BRAZILIAN JOURNAL OF IMPLANTOLOGY AND HEALTH SCIENCES

ISSN 2674-8169

Scientific evidence available after 18 years of application of fibrin rich in platelets and leukocytes in the repair of surgical wounds: An integrative review

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ABSTRACT

Introduction: In the last 18 years, Platelet and Leukocyte Rich Fibrin (L-PRF) has emerged as an innovative biomaterial in regenerative medicine and dentistry, standing out for its ability to continuously release growth factors and promote more efficient healing. However, the variability in the preparation and application of L-PRF, together with the lack of standardization, represent major challenges, increasing the need for further research to improve and standardize its clinical use. Materials and Methods: This study is an integrative review, with no need to submit it to the Research Ethics Committee. The guiding question was: "What is the main evidence in the literature on the applications of platelet- and leukocyte-rich fibrin in dentistry?". Results and Discussion: L-PRF has proved effective in various areas of dentistry. In implantology, it accelerates bone healing and improves implant integration. In periodontics, it promotes regeneration of bone damage and improves the quality of periodontal tissue. In gingival recessions and soft tissue lesions, it accelerates regeneration and reduces post-operative discomfort. In periodontal and maxillofacial surgery, it contributes to a faster and more comfortable recovery from swelling and pain. Variability in the preparation and application of L-PRF is still a challenge, and standardization of protocols is essential to ensure more consistent and predictable results. Conclusion: After 18 years, L-PRF has shown beneficial effects in dentistry, especially in terms of bone regeneration and improved post-operative healing. However, the standardization of protocols seems to be crucial in order to improve its clinical results.

Keywords: Platelet-Rich Fibrin. Dentistry. Evidence-Based Dentistry and L-PRF

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Dados da publicação: *Artigo recebido em 03 de Julho e publicado em 23 de Agosto de 2024.*
DOI: *https://doi.org/10.36557/2674-8169.2024v6n8p-3902-3916*
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INTRODUCTION

Over the past 18 years, Leukocyte-Platelet Rich Fibrin (L-PRF) has emerged as an innovative biomaterial, gaining prominence in regenerative medicine and surgical practices, particularly in dentistry and oral and maxillofacial surgery.[RM1] Since its introduction, L-PRF has been recognized for its unique ability [RM2] to continuously release growth factors, promoting apparently more efficient and predictable tissue regeneration. This biomaterial is derived from the centrifugation of autologous blood, generating a three-dimensional matrix composed of a fibrin network that encapsulates platelets and leukocytes, which play fundamental roles in the healing process [1-5].

L-PRF has proven particularly effective in several clinical applications, including the regeneration of bone defects, the treatment of periodontal lesions, and the acceleration of complex wound healing. Preclinical and clinical studies have consistently demonstrated that the use of L-PRF not only facilitates healing, but also significantly reduces recovery time and minimizes postoperative complications such as persistent infections and inflammation. Its biocompatibility and ease of use have made L-PRF a preferred choice for many healthcare professionals [6-8].

The mechanism of action of L-PRF involves the sustained release of growth factors, such as TGF-β, PDGF and VEGF, which are critical for angiogenesis, cell proliferation and collagen synthesis. These growth factors are gradually released from the fibrin matrix, which ensures more effective healing and regeneration of damaged tissues. Furthermore, the presence of leukocytes in the L-PRF matrix contributes to the modulation of the immune response, promoting an anti-inflammatory environment that favors tissue repair [9-12].

The application of L-PRF has also been explored in other areas of medicine, such as orthopedics, dermatology and plastic surgery, where its ability to promote tissue regeneration and modulate the inflammatory response has been valued. The success of L-PRF in these areas expands its potential for clinical application, encouraging further research to explore new uses and optimize existing protocols. The versatility and efficacy of L-PRF make it a promising biomaterial for treatments that require rapid and efficient healing [13,14]. However, despite significant advances in the use of L-PRF, some questions remain open. Variability in the methods of preparation and application of L-

PRF can influence clinical results, and the lack of standardization makes comparison between studies difficult. In addition, individual differences, such as genetic variability and health status of patients, can affect the efficacy of L-PRF, suggesting the need for personalized approaches in the use of this biomaterial. These challenges highlight the importance of additional studies to standardize and optimize the use of L-PRF [15-18]. Another relevant aspect to be considered is the impact of L-PRF on the modulation of the inflammatory microenvironment. Recent studies suggest that L-PRF can influence macrophage polarization, promoting a shift from the pro-inflammatory M1 phenotype to the anti-inflammatory M2 phenotype. This modulation is crucial for the resolution of inflammation and tissue regeneration, highlighting the potential of L-PRF in treatments where chronic inflammation is a problem. Exploring these mechanisms may open new frontiers for the use of L-PRF in a variety of clinical conditions [19,20].

In addition, L-PRF may play an important role in reducing the use of anti-inflammatory drugs and antibiotics in the postoperative period. Its ability to accelerate healing and modulate the immune response may reduce the need for pharmacological interventions, minimizing the risks associated with prolonged use of medications [21-23].

This study aims to review the main scientific evidence accumulated over the 18 years since the discovery of L-PRF. The review aims to critically evaluate the efficacy, safety and biological mechanisms underlying the use of L-PRF in various clinical applications. In addition, it seeks to identify the main gaps in current knowledge and suggest future directions for research, with the aim of optimizing the use of L-PRF and expanding its therapeutic potential in different areas of Dentistry.

