study by Giudice *et al.* [25], which adopted 18 minutes of centrifugation time. This review aimed to provide a comprehensive analysis of the available literature on the use of L-PRF in promoting healing in extraction sockets.

2.1. Evaluation of Hard Tissue Regeneration

Seven of the included articles [18] [20] [21] [23] [26] [27] [29] evaluated the hard tissue regeneration. In the study by Suttapreyasri *et al.* [29], cast analysis was used to evaluate the dimensional resorption of the ridge after an 8-week period, comparing the L-PRF group to the non-L-PRF group. The results did not show any significant difference between the two groups. Canellas *et al.* [20] and

Table 1. Centrifugation protocols for L-PRF preparation in included studies.

Study	Design	RPM	Centrifugation Time (min)
Castro *et al.* [18]	Split Mouth RCT	2700 rpm	12
Mourao *et al.* [19]	Parallel RCT	2700 rpm	12
Canellas *et al.* [20]	Parallel RCT	2700 rpm	12
Srinivas *et al.* [21]	CCT Split Mouth	3000 rpm	10
Ahmed *et al.* [22]	Parallel RCT	3000 rpm	10
Areewong *et al.* [23]	Parallel RCT	2700 rpm	12
Ustaoglu *et al.* [24]	Parallel RCT	2700 rpm	12
Giudice *et al.* [25]	Split Mouth RCT	2700 rpm	18
Zhang *et al.* [26]	Parallel CCT	2700 rpm	10
Temmerman *et al.* [27]	Split Mouth RCT	2700 rpm	12
Marenzi *et al.* [28]	Split Mouth RCT	2700 rpm	12
Suttapreyasri *et al.* [29]	Split Mouth RCT	3000 rpm	10

Temmerman *et al.* [27] used Cone Beam Computed Tomography (CBCT) to evaluate the hard tissue regeneration after three months. Canellas *et al.* [20] found a significant overall volume difference in favor of the L-PRF group, particularly in the buccal wall, but no difference in the horizontal bone resorption. Temmerman *et al.* [27] also found a significant difference in the L-PRF group, with less vertical and horizontal bone resorption.

Castro *et al.* [18] used CBCT to measure socket bone fill after three months and found a significant difference in favor of the L-PRF group compared to the control group. Srinivas *et al.* [21] used CBCT to evaluate bone density and found it higher in the L-PRF group, but no difference in bone height was found. Zhang *et al.* [26] evaluated the resorption rate of the bone using CBCT after three months and found a markedly lower resorption rate in the L-PRF group compared to the control group, although the difference was not statistically significant.

Histologic evaluation was performed by Canellas *et al.* [20] and Zhang *et al.* [26] using histomorphometry of the newly formed bone after three months. They found a more significant new bone formation in the L-PRF group compared to the control group. On the other hand, Areewong *et al.* [23] performed the same evaluation after an 8-week healing period and found no significant difference in new bone formation between the two groups.

2.2. Soft Tissue Healing Evaluation

Six studies [19] [21] [22] [24] [25] [28] evaluated the soft tissue healing using the Landry *et al.* Healing Index. The studies are summarized in **Table 2**. Out of these, 33% of the studies [22] [24] [25] found no significant difference in soft tissue healing after one week between the L-PRF and non-L-PRF groups. On the other hand, 50% of the studies [19] [21] [28] showed a significant difference in the healing of the soft tissue in the L-PRF group in the early healing time (one week). Although Ustaoglu *et al.* [24] did not find a significant difference in soft tissue healing, they measured the percentage of epithelization and found a faster epithelization in the L-PRF group.

Table 2. Soft tissue healing evaluation results from six studies.

Study	Result (L-PRF)	Result (Control)	Significant Difference
Mourao *et al.* [19]	Week 1: 3.81 ± 0.65 Week 2: 4.75 ± 0.44	Week 1: 3.18 ± 0.54 Week 2: 4.5 ± 0.51	Week 1: Yes Week 2: No
Srinivas *et al.* [21]	At day 7: 3.8 ± 0.40	At day 7: 3.0 ± 0.53	Yes
Ahmed *et al.* [22]	94.1%	86.7%	No
Ustaoglu *et al.* [24]	Week 1: 3.58 ± 0.63 Week 2: 4.59 ± 0.51	Week 1: 3.21 ± 0.66 Week 2: 4.38 ± 0.49	Week 1: No Week 2: No
Giudice *et al.* [25]	Week 1: 1 Week 2: 0.25	Week 1: 1.05 Week 2: 0.33	No
Marenzi *et al.* [28]	Day 3: 4.8 ± 0.6 Day 7: 4.5 ± 0.5 Day 14: 4.2 ± 0.2 Day 21: 4.1 ± 0.1	Day 3: 5.1 ± 0.9 Day 7: 4.9 ± 0.3 Day 14: 4.3 ± 0.3 Day 21: 4.2 ± 0.2	Day 3: No Day 7: Yes Day 14: Yes Day 21: Yes

