Universidad Europea

GRADUATION PROJECT

Degree in Dentistry

TITLE

PRP IN PERIODONTICS

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ABSTRACT

Introduction: In recent years, the search for less invasive and biologically driven treatments has transformed periodontics. Platelet-rich derivatives have emerged being capable of leveraging the body's natural regeneration capacity. Platelet-Rich Plasma (PRP), Platelet-Rich Fibrin (PRF), and Concentrated Growth Factors (CGF) are autologous blood products high in growth factors that promote healing, angiogenesis, and new tissue creation. **Objective:** This study aimed to assess the effectiveness of PRP in periodontal regeneration and compare its performance with PRF and CGF, analyzing their clinical efficacy in managing intrabony defects. **Material and Methods:** A systematic review was conducted following PRISMA guidelines. Databases including Medline, Scopus, Cochrane, and Dentistry & Oral Sciences Source were searched using relevant MeSH terms. Selection included randomized controlled trials and clinical studies involving PRP, PRF, and CGF in periodontal therapy. Clinical parameters such as clinical attachment level (CAL), probing depth (PD), and bone regeneration were evaluated. **Results:** The study found that using PRP in conjunction with regenerative treatments improved CAL and PD results. However, PRF and CGF produced better long-term results due to sustained growth factor release and scaffold stability. The efficacy of these platelet concentrates was determined by defect morphology, application procedures, and individual patient characteristics. **Conclusion:** While PRP promotes periodontal regeneration, PRF and CGF tend to provide better and more consistent long-term effects. However, present evidence is limited due to methodological diversity. As a result, more study is needed to provide definite therapeutic guidelines, optimize application methodologies, and identify the most effective derivative for certain clinical settings.

KEYWORDS

Dentistry, Periodontal regeneration, Platelet Rich Plasma, Platelet Rich Fibrin, Concentrated Growth Factors, Intrabony Defects

RESUMEN

Introducción: En los últimos años, la búsqueda de tratamientos menos invasivos y con enfoque biológico ha transformado la periodoncia. Derivados como el plasma rico en plaquetas (PRP), la fibrina rica en plaquetas (PRF) y los factores de crecimiento concentrados (CGF) han demostrado aprovechar el potencial regenerativo del organismo, promoviendo la cicatrización, la angiogénesis y la formación de nuevos tejidos. **Objetivo:** Evaluar la eficacia del PRP en la regeneración periodontal y compararlo con el PRF y el CGF en el tratamiento de defectos intraóseos. **Material y Métodos:** Se realizó una revisión sistemática siguiendo las directrices PRISMA. Se buscaron estudios clínicos y ensayos controlados aleatorizados en bases de datos como Medline, Scopus, Cochrane y Dentistry & Oral Sciences Source. Se analizaron parámetros clínicos como el nivel de inserción clínica, la profundidad de sondaje y la regeneración ósea. **Resultados:** El uso del PRP como coadyuvante mejoró el nivel de inserción clínica y la profundidad de sondaje. No obstante, el PRF y el CGF mostraron mejores resultados a largo plazo por su liberación sostenida de factores bioactivos y mayor estabilidad estructural. Su eficacia depende de la morfología del defecto, la técnica aplicada y las características del paciente. **Conclusión:** Aunque el PRP favorece la regeneración periodontal, el PRF y el CGF tienden a ofrecer efectos más duraderos y consistentes. No obstante, la evidencia actual es limitada debido a la diversidad metodológica. Por ello, se requiere más investigación para establecer pautas terapéuticas definitivas, optimizar las técnicas de aplicación y determinar el derivado más eficaz según el caso clínico.

PALABRAS CLAVE

Odontología, Regeneración periodontal, Plasma rica en plaquetas, Fibrina rica en plaquetas, Factores de crecimiento concentrados, Defectos intraóseos

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1. INTRODUCTION

1.1. Pathogenesis in Periodontitis

Periodontitis, an inflammatory condition that causes the alveolar bone, periodontal ligament, and tooth supporting tissues to gradually deteriorate (1). Gingivitis is a reversible form of gum inflammation that precedes periodontitis, which is caused by intricate interactions between dental biofilms and host immunological responses (2). if treatment is not received It can develop into periodontitis, which causes irreparable damage. The development of this condition is significantly influenced by microbial dysbiosis, which is the change from a balanced oral microbiome to one that is dominated by pathogenic bacteria (3).

The diagnosis entails thorough evaluations, such as radiographic imaging to measure bone loss, clinical attachment loss, and probing pocket depth (PPD) clinical tests. A more sophisticated method was introduced by the 2017 World Workshop on the Classification of Periodontal Diseases, which grades periodontitis from A to C to show the rate of advancement and stages it from I to IV according to the level of damage. While Stage IV indicates advanced illness with possible tooth loss, Stage I indicates early periodontitis. Grading aids medical professionals in predicting the course of an illness and considering variables like smoking, genetic predispositions, and systemic diseases like diabetes. Grade I indicates slow progression with minimal bone loss relative to age, Grade II reflects moderate progression aligned with the patient's age, and Grade III represents rapid progression with significant bone loss and potential tooth loss. Grade IV is reserved for complex cases involving severe bone loss, extensive tooth loss, and additional rehabilitation challenges like occlusal trauma or masticatory dysfunction (1).

1.2. Advances in Periodontal Defect Classification

Clinical professionals now have more treatment choices in addition to better diagnostic clarity thanks to developments in the understanding and classification of periodontal bone defects. The groundbreaking classification developed by Goldman and Cohen in 1958, which categorized infrabony defects according to the number of surviving walls, established the foundation for assessing these defects. This method demonstrated the regenerative potential of three-wall defects, which provided ideal healing conditions and natural confinement for graft materials. On the other hand, because of their open structure, one-wall defects posed serious difficulties that called for creative solutions like guided tissue regeneration (GTR) or graft-growth factor combinations. Their research established a crucial benchmark for decades by highlighting the clear connection between treatment results and defect shape. The classification also addresses combination defects, which transition between configurations along their depth. For instance, a defect may begin as a three-wall defect apically and become a two-wall or one-wall defect coronally. These require tailored approaches to maximize regeneration in the favorable apical regions while addressing the less supportive coronal areas. The Goldman and Cohen classification remains fundamental in periodontal therapy due to its simplicity and its clear connection to treatment outcomes, although it does not account for other influencing factors such as defect depth, angle, or anatomical irregularities (4).

