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Review Article

The biological edge in periodontal therapy: Revolutionizing periodontal treatment with autologous blood products

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ABSTRACT

This review delves into the pivotal role of autologous blood products—such as platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and injectable platelet-rich fibrin (i-PRF)—in revolutionizing periodontal therapy by seamlessly integrating biological principles with clinical applications. These blood derivatives enhance key regenerative processes, including cellular proliferation, angiogenesis, and extracellular matrix remodelling, thereby significantly improving outcomes in soft and hard tissue healing. By synthesizing the latest research, clinical studies, and practical experiences, the review underscores the growing importance of these therapies in modern periodontics while advocating for standardized protocols and further research to maximize their clinical efficacy and long-term benefits.

1. Introduction

The evolution of periodontal therapy has witnessed significant strides over the past few decades, with a growing emphasis on biological approaches that harness the body's natural healing mechanisms. Among these advancements, the application of autologous blood products, particularly Platelet-Rich Fibrin (PRF) and its various derivatives, has revolutionized the field.[1] These products are obtained from the patient's own blood, they are abundant in growth factors and cytokines that stimulate tissue regeneration and enhance wound healing, and enhance overall clinical outcomes. The shift from synthetic and allogenic materials to autologous options has not only minimized risks associated with foreign body reactions but also tapped into the inherent regenerative potential of the patient's biology, leading to more predictable and successful periodontal treatments.

The integration of autologous blood products into periodontal therapy represents a paradigm shift towards more natural and patient-specific treatment modalities. This review delves into the types and classifications of PRF, recent advancements in its application, and the role of platelet concentrates in various periodontal procedures.[2] It also explores the impact of these biologically active products on bone regeneration and dental implant success, providing a comprehensive overview of how these innovations are shaping the future of periodontal therapy. By examining the pioneering efforts and clinical outcomes associated with each generation of PRF, this article aims to underscore the significance of autologous blood products in achieving superior regenerative results and advancing the field of periodontics.

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1.1. Types and classification of platelet-rich fibrin (PRF)

1.1.1. Leukocyte- and platelet-rich fibrin (L-PRF)

L-PRF, developed by Dr. Choukroun, is a second-generation platelet concentrate that forgoes the utilisation of anticoagulants, allowing for a natural coagulation process. This results in a fibrin matrix rich in platelets and leukocytes, which are critical for promoting wound healing and tissue regeneration.[3]

1.1.2. Advanced platelet-rich fibrin (A-PRF)

Advanced Platelet-Rich Fibrin (A-PRF) represents a refinement of L-PRF, introduced by Ghanaati et al. By modifying centrifugation protocols—specifically, reducing the speed and extending the duration—A-PRF yields a fibrin matrix with a higher concentration of leukocytes and regenerative cells, which enhances the release of growth factors over a longer period.[4] This modification results in superior regenerative outcomes, particularly in periodontal and implant procedures.

1.1.3. Injectable platelet-rich fibrin (i-PRF

Injectable PRF (i-PRF) is a more recent innovation that allows PRF to be delivered in a liquid form, which is advantageous for direct injection into tissues. This form of PRF, developed by Miron and colleagues, provides a scaffold-free approach, enhancing cellular proliferation and tissue regeneration in challenging anatomical locations.[5]

1.1.4. Titanium-prepared platelet-rich fibrin (T-PRF)

Titanium-Prepared Platelet-Rich Fibrin (T-PRF), introduced by Tunalı et al., employs titanium tubes rather than conventional glass tubes for PRF preparation. The use of titanium is believed to improve the quality of the fibrin matrix and enhance the biocompatibility of the PRF, leading to more effective tissue regeneration.[6]

1.2. Generations of platelet-rich fibrin

1.2.1. First-generation: Platelet-rich plasma (PRP)

The first generation of platelet concentrates, PRP, involves separating and concentrating platelets using centrifugation and then mixing them with an anticoagulant. While PRP enhances soft tissue healing and inflammation reduction, its reliance on external activators and the addition of anticoagulants limit its natural regenerative potential.[7]