METODOLOGY

This study is configured as an integrative review, dispensing with submission to the Research Ethics Committee. The primary objective of the review is to systematize and synthesize information on a specific topic, employing a rigorous research method that ensures critical evaluation of the relevance and validity of the findings. Initially, a control protocol was developed, encompassing the delimitation of the problem-question and the search strategies. The review followed six methodological steps, as described by Sousa et al. (2018) [24]: 1) identification of the topic; 2) establishment of

rigorous inclusion and exclusion criteria; 3) analytical categorization of the studies; 4) meticulous evaluation of the selected studies; 5) careful interpretation of the results; 6) presentation of the synthesis of knowledge. The guiding question established was: "What is the main evidence in the literature on the applications of Platelet-Rich Fibrin and Leukocytes in Dentistry?" To elucidate this issue, comprehensive searches were conducted in three databases: PubMed via MEDLINE, Web of Science and Google Scholar. The search was conducted using the following descriptors from the controlled vocabulary Health Sciences Descriptors (DeCS): "Platelet-Rich Fibrin", "Dentistry", "Evidence-Based Dentistry" and "L-PRF" in English, combined using the Boolean operators "AND" and "OR". The search strategies included studies that answered the guiding question of this research. During the search stage in the databases, exclusion criteria were adopted, such as: course completion papers (monographs, dissertations and theses), duplicates, editorials, previous notes, abstracts published in conference proceedings and manuals. The research and analysis of the works in the selected databases were carried out by two independent researchers on May 30, 2024. Of the 498 results obtained, 67 duplicate studies were identified, which were resolved using the Rayyan software, with a total of 24 articles included in this review. To present the results found in the literature, it was decided to describe them in a structured manner in topics, highlighting the applications of this autologous material in dentistry.

RESULTS AND DISCUSSION

L-PRF has been extensively investigated for its remarkable ability to enhance bone regeneration, especially in dental implant procedures. Rigorous studies have demonstrated that L-PRF not only accelerates bone healing but also optimizes implant integration, resulting in a higher success rate when compared to other autologous concentrates. This biomaterial significantly contributes to the formation of better quality new bone, facilitating insertion, long-term stability of implants and promoting stronger bone anchorage [25-29].

In periodontics, L-PRF has demonstrated remarkable efficacy in the regeneration of periodontal bone defects. The application of this material in combination with bone grafts not only resulted in a significant reduction in probing depth but also promoted a substantial improvement in the quality and quantity of bone formation. L-PRF plays a

crucial role in promoting osteogenesis and vascularization in the defect area, creating a bioactive environment that favors tissue regeneration. Furthermore, the gradual release of growth factors through L-PRF enhances tissue repair, contributing to the long-term stability of periodontal tissue and significantly improving clinical results in periodontal regeneration procedures [30-34].

In relation to gingival recessions, L-PRF has demonstrated substantial benefits; its combined use with grafts for the treatment of gingival recessions has shown a significant improvement in root coverage, as well as in the healing of gingival tissue. L-PRF acts by accelerating the regeneration process, optimizing the biological response by promoting angiogenesis and the formation of healthy connective tissue. In addition, its application reduces postoperative discomfort, providing superior aesthetic and functional results, with faster recovery and fewer associated complications [35-39].

In periodontal surgery, L-PRF has been shown to be highly effective in accelerating the healing of periodontal tissues. The use of L-PRF not only promotes faster healing but also significantly reduces postoperative discomfort after periodontal surgical procedures. The application of L-PRF contributes to a more efficient recovery, favoring tissue regeneration through the sustained release of growth factors and cytokines, which results in a lower incidence of complications and a better postoperative experience for patients [40-42]. L-PRF has been shown to be particularly valuable in maxillofacial surgeries due to its ability to attenuate postoperative edema and pain. The application of L-PRF has resulted in a significant decrease in edema and pain, which has facilitated a faster and more comfortable recovery for patients. This efficacy is due to the prolonged release of growth factors, which promote tissue regeneration and modulate the inflammatory response. As a result, L-PRF not only accelerates healing but also reduces the need for postoperative analgesics, contributing to more efficient pain management and a recovery with fewer complications [43-48].

The variability in the preparation and application of L-PRF continues to represent a specific challenge in clinical practice. The lack of standardization in protocols can compromise the efficacy of the treatment, leading to inconsistent results. Studies such as that of Zhao et al. (2020) highlight the importance of standardizing the methods of

preparation and application of L-PRF to improve its clinical benefits. The standardization of processes not only ensures greater consistency in results, but also improves the predictability and applicability of L-PRF in a variety of clinical settings, facilitating its integration and effectiveness in different areas of medicine and dentistry.

FINAL CONSIDERATIONS

The articles reviewed demonstrated that since its clinical application in surgical wound repair, leukocyte-rich platelet fibrin (L-PRF) has benefits in dentistry, including bone regeneration, treatment of gingival recessions, and improvement of postoperative healing. L-PRF appears to improve the quality of newly formed bone and possibly pain and edema. However, the lack of standardization in preparation and application protocols still represents a challenge. Standardization of methods and further studies are needed to maximize its benefits and ensure studies with more consistent results.

ETHICAL APPROVAL

As this is an integrative review, it was not necessary to obtain approval from the research ethics committee for this study.

FUNDING SOURCES

This review received no funding.

AUTHORS' CONTRIBUTION

Study design: all authors; Assessment of the overall quality of the study: all authors. Writing the article: all authors. Approval of the study: all authors. Correction and final revision: all authors.

DISCLOSURE OF CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

DECLARATION OF DATA AVAILABILITY

All datasets arising from this study are available upon reasonable request to the corresponding author. The datasets generated and/or analyzed during this study are available from the corresponding author upon reasonable request.

STUDY DESIGN

Integrative review.

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