2.3. Pain Comparison between L-PRF and Control Groups

Four studies (Mourao *et al.* [19], Ustaoglu *et al.* [24], Temmerman *et al.* [27], Marenzi *et al.* [28]) assessed the pain levels using visual analogue scale (VAS) and compared the results between L-PRF and control groups. All studies showed a significant difference in pain levels in favor of the L-PRF group on the first day after treatment as shown in **Table 3**. However, the difference in pain levels reduced by the second day according to Ustaoglu *et al.* [24] and by the fourth day according to Marenzi *et al.* [28]. Significant differences in pain levels between the two groups were still present at day three according to Tammerman *et al.* [27] and at day seven according to Maurao *et al.* [19].

3. Discussion

In this study, we evaluated the effect of L-PRF on the healing of the sockets after tooth extraction. Although there have been few qualified clinical trials regarding the evaluation of the effect of L-PRF on extraction socket preservation, we aimed to summarize the available evidence.

We selected twelve studies for our analysis, which met the inclusion criteria and used L-PRF only to minimize the heterogeneity of the data. We measured three outcomes: hard tissue healing, soft tissue healing, and pain assessment.

In terms of hard tissue healing, seven of the studies used various methods of evaluation and we found a range from no significant difference to a significant difference in favor of the L-PRF groups during the early healing stage. For soft tissue healing, a more constant method of evaluation was used, the Landry *et al.* Healing Index, which showed significant results in the L-PRF groups in 50% of the studies that measured soft tissue healing. In all four studies that measured pain score using the Visual Analog Scale (VAS), a positive effect was seen in the L-PRF groups.

L-PRF contains growth factors and cytokines, such as platelet-derived growth factor, transforming growth factor, vascular endothelial growth factor, and insulin-like growth factor, which are released slowly over 7 to 14 days [30] [31]. Additionally, many studies have shown the effect of PRF in preserving the keratinized gingiva in various surgical procedures [32] [33], which supports the positive effect of L-PRF on soft tissue healing.

Table 3. Visual Analogue Scale (VAS) pain assessment results.

Study	Result test (with L-PRF)	Result control (Normal healing)	Significance statistics
Mourao *et al.* [19]	At 7 days: 4 ± 1.15	7 days: 5.12 ± 1.08	Yes
Ustaoglu *et al.* [24]	Day 1: 3.30 ± 2.07 Day 2: 0.48 ± 0.92	Day 1:5.11 ± 1.60 Day 2	Day 1: yes Day 2: no
Temmerman *et al.* [27]	Day 3: 2,81	Day 3: 3,52	yes
Marenzi *et al.* [28]	3.2 ± 0.3	4.5 ± 0.7	yes

However, the effect of L-PRF on hard tissue healing cannot be definitively approved based on the available data and previous reviews [34] [35], as the methods of evaluation used in these studies were not standardized. Future studies should consider standardizing these methods to provide clearer evidence.

It is important to note that socket healing can be influenced by various factors, such as the indication for extraction, which can play a role in the healing of the alveolar bone [36]. Additionally, smokers have a significant reduction in both the quality and quantity of bone in extraction sockets compared to non-smokers [37] [38]. These factors should be taken into consideration in future studies.

4. Conclusion

In conclusion, the available data suggests that the use of L-PRF has a positive impact on the healing of extraction sockets, particularly in terms of soft tissue healing and pain reduction. Results showed a significant improvement in the early stages of healing, with 50% of the studies demonstrating a significant improvement in soft tissue healing in the first week. While the effects on hard tissue healing were less conclusive, there was a trend towards a positive impact in the early stages of healing. However, the results should be interpreted with caution due to the heterogenicity of the studies, including the varied methods of preparation and evaluation. Further studies with standardized protocols and considering factors that affect the healing process are needed to provide more robust evidence for the benefits of L-PRF in socket preservation.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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