1.3. Second-generation: Leukocyte- and platelet-rich fibrin (L-PRF)

L-PRF, the second generation, eliminates the need for anticoagulants, allowing for a more natural healing process. The fibrin matrix in L-PRF traps platelets and leukocytes, which gradually release growth factors, promoting sustained tissue regeneration. This generation has been instrumental in enhancing the outcomes of periodontal regenerative procedures.[8]

1.3.1. Third-generation: Advanced platelet-rich fibrin (A-PRF) and Injectable PRF (i-PRF)

The third generation of PRF, including A-PRF and i-PRF, focuses on optimizing the concentration of regenerative cells and the extended release of growth factors. A-PRF is characterized by a slower centrifugation process, leading to a more effective and prolonged regenerative response. i-PRF, in its liquid form, facilitates easier application and direct injection into tissues, making it particularly useful for targeted regeneration.

1.4. Recent advances in PRF

The field of PRF has seen significant advancements in recent years, particularly in the optimization of preparation protocols and the expansion of clinical applications. The development of T-PRF, with its enhanced fibrin matrix quality, represents a major step forward in improving the biocompatibility and regenerative potential of PRF. Additionally, the combination of PRF with bone graft materials has been explored to further improve outcomes in periodontal regeneration and implant stability.[9]

1.5. Platelet products in periodontal procedures

1.5.1. Periodontal regeneration

PRF has become an essential component of periodontal regeneration, especially in procedures such as guided tissue regeneration (GTR) and bone grafting. The high concentration of growth factors in PRF promotes key regenerative processes, including cellular proliferation, angiogenesis, and extracellular matrix remodelling, which are critical for the regeneration of periodontal tissues.[10] When used in conjunction with bone grafts, PRF significantly enhances bone regeneration, leading to improved clinical outcomes and faster healing times.[11]

1.5.2. Soft tissue augmentation

PRF is widely used in soft tissue augmentation procedures, including root coverage and gingival recession treatment. The application of PRF in these procedures has shown improved clinical outcomes, such as increased tissue thickness, enhanced aesthetic results, and reduced patient discomfort. The sustained release of growth factors from PRF supports fibroblast proliferation and collagen synthesis, leading to more effective soft tissue healing.[12]

1.5.3. Dental implants

In implant dentistry, PRF has been shown to play a crucial role in improving the osseointegration process and reducing healing time. The application of PRF in conjunction with dental implants enhances the stability of the implant and promotes the regeneration of peri-implant tissues. PRF can be used as a membrane to cover the implant site or mixed with bone graft material to improve graft integration, leading to more predictable and successful implant outcomes.[13]

1.5.4. Bone regeneration

One of the most significant applications of PRF is in bone regeneration, particularly in the context of periodontal therapy and dental implantology. The fibrin matrix within PRF functions as a scaffold, supporting the proliferation and differentiation of osteoblasts, which are essential for new bone formation. Studies have shown that PRF can enhance the integration of bone grafts, reduce bone resorption, and accelerate the healing of bone defects.[14] The use of PRF in sinus augmentation, ridge preservation, and alveolar bone grafting has demonstrated its ability to promote faster and more complete bone regeneration, making it a valuable tool in both periodontal therapy and implantology.[15]

1.6. Centrifugation Protocols for Different Types of PRF

1. L-PRF
   - (a) Centrifugation Speed: 2,700 rpm
   - (b) Time: 12 minutes
   - (c) Result: A fibrin matrix with high concentrations of platelets and leukocytes, ideal for wound healing and tissue regeneration.
2. A-PRF
   - (a) Centrifugation Speed: 1,500 rpm
   - (b) Time: 14 minutes
   - (c) Result: A denser fibrin matrix with a higher concentration of regenerative cells and prolonged growth factor release, suitable for enhanced tissue regeneration.[16]
3. I-PRF
   - (a) Centrifugation Speed: 700 rpm
   - (b) Time: 3 minutes
   - (c) Result: A liquid PRF form that retains more regenerative cells and can be injected directly, allowing for targeted tissue regeneration.
4. T-PRF
   - (a) Centrifugation Speed: 3,100 rpm
   - (b) Time: 12 minutes
   - (c) Result: A fibrin matrix with enhanced biocompatibility and regenerative potential, providing superior outcomes in tissue healing and regeneration.