A new dimension was introduced by Clarke's anatomical classification (1971), which concentrated on the connection between nearby tissues and bony abnormalities. By introducing concepts like hemisected defects and craters, Clarke gave medical professionals a more sophisticated grasp of how the shape of defects may affect surgical access and treatment planning. In order to repair periodontal tissues while maintaining anatomical integrity, Clarke also promoted the use of bone grafts and minimally invasive flap procedures (5).

By highlighting the connection between clinical presentation, defect morphology, and systemic variables, Papanou and Tonetti made a substantial contribution to the comprehension and categorization of periodontal disorders. They worked to improve diagnosis and treatment planning by combining clinical and radiographic examinations. They emphasized that regenerative results are influenced by the morphology of periodontal abnormalities, such as furcation involvement, craters, and infrabony defects. They highlighted a comprehensive approach to periodontal care by connecting smoking and other systemic diseases like diabetes to the advancement of the disease. By integrating accurate morphological evaluation with the identification of patient-specific risk factors for the best possible periodontal regeneration, their categorization system set the foundation for personalized treatment plans (6).

Building upon these frameworks, Vandana and Bharath (2017) created a contemporary classification system that combined clinical concerns with morphological characteristics. Their complete method addressed complex or combination flaws involving numerous wall types inside a single lesion, periodontal problems based on wall configurations, and developmental defects such as fenestrations. Defect-specific therapeutic approaches, including the application of sophisticated regenerative materials like concentrated growth factors (CGF), platelet-rich fibrin (PRF), and enamel matrix derivatives (EMDs), were also highlighted by this classification.

They gave clinicians a useful framework for treating problems of different complexity by matching classification with customized remedies (7).

Regarding Radiographic Classification, we have three classifications of osseous defects based on angles and depth. Steffensen & Weber 1989 focus on small versus wide angles, Papapanou & Wennstrom 1991 on defect depth, and Tsitoura et al. 2004 on narrow, intermediate, and wide angles. These systems guide diagnosis and treatment planning in periodontal regeneration (8–10) (Fig 1.).

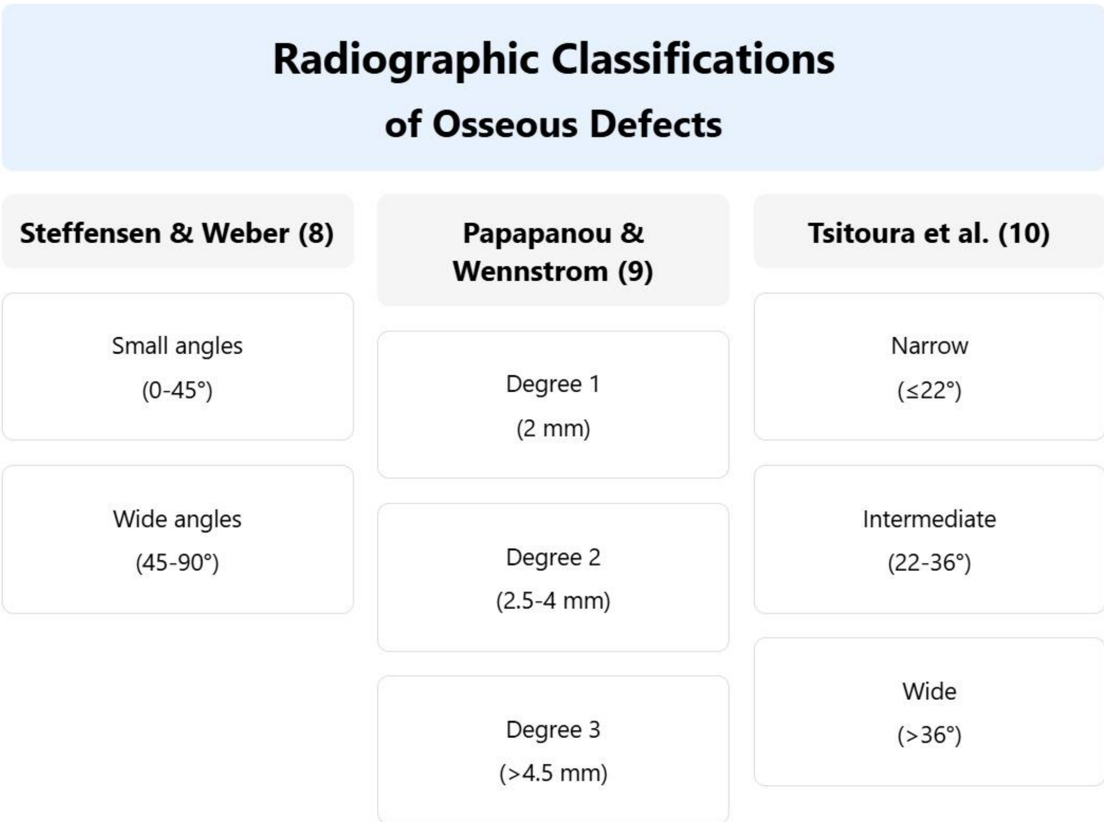

Figure. 1. Radiographic classification of osseus defects (8–10)

The most recent development, the physiologically driven methods of Velasquez-Plata et al. (2022), highlighted how osseous topography directs minimally invasive surgical (MIS) procedures. Cone-beam computed tomography (CBCT) and other contemporary imaging technologies were included into this classification to provide intricate three-dimensional representations of defects. It promoted customized flap designs according to the shape of the defect, like restricted reflection techniques to support grafts in three-wall defects or papilla preservation flaps for interproximal defects. By emphasizing on less traumatic procedures, improved wound stability, and long-term regeneration effects, the biologically driven model also demonstrated the synergy between cutting-edge biomaterials and surgical procedures (11).

1.3. Biomaterials in Regenerative Periodontics

Expanding upon these categories, the incorporation of cutting-edge biomaterials has greatly improved defect control. A cutting-edge biomaterial refers to an advanced material designed to interact with biological systems for medical purposes, such as tissue regeneration, healing, or repair. In periodontics for example, PRF and CGF have shown promising results in restoring difficult defects such one-wall or combination lesions because they offer continued growth factor release and structural support. These biomaterials have made regenerative outcomes more predictable, especially when long-term stability and better healing capability are needed. These developments are now incorporated into personalized treatment plans, which emphasize the distinct clinical and anatomical features of each defect to maximize regenerative therapies using minimally invasive and biologically motivated techniques (12). Non-surgical treatments like scaling and root planning (SRP), which attempt to remove calculus and biofilm in order to limit infection, are frequently the first line of treatment for periodontitis (13). In extreme situations, surgical techniques like bone grafting and guided tissue regeneration might be required. PRP has demonstrated promise in boosting both soft and hard tissue regeneration when used as an adjuvant to these treatments, complementing conventional methods by facilitating quicker and more thorough recovery (14,15).

1.4. Periodontal Regeneration and Challenges

Recent developments have focused on encouraging actual periodontal regeneration as well as reducing inflammation. This entails promoting the regeneration of new bone, cementum, and connective tissue by utilizing bioactive substances like PRP, PRF and CGF (2,14). Regenerative methods in periodontics aim to restore periodontal structures, going beyond symptom management (16). True regeneration is a complex biological problem that necessitates specific treatments to overcome variables such as bacterial contamination, tissue inflammation, and the presence of non-regenerative cells. While periodontal therapies frequently result in the production of lengthy junctional epithelium, true regeneration is the objective in advanced periodontal care. The incorporation of sophisticated surgical procedures, biomaterials, and physiologically active substances has substantially enhanced the potential for effective regeneration, encouraging a multidisciplinary approach in modern periodontics (11).

Open flap debridement (OFD) is a fundamental method in periodontal surgery. This method involves reflecting soft tissue flaps to gain access to the root surfaces and osseous defects, allowing for complete debridement of biofilm, calculus, and granulation tissue. The main goals of OFD are infection prevention and periodontal pocket reduction, which frequently leads to healing through repair as opposed to regeneration. Although OFD greatly enhances clinical criteria like attachment level and probing depth, its limited capacity to restore damaged periodontal structures has led to the creation of more sophisticated techniques (4,5).

Guided tissue regeneration (GTR) is a significant improvement in periodontal therapy, aiming to selectively repopulate cells capable of rebuilding the periodontium. The method uses barrier membranes to keep rapidly proliferating connective tissue and epithelial cells out of the defect, making room for osteoblasts, cementoblasts, and periodontal ligament fibroblasts to grow. Early GTR applications used non-resorbable membranes, which gave great regenerative results but carried the danger of membrane exposure and infection. Contemporary resorbable membranes, frequently enhanced with growth agents or nanomaterials, have decreased problems and increased GTR predictability. This method has been especially successful in treating Grade II furcation involvement and intrabony abnormalities, where regulated cell repopulation is essential to establishing regeneration (12,17).

The concepts of guided bone regeneration (GBR) are expanded upon by GTR, with a particular emphasis on alveolar bone regeneration. GBR is mostly utilized for bone abnormalities, particularly those related to implant therapy, whereas GTR seeks to reconstruct the whole periodontium. To promote osteoblast activity and bone regeneration, GBR combines barrier membranes with bone grafts or substitutes. When combined with biomaterials like autografts, allografts, or xenografts, this method is extremely effective in correcting vertical deformities and ridge augmentation. In big or complex lesions, GBR has also been successfully used in conjunction with growth factors such as platelet concentrates to promote angiogenesis and osteogenesis. Minimally invasive surgical techniques, coupled with advanced imaging modalities like cone-beam computed tomography (CBCT), have also enabled precise defect assessment and targeted regenerative interventions. The synergy between these approaches continues to redefine the standards of care in periodontal therapy, ensuring that regeneration is not only achievable but increasingly predictable (7,11).

periodontal regeneration encompasses a range of modalities, each tailored to specific clinical scenarios. From foundational approaches like OFD to advanced techniques such as GTR, GBR, and biomaterial integration, the field has evolved to offer a sophisticated array of tools for restoring periodontal structures. The inclusion of biologically driven therapies and emerging technologies ensures that clinicians can address even the most complex defects, driving the future of regenerative periodontics.

1.5. Significance of platelet concentrates in periodontics

Incorporation of Autologous platelet concentrates into periodontal therapy has become a viable strategy to promote tissue regeneration and repair. In the pursuit of less invasive dentistry, Emerging evidence suggests that Platelet concentrates may enhance clinical outcomes, warranting further investigation into its comparative efficacy (18–20). Growth factors including transforming growth factor-beta (TGF-β) and platelet-derived growth factor (PDGF) are abundant in platelet concentrates and are crucial for fostering angiogenesis, cell division, and the development of new tissue (21,22). The use of platelet concentrates in periodontics goes beyond simple wound healing; it signifies a change to regenerative techniques meant to restore cellular health and function leveraging the body's natural healing mechanisms, presenting a promising alternative to traditional surgical approaches (2).

Dental professionals may find that PRP is explored as a method that has the potential to improve clinical outcomes, including patient satisfaction and recovery time (15). This method aligns with the broader exploration in modern dentistry of biologically driven therapies. In addition to highlighting platelet concentrates clinical benefits, highlighting its significance in periodontal treatment promotes the development of cutting-edge, evidence-based care (22,23).

1.6. First generation blood concentrate or Platelet Rich Plasma

Autologous blood concentrates are well-known for having high concentration of platelets, which release growth factors essential for tissue regeneration and repair (14,24). PRP was first used in orthopedic and maxillofacial surgery, but its ability to promote healing has made it a popular option in periodontics (16,21). Alpha granules found in platelet concentrates are loaded with growth factors like Platelet derived growth factors (PDGF), Transforming growth factor-beta (TGF-β), Vascular endothelial growth factor (VEGF) and insulin-like growth factor (IGF) all of which contribute to the complex processes of tissue repair and regeneration. PDGF promotes the recruitment and proliferation of mesenchymal stem cells, while TGF-β plays a dual role by stimulating collagen production and modulating the immune response to minimize inflammation, creating an environment conducive to healing. VEGF, on the other hand, is

essential for angiogenesis, facilitating the formation of new blood vessels to sustain regenerating tissues. Insulin-like growth factor (IGF) complements these processes by enhancing cellular metabolism and matrix remodeling, crucial for restoring tissue integrity (17,25).
Platelets first clump together to form a clot during wound healing, which acts as a structural scaffold for cellular activity. The healing process is accelerated by growth factors released from the clot, which promote fibroblast proliferation, collagen deposition, and vascularization. Furthermore, platelet concentrates alter the local immune response by increasing anti-inflammatory activity and decreasing pro-inflammatory cytokines, both of which are essential for halting the formation of scar tissue and fostering effective tissue regeneration (21). Autologous platelets are used in concentrated forms, such as platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and concentrated growth factors (CGF).

Venous blood is drawn in order to prepare PRP, and anticoagulants such as citrate are used to stop premature clotting (26). The platelet-rich fraction is then separated from red blood cells and plasma by centrifuging the blood at regulated rates (24). By concentrating platelets to a far higher levels than baseline, this procedure makes it possible to apply growth factors specifically to periodontal areas (14,21). The release of growth factors can be further enhanced by activation with thrombin or calcium chloride.

PRP's growth factor content can deteriorate over time, it works best when used fresh (23). To optimize PRP's regenerative potential, physicians are encouraged to prepare it as near to application time as possible, even though it can be stored for a brief period of time under refrigeration (16). PRP preparations vary based on their leukocyte content and activation methods, Leukocyte-Rich PRP (LR-PRP) and Leukocyte-Poor PRP (LP-PRP) respectively contains white blood cells, which may aid wound debridement but could exacerbate inflammation while latter excludes most leukocytes, minimizing pro-inflammatory effects while focusing on growth factor delivery (16).

PRP is used in periodontics for treatments such bone grafting, tooth extractions, and periodontal flap surgery. PRP's main benefits are its ability to release a concentrated burst of growth factors and its autologous nature, which reduces the possibility of unfavorable immunological reactions (21). PRP has drawbacks despite its advantages. Inconsistent platelet concentrations resulting from different preparation methods can compromise the effectiveness of treatment. Clinical workflows are further complicated operationally by the need for immediate usage following preparation (24). Additionally, underlying medical disorders that may affect platelet activity or other patient-specific factors may affect how successful PRP is (16).

1.7. Second generation blood concentrate or Platelet Rich Fibrin

For regenerative therapies, Platelet-rich plasma (PRP), the first-generation platelet concentrate is one of various platelet concentrates that are available. This idea is furthered by the second generation, platelet-rich fibrin (PRF), which eliminates anticoagulants and permits fibrin to naturally polymerize during centrifugation. PRF creates a reservoir for the prolonged release of growth factors over a period of 7–10 days by forming a fibrin clot with platelets and leukocytes (17). In contrast to PRP's transient growth factor burst, this continuous release promotes longer tissue recovery.

PRF is ideal for regenerative periodontal therapy as it is very good at promoting angiogenesis, supporting bone grafts, and offering a scaffold for cellular migration (20). The adaptability of PRF in clinical settings is a major benefit. It can be used with graft materials for sinus augmentation and bone defect repair through the making of sticky bone, or it can be formed into membranes for directed tissue regeneration (Figs 2. And 3.). In addition to acting as a scaffold for cellular migration, the fibrin matrix that forms in PRF and CGF stabilizes the defect site and gives transplant materials mechanical support. This matrix is very helpful in difficult defect morphologies, like one-wall or combination defects, because it improves wound stability and lowers the chance of graft displacement or infection (25).

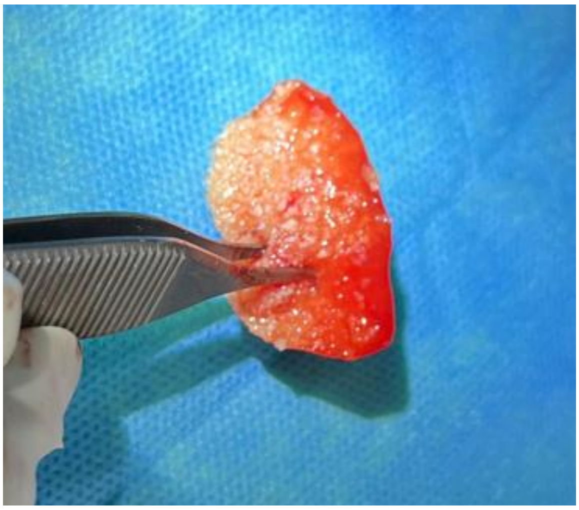

Figure. 2. Sticky bone (Courtesy by Prof. Talebi)

Figure. 3. A-PRF or PRF membrane (Courtesy by Prof. Talebi)

PRF has been applied in diverse fields including Periodontal therapy through enhancing clinical attachment levels and bone regeneration in intrabony defects, oral surgery by promoting soft tissue healing in extraction sites, implant placement and aesthetic dentistry by improving skin texture and reducing scarring through collagen induction. Although PRF technologies continued to evolve introducing new variants such as, Injectable-PRF (I-PRF) which offers a liquid form for easy application in minimally invasive procedures whereas Advanced-PRF (A-PRF) enhances growth factor release with modified centrifugation protocols which are helpful depending on clinical needs (16,26)(Fig 4.).

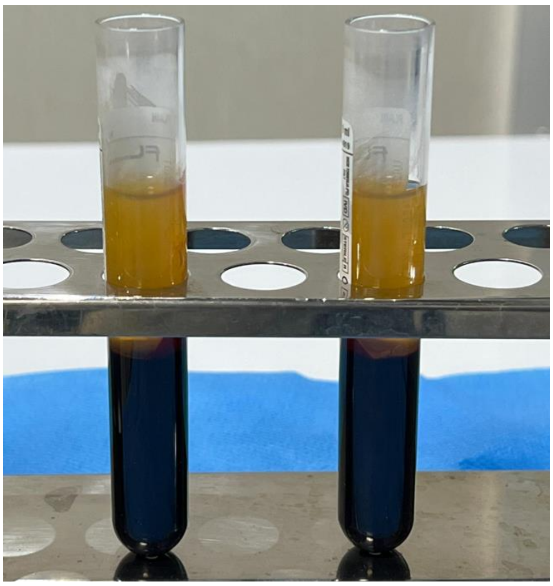

Figure. 4. I-PRF (Courtesy by Prof. Talebi)

1.8. Third generation blood concentrate or CGF

By improving the centrifugation procedure to create a denser fibrin matrix, concentrated growth factor (CGF), the third-generation platelet concentrate, expands on PRF. Different centrifugation rates are used in the procedure, which produces a product with increased growth factor concentrations and enhanced mechanical strength. Greater amounts of growth factors like VEGF, TGF-β, insulin-like growth factor (IGF-1) and hepatocyte growth factor (HGF) are released by CGF, while other bioactive molecules like fibronectin and thrombospondin help with cell adhesion, matrix remodelling and facilitating intricate treatments like ridge augmentation and the repair of extensive periodontal defects meaning its more suitable for large scale regenerative applications. While PRF offers excellent results in moderate defects (20,25).

1.9. Other Biomaterials

Emdogain one of the newer biomaterials available, an enamel matrix derivative (EMD), is a very successful treatment for intrabony periodontal abnormalities. By simulating the natural tissue growth that occurs during tooth formation, it aids in the regeneration of missing periodontal structures, including as the cementum, periodontal ligament, and alveolar bone. EMD promotes tissue regeneration and repair by activating vital cells such as osteoblasts, cementoblasts, and fibroblasts. When applied to root surfaces, it inhibits undesired epithelial growth while promoting new connective tissue attachment. Combining EMD with bone grafts, such as natural bone mineral (NBM), improves regeneration by creating a stable framework for bone growth. Better clinical attachment levels and increased bone regeneration in defects are the results of this method. Emdogain is an essential tool for attaining full periodontal regeneration because of its combination with minimally invasive surgical procedures (27)(Fig 5.).

Figure. 5. Enamel Matrix derivative (EMDOGAIN)(Courtesy by Prof. Talebi)

1.10. Gaps in Knowledge

In a nutshell autologous platelets are crucial instruments in regenerative dentistry because of their distinct biological and physical properties. The treatment of complicated defects has changed because of their capacity to moderate inflammation, enhance wound stabilization, and administer tailored growth factors. The efficacy of platelet concentrate formulations is always being improved, giving physicians flexible and practical choices for attaining the best possible restorative results. Although the existing literature provides encouraging evidence regarding the efficacy of these platelet concentrates, gaps remain in understanding their comparative benefits across different defect morphologies and patient profiles. Additionally, more research is needed to determine how elements like application techniques, systemic health problems, and defect characteristic affect therapy results. To maximize patient benefits and optimize therapy regimens, these gaps must be filled. The purpose of this thesis was to compare the effectiveness of PRP with PRF and CGF and to thoroughly assess its involvement in periodontal regeneration. The study aims to give clinicians evidence-based insights on the benefits and limitations of these therapies. By bridging the gap between encouraging laboratory results and useful clinical applications, this research ultimately hopes to advance less invasive and biologically inspired periodontal treatments.

2. OBJETIVE

2.1. Primary Objective

- Analyze whether there are differences in the effectiveness of treating periodontal defects with and without the use of PRP (Platelet-Rich Plasma)

2.2. Secondary Objective

- Analyze and compare PRP vs PRF vs CGF
- Analyze factors influencing PRP, PRF and CGF efficacy, including defect type and application methods

3. MATERIAL AND METHODS

This review was carried out following the PRISMA 2020 guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.

3.1. Focused question

To guide our search, we began by formulating the following PICO question: *"In Patients with moderate to severe Periodontal disease, does adjunctive use PRP with regenerative therapies results in a more efficient periodontal regeneration and CAL improvement compared to therapies without adjunctive use of PRP?"*

3.2. Search strategy

Search was conducted across several electronic databases, including Medline, Dentistry & Oral Sciences Source, Scopus, and Cochrane. The search was limited to English-language studies with available full-texts. Additional relevant articles were identified through a manual review of the reference lists of included studies and previous systematic reviews. The search was performed using the following equation: [[[[[Dentistry] AND [Periodontal regeneration]] AND [Platelet Rich plasma]] OR [Platelet Rich Fibrin]] OR [Concentrated Growth Factors]] AND [Intrabony defects]

3.3. Selection process

This review includes randomized controlled trials and clinical studies evaluating the role of PRP, PRF, and CGF in periodontal therapy. Eligible studies involved human participants with moderate to severe periodontal disease and assessed these treatments either alone or in combination, reporting outcomes such as Clinical Attachment Level (CAL) gain, Probing Depth (PD) reduction, or bone regeneration. Studies focused solely on soft tissue healing, non-periodontal applications, or lacking quantitative outcomes were excluded. The review also examined factors influencing the efficacy of these platelet concentrates, including defect morphology, preparation protocols, and application methods.

The selection process followed the PRISMA 2020 guidelines. Titles and abstracts retrieved from the database search were independently screened by the author. Full-text articles of potentially relevant studies were then thoroughly reviewed against the eligibility criteria. As the review was conducted solely by the author, no inter-reviewer discrepancies were present.

3.3.1. Inclusion criteria

- Randomized controlled trials, clinical and radiographic studies, cross-sectional studies, prospective studies
- Human participants with moderate to severe periodontal disease.
- Studies involving PRP, PRF, CGF, or their combinations in periodontal regenerative therapies.
- Reports on Clinical Attachment Level (CAL) gain, Probing Depth (PD) reduction, or bone regeneration.
- Comparisons between PRP, PRF, CGF, or standard therapies.

3.3.2. Exclusion criteria

- Studies only on soft tissue healing (e.g., root coverage) without hard tissue regeneration outcomes.
- Animal studies or participants with systemic conditions interfering with periodontal outcomes.
- Studies not evaluating PRP, PRF, or CGF or focused on non-periodontal applications.
- Articles without quantitative clinical data (e.g., narrative reviews or conceptual papers).

3.4. Risk of Bias Assessment

The risk of bias in the included randomized controlled trials was determined using the Revised Cochrane Risk of Bias Tool (RoB 2.0), specifically the version for individually randomized, parallel-group trials (22 August 2019 template)(28). The assessment was completed manually, guided by the signalling questions and domain-specific criteria provided in the Cochrane methodology.

Each study was evaluated across five core domains:

1. Bias arising from the randomization process
2. Bias due to deviations from intended interventions
3. Bias due to missing outcome data
4. Bias in measurement of the outcome
5. Bias in selection of the reported result

For each domain, studies were judged as having a low risk of bias, some concerns, or high risk of bias, and these judgments contributed to an overall risk of bias rating per study. Although the review was conducted by a single author, all assessments followed the Cochrane RoB 2 template systematically, ensuring consistency and transparency.

3.5. Data collection

Data were extracted manually, using a structured data extraction table created prior to the review. Relevant information for each trial was gathered, including the study design, participant demographics, interventions (PRP, PRF, CGF), control/comparator groups, clinical outcomes (CAL gain, PD reduction, bone regeneration), and follow-up periods. All data were thoroughly examined to guarantee consistency and accuracy.

3. RESULTS

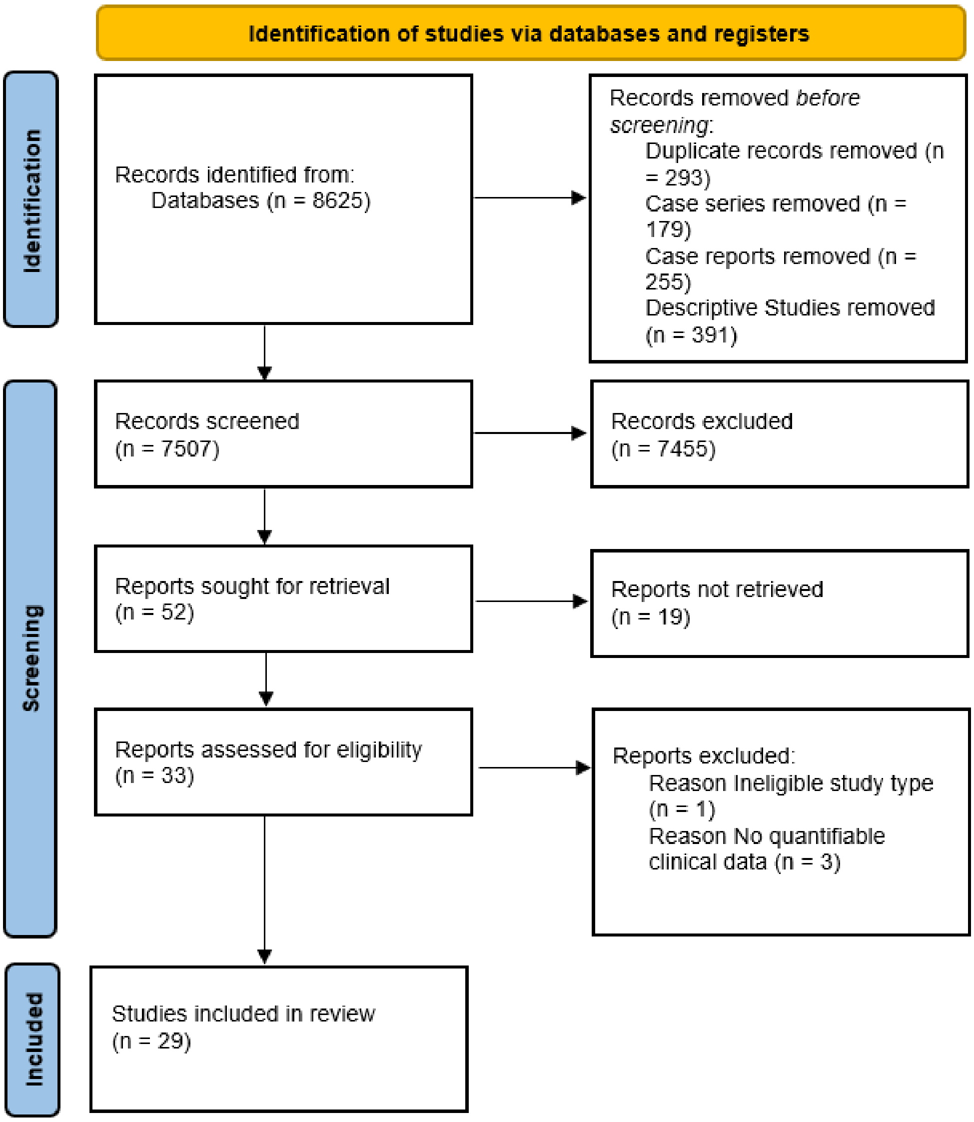

Figure. 4. Search strategy flowchart(29)

This review included 13 randomized clinical trials (RCT) evaluating the effects of Platelet-Rich Plasma (PRP), 13 RCTs assessing Platelet-Rich Fibrin (PRF), and 3 RCTs examining Concentrated Growth Factors (CGF) in periodontal therapy, specifically targeting intrabony defects (IBDs). The initial database search identified 8,625 records. Following the removal of 293 duplicates, 179 case series, 255 case reports, and 391 descriptive studies, a total of 7,507 records were screened. Of these, 7,455 were excluded based on title and abstract. Fifty-two reports were sought for retrieval, but 19 could not be obtained. After full-text review of 33 reports, 4 were excluded due to ineligible study type (n = 1) or lack of quantifiable clinical data (n = 3), resulting in 29 RCTs being included in this review.

The included studies were assessed based on outcomes such as radiographic bone level (RBL), clinical attachment level (CAL), and pocket probing depth (PPD), with follow-up periods ranging from 6 months to 1 year. Several studies also compared PRP, PRF, and CGF with other regenerative biomaterials, including Demineralized Freeze-Dried Bone Allograft (DFDBA), Anorganic Bovine Bone Mineral (ABBM), β-Tricalcium Phosphate (β-TCP), Emdogain (EMD), Bovine Porous Bone Mineral (BPBM), Natural Bone Mineral (NBM), Demineralized Bone Matrix (DBM), Demineralized Freeze-Dried Bone Xenograft (DFDBX), Hydroxyapatite (HA), Nano-crystalline Hydroxyapatite (NcHA), and Autologous Bone Graft (ABG). And the use of membranes such as expanded Polytetrafluoroethylene (ePTFE). These comparisons provided further insight into the potential synergistic or additive effects of combining platelet concentrates with conventional biomaterials in enhancing periodontal regeneration.

Table 1 Risk of Bias Assessment (Table 3)

Study	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall Risk of Bias
Döri et al. (2008)(27)	Low	Low	Low	Low	Low	Low
Döri et al. (2007)(30)	Some concerns	Low	Low	Low	Low	Some concerns
Piemontese et al. (2008)(31)	Low	Low	Low	Low	Low	Low
Döri et al. (2007)(32)	Some concerns	Low	Low	Low	Low	Some concerns
Thangavelu et al. (2015)(33)	Some concerns	Some concerns	Low	Low	Low	Some concerns
Md. Jalaluddin et al. (2017)(34)	Low	Low	Low	Low	Low	Low
Döri et al. (2008)(35)	Low	Low	Low	Low	Low	Low
Camargo et al. (2009)(36)	Low	Low	Low	Low	Low	Low
Harnack et al. (2009)(37)	Some concerns	Some concerns	Low	Low	Low	Some concerns
Agarwal et al. (2016)(38)	Low	Low	Low	Low	Low	Low
Amin et al. (2022)(39)	Low	Low	Low	Low	Low	Low
Pradeep et al. (2012)(40)	Low	Low	Low	Low	Low	Low
Camargo et al. (2005)(41)	Some concerns	Low	Low	Low	Some concerns	Some concerns

Table 2 Risk of Bias Assessment (Table 4)

Study	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall Risk of Bias
Csifó-Nagy et al. (2021)(42)	Low	Low	Low	Low	Low	Low
Chandradas et al. (2016)(43)	Low	Low	Low	Low	Low	Low
Ozkal Eminoglu et al. (2024)(44)	Low	Low	Low	Low	Some concerns	Some concerns
Alshoiby et al. (2023)(45)	Some concerns	Low	Low	Low	Low	Some concerns
Liu et al. (2021)(46)	Low	Low	Low	Low	Low	Low
Patel et al. (2017)(47)	Low	Low	Low	Low	Low	Low
Ajwani et al. (2014)(48)	Low	Low	Low	Low	Low	Low
Chaudhary et al. (2023)(49)	Low	Low	Low	Low	Low	Low
Pavani et al. (2021)(50)	Low	Low	Low	Low	Low	Low
Naidu et al. (2024)(51)	Low	Low	Low	Low	Some concerns	Some concerns
Mathur et al. (2015)(52)	Some concerns	Low	Low	Low	Low	Some concerns
Elgendy and Abo Shady et al. (2014)(53)	Low	Low	Low	Low	Low	Low
Atchuta et al. (2020)(54)	Low	Low	Low	Low	Low	Low
Qiao et al. (2016)(55)	Low	Low	Low	Low	Low	Low
Xu et al. (2019)(56)	Low	Low	Low	Low	Low	Low
Alshujaa et al. (2024)(57)	Low	Low	Low	Low	Low	Low

Table 3 Main characteristics of the 13 PRP RCTs included in the present study

Authors (years)	Study design	No. patients & gender	Groups	Outcomes
Döri et al. (2008)(27)	Controlled Clinical Trial	26 Patients 14 F, 12 M	T: EMD + NBM + PRP C: EMD + NBM	PRP did not show statistically significant enhancements compared to EMD + NBM alone.
Döri et al. (2007)(30)	Randomized controlled clinical trial (RCT)	24 Patients 14 F, 10 M	T: PRP + ABBM + GTR C: ABBM + GTR	No statistically significant difference between the groups
Piemontese et al. (2008)(31)	Randomized, double-masked, clinical trial	60 Patients 29 F, 31 M	T: DFDBA + PRP C: DFDBA + Saline solution	PPD: Statistically significant greater reduction in the test group ($P < 0.05$) CAL: Statistically significant greater gain in the test group ($P < 0.001$). RBL: No statistically significant difference between groups with regards to HTF and BDR.
Döri et al. (2007)(32)	RCT	30 Patients 16 F, 14 M	T: NBM + PRP + GTR C: NBM + GTR	No statistically significant difference between groups.
Thangavelu et al. (2015)(33)	Split-mouth randomized controlled clinical trial (SMRCT)	30 Patients (F or M not explicitly mentioned)	T: Autogenous bone grafts C: DFDBX + PRP	PPD: Greater reduction in Test group, statistically significant ($P < 0.001$). CAL: Greater gain in Test group, statistically significant ($P < 0.001$). RBL: Greater bone fill in Test group, statistically significant ($P < 0.001$).
Md. Jalaluddin et al. (2017)(34)	Randomized Controlled Clinical Trial	10 Patients (20 IBD) 4 F, 6 M	T: PRP C: OFD	No statistically significant difference between groups.
Döri et al. (2008)(35)	Randomized Controlled Clinical Trial	28 Patients 16 F, 12 M	T: β-TCP + PRP + GTR + ePTFE C: β-TCP + GTR + ePTFE	No statistically significant difference between groups.
Camargo et al. (2009)(36)	SMRCT	23 Patients 14 F, 9 M	T: BPBM + GTR + PRP C: BPBM + GTR	Differences between all groups were not statistically significant.

Harnack et al. (2009)(37)	Prospective Randomized Double-Blind Clinical Trial	22 Patients (F or M not explicitly mentioned)	T: β-TCP + PRP C: β-TCP	No statistically significant difference between all groups.
Agarwal et al. (2014)(38)	SMRCT	24 Patients (48 IBD) 10 F, 14 M	T: DFDBA + PRP C: DFBDA + Saline solution	PPD: No statistically significant difference between groups. CAL & RBL: The test group showed statistically significantly greater improvement (P < 0.001).
Amin et al. (2022)(39)	RCT	70 patients 3 groups, PRP: 30 patients 14 F, 16 M I-PRF: 30 patients 14 F, 16 M C: 10 patients 4 F, 6 M	T1: PRP + SRP T2: iPRF + SRP C: SRP	iPRF showed the most significant improvements in both PPD and CAL reduction compared to PRP and the control group. PRP was second in effectiveness, while the control group (SRP alone) demonstrated the least improvement.
Pradeep et al. (2012)(40)	RCT	54 Patients (90 IBD) 27 F, 27 M	T1: PRF + OFD T2: PRP + OFD C: OFD	PPD: PRF and PRP showed significantly greater PPD reduction compared to the control group (P ≤ 0.05). CAL: No statistically significant difference in CAL gain between PRF and PRP groups. RBL: PRF and PRP groups demonstrated significantly greater bone fill compared to the control group (P < 0.001).
Camargo et al. (2005)(41)	SMRCT	28 Patients 12 F, 16 M	T: BPBM + GTR + PRP C: OFD	PPD: Statistically significant reduction in favor of the test group (P < 0.001). CAL: Statistically significant improvement in favor of the test group (P < 0.001). RBL: Statistically significant improvement in favor of the test group (P < 0.001).

Table 4 Main characteristics of the 13 PRF & 3 CGF RCTs included in the present study

Authors (years)	Study design	No. patients & gender	Groups	Outcomes
Csifó-Nagy et al. (2021)(42)	RCT	18 patients 9 F, 9 M	T: A-PRF+ C: EMD	There is no statistically significant difference between the groups.
Chandradas et al. (2016)(43)	RCT	36 patients 18 F, 18 M	T1: PRF + DBM T2: PRF C: OFD	PPD: The reduction in PD was greater in T1 and T2 compared to Control. CAL: Statistically significant improvement was observed in T1 and T2 compared to Control.
Ozkal Eminoglu et al. (2024)(44)	SMRCT	20 patients 9 F, 11 M	T: T-PRF + OFD C: OFD	PPD: Statistically significant improvement in the test group (p = 0.010) CAL: No statistically significant difference between groups (p = 0.118) Bone Fill: Statistically significant higher bone-filling rate in the test group (p < 0.001)
Alshoiby et al. (2023)(45)	RCT	20 patients 13 F, 7 M	T: I-PRF + DFDBA C: DFDBA	No statistically significant difference was noted between the groups.
Liu et al. (2021)(46)	SMRCT	14 patients 10 F, 4 M	T: GTR + BPBM + PRF C: GTR + BPBM	PPD & CAL: Statistically significant differences favoring the test group (p < 0.05). RBL: No significant differences in radiographic measurements between groups
Patel et al. (2017)(47)	SMRCT	13 patients 9 F, 4 M	T: OFD + PRF C: OFD	PPD & CAL & RBL: Significant improvement in the test group compared to the control group (p < 0.001).
Ajwani et al. (2014)(48)	SMRCT	20 patients 10 F, 10 M	T: OFD + PRF C: OFD	PPD & CAL & RBL: Significant improvement in the test group compared to the control group

Chaudhary et al. (2023)(49)	RCT	34 patients T: 9 F, 8 M C: 7 F, 10 M	T: I-PRF + HA C: HA	PPD: not statistically significant ($p = 0.054$) CAL: not statistically significant ($p = 0.088$) RBL: T showing significantly better results ($p = 0.004$)
Pavani et al. (2021)(50)	RCT	30 Patients Gender not specified	T1: β-TCP + PRF T2: β-TCP C: OFD	PPD: T1 showing the greatest reduction ($p < 0.05$) Bone Fill: highest bone fill compared to the other groups
Naidu et al. (2024)(51)	Single-blind, SMRCT	12 patients 4 F, 8 M	T: OFD + DFDBA + PRF C: OFD + DFBDA	PPD: No statistically significant difference in PPD reduction between groups ($p = 0.780$) CAL: No statistically significant difference in CAL improvement between groups ($p = 0.333$) RBF: No statistically significant difference in between groups ($p = 0.819$)
Mathur et al. (2015)(52)	RCT	25 patients 11 F, 14 M	T1: OFD + PRF T2: OFD + ABG	PPD & CAL: Statistically significant reduction for both groups ($p = 0.001$), with no significant intergroup differences RBF: T1 showed greater radiographic defect fill compared to T2 with statistical significance ($p < 0.05$).
Elgendy and Abo shady et al. (2014)(53)	SMRCT	20 patients Gender not specified	T: NcHA + PRF C: NcHA	PPD: T demonstrated a significantly greater reduction in PPD compared to Group II ($p = 0.020$) CAL: demonstrated a significantly greater gain in CAL compared to Group II ($p = 0.027$) Bone density: showed a significantly greater increase in BD compared to Group II ($p < 0.001$)
Atchuta et al. (2020)(54)	RCT	39 patients	T1: DFDBA	PPD: statistically significant differences between T2 and C ($p < 0.05$).

		Gender not specified	T2: DFDBA + PRF C: OFD	RBL: T2 statistically significant differences compared to C ($p < 0.05$)
Qiao et al. (2016)(55)	RCT	17 patients 10 F, 7 M	T: CGF + BPBM C: BPBM	PPD: T group showed significantly greater PPD reduction compared to the control group ($p = 0.016$) CAL: T group exhibited significantly greater CAL gain compared to the control group ($p = 0.013$) RBF: T group had a higher, though not statistically significant, radiographic bone fill compared to the control group ($p = 0.087$)
Xu et al. (2019)(56)	RCT	54 patients 24 F, 30 M	T1: Flap surgery + CGF T2: Flap surgery + Bio-Oss T3: Flap surgery + CGF + Bio-Oss C: Flap surgery	PPD: Significant PPD reduction was observed in all groups, with T3 showing the greatest reduction ($p < 0.05$) CAL: T3 demonstrated the highest CAL gain, significantly better than the other groups ($p < 0.05$) RBL: T3 achieved the most significant defect depth reduction compared to the other groups ($p < 0.05$)
Alshujaa et al. (2024)(57)	SMRCT	20 patients (80 defects) 13 F, 7 M	T1: OFD + PRF T2: OFD + CGF T3: OFD + ABG C: OFD	PPD: T3 showed the most significant reduction, followed by T2, T1 and Control ($p < 0.001$) CAL: T3 showed the highest improvement, followed by T2, T1 and Control ($p < 0.001$) RBG: T3 achieved the greatest alveolar bone gain, followed by T2, T1, and Control ($p < 0.001$)

4. DISCUSION

This discussion analyzes the comparative regenerative potential of PRP, PRF, and CGF, focusing on their clinical outcomes in relation to defect morphology and biomaterial combinations

4.1. Effectiveness of PRP in Periodontal Regeneration

Platelet-rich plasma (PRP) has been widely explored as a potential enhancer for periodontal regeneration, though its success rates have been inconsistent. Studies by Döri et al. (2008) and Döri et al. (2007) examined the combination of PRP with Enamel Matrix Derivative (EMD) and Natural Bone Mineral (NBM), as well as with Anorganic Bovine Bone Mineral (ABBM) and Guided Tissue Regeneration (GTR), respectively. However, both studies found that PRP did not provide statistically significant improvements in probing pocket depth (PPD) reduction, clinical attachment level (CAL) gain, or radiographic bone level (RBL) enhancements (Table 3)(27,30).

Conversely, Piemontese et al. (2008) and Agarwal et al. (2016) reported significant improvements when PRP was combined with Demineralized Freeze-Dried Bone Allograft (DFDBA). These studies showed statistically significant reductions in PPD ($P < 0.05$) and greater CAL gains ($P < 0.001$) in PRP-treated groups (16,34). However, no significant differences were found in radiographic hard tissue fill (HTF) and bone defect resolution (BDR), indicating that PRP's regenerative effects may be limited primarily to soft tissue rather than bone regeneration. Despite conflicting findings in the literature, PRP remains a valuable adjuvant in regenerative therapy, especially for soft tissue enhancement and when used in conjunction with grafting materials, which maximizes its capacity for early healing.

4.2. Comparison of PRP vs. PRF

PRP and platelet-rich fibrin (PRF) are both autologous platelet concentrates utilized in regenerative medicine, but their mechanisms of action are distinct. PRF lacks anticoagulants, resulting in the formation of a fibrin clot, which allows for the extended release of growth factors over 7 to 10 days. Studies comparing PRP and PRF in periodontal therapy have reported mixed results. Pradeep et al. (2012) demonstrated that both PRP and PRF significantly improved PPD reduction and bone fill compared to open flap debridement (OFD) alone ($P < 0.05$). However, there was no statistically significant difference in CAL gain between the two groups (40). Patel et al. (2017) and Ajwani et al. (2014) reported that PRF provided superior clinical outcomes compared to OFD alone, reinforcing its regenerative potential (47,48). Furthermore, Amin et al. (2022) found that injectable platelet-rich fibrin (iPRF) demonstrated greater PPD and CAL improvements compared to PRP, suggesting that PRF’s extended release of bioactive factors may enhance wound healing more effectively than PRP's short burst of growth factors. In line with the hypothesis of this review, these findings support the notion that second-generation platelet concentrates offer more predictable outcomes in periodontal regeneration than PRP (39). For consistent regeneration results in periodontal therapy, PRF is a more clinically reliable alternative to PRP due to its scaffold stability and sustained release of growth factors.

4.3 Comparison