1.7. Unlocking the regenerative potential in periodontics through slow-speed centrifugation

1.7.1. The advancing frontier of PRF

Platelet-rich fibrin (PRF) has evolved significantly since its initial introduction in the early 2000s by Dr. Joseph Choukroun. PRF, an autologous blood product, has gained increasing recognition in periodontics for its regenerative potential, particularly in the treatment of periodontal and peri-implant defects.[3] Over time, different generations of PRF have emerged, primarily distinguished by the centrifugation protocols used to obtain them. Traditional PRF, also known as L-PRF (leukocyte-rich PRF), involves high-speed centrifugation, while newer forms, such as advanced PRF (A-PRF) and injectable PRF (i-PRF), utilize slower centrifugation speeds to enhance regenerative capacity.[4]

1.7.2. Slow-speed centrifugation concept

The concept of slow-speed centrifugation emerged as a pivotal advancement in the field of autologous blood products. Traditional PRF uses higher centrifugal forces (around 3000 RPM) for longer durations to separate platelets and other cellular components. However, research revealed that higher centrifugal forces reduce the viability of leukocytes and growth factors critical for tissue regeneration. As a response, slow-speed centrifugation protocols (around 1300 RPM for A-PRF or 700 RPM for i-PRF) were developed, retaining a higher concentration of white blood cells, platelets, and bioactive molecules within the PRF matrix.[17]

1.8. Advantages of slow-speed centrifugation

1.8.1. Higher concentration of growth factors

Slower centrifugation preserves key growth factors such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor-beta (TGF-β). These molecules play critical roles in promoting cell proliferation, angiogenesis, and extracellular matrix formation, which are essential for effective periodontal regeneration.[4]

1.8.2. Improved cell viability

The slower centrifugation process enhances the preservation of leukocytes, which contribute to the body's immune response and further facilitate wound healing. The improved cell viability in A-PRF and i-PRF compared to traditional PRF makes them more effective in promoting tissue regeneration and inflammation control.[18]

1.8.3. Enhanced fibrin network structure

Slow-speed centrifugation results in a more porous fibrin scaffold, which allows for better entrapment and sustained release of growth factors. This fibrin structure provides a superior matrix for cell migration, making it ideal for soft tissue regeneration in periodontal procedures.[19]

1.8.4. *Injectability and versatility*

The introduction of i-PRF, obtained through very low-speed centrifugation, marked a significant leap in the versatility of autologous blood products. i-PRF remains in liquid form and can be easily injected into targeted periodontal sites, making it ideal for non-invasive and minimally invasive procedures. Its injectable nature allows for more precise delivery of growth factors to areas of tissue injury, maximizing the therapeutic effects.[20]

1.9. *Impact in periodontics*

Slow-speed centrifugation has revolutionized the use of PRF in periodontics by significantly enhancing the regenerative outcomes in both soft and hard tissue treatments. Periodontal surgeries, such as guided bone regeneration, sinus augmentation, and root coverage procedures, have all benefited from the enhanced biological properties of A-PRF and i-PRF. Clinical studies have shown superior wound healing, faster recovery times, and greater bone and tissue regeneration in patients treated with slow-speed PRF preparations compared to traditional high-speed PRF.[21]

Moreover, the use of advanced PRF formulations has led to improved patient outcomes in peri-implantitis management, recession defects, and complex periodontal surgeries.[22] The slow-speed centrifugation concept has also enabled a more predictable and biologically driven approach to periodontal regeneration, making it a cornerstone in modern periodontal therapy.

2. Discussion

The application of autologous blood products, particularly platelet-rich fibrin (PRF) and its derivatives, has introduced an innovative approach to periodontal therapy that aligns closely with the principles of regenerative biology. Unlike traditional synthetic grafts or allogenic materials, these products derive directly from a patient's own blood, containing an array of growth factors and cytokines that are essential for cellular proliferation, angiogenesis, and tissue regeneration.[23] This biological edge minimizes the risks of foreign-body reactions and enhances patient-specific healing. As these autologous products stimulate the body's natural repair mechanisms, they offer a promising alternative to conventional treatments by yielding highly individualized outcomes in soft and hard tissue healing.

In periodontal applications, PRF and its forms—such as leukocyte-rich PRF (L-PRF), advanced PRF (A-PRF), and injectable PRF (i-PRF)—have been shown to accelerate wound healing, promote bone regeneration, and improve outcomes in dental implantology. These products differ in preparation methods, particularly centrifugation speeds, which influences the concentration of regenerative cells and the release duration of growth factors. The slower centrifugation techniques utilized in A-PRF and i-PRF, for instance, retain a higher concentration of leukocytes and platelets, enhancing both the structural and biological quality of the fibrin matrix.[24] This adaptation makes PRF highly effective for periodontal procedures, as it supports sustained tissue regeneration and a more controlled healing environment.

Further, these advances in PRF technology, including T-PRF and i-PRF, are revolutionizing regenerative periodontics by providing clinicians with flexible applications that range from injectable forms for non-invasive treatments to denser matrices for soft and hard tissue augmentation.[25] The versatility and safety of autologous blood products emphasize their value as foundational tools in periodontal therapy, potentially reducing the need for additional biomaterials and offering superior biocompatibility. Future studies focused on standardized preparation protocols and long-term clinical evaluations are crucial to optimizing their therapeutic potential, as they continue to reshape the landscape of periodontal treatment through biologically driven solutions.

PRF has demonstrated considerable success in enhancing tissue regeneration due to its autologous nature and capacity to release growth factors. However, certain limitations affect its efficacy in specific patient populations. For instance, in elderly patients or individuals with hematological conditions like leukemia, PRF quality can be compromised, resulting in less effective fibrin matrices.[26] Obtaining platelet-rich fibrin (PRF) in older patients can present limitations due to age-related factors affecting the quality and regenerative potential of the fibrin matrix. As people age, physiological changes lead to a natural decline in platelet count and growth factor concentrations, which can reduce the overall efficacy of PRF in promoting wound healing and tissue regeneration. Additionally, older patients may experience compromised immune function and slower cellular turnover, factors that can impact the structural integrity of the PRF matrix.[26]The fibrin quality itself may be less robust, potentially leading to reduced stability and longevity of the PRF when applied to periodontal or other surgical sites, making it a consideration for clinicians when planning regenerative procedures in geriatric patients.

These biological constraints have driven interest in alternative biomaterials to ensure optimal clinical outcomes. Among these, synthetic products like Gem21S, which combines platelet-derived growth factor (PDGF) with a bone matrix, offer targeted regenerative benefits and have shown efficacy in patients where PRF may be less effective.[27] Other available substitutes, such as Emdogain (enamel matrix derivative) and synthetic bone graft materials, further expand treatment options. These alternatives enable clinicians to tailor regenerative approaches to meet individual patient needs, particularly when PRF may not achieve the desired outcomes due to underlying health factors.

3. Conclusion

The evolution from PRP to the advanced forms of PRF has revolutionized periodontal therapy, providing clinicians with powerful tools for promoting tissue regeneration and improving clinical outcomes. As research continues to refine PRF technology and expand its applications, PRF is likely to remain at the forefront of regenerative dentistry. Future studies should focus on standardizing preparation techniques, exploring new clinical applications, and further elucidating the biological mechanisms underlying the success of PRF.

4. Source of Funding

None.

5. Conflict of Interest

None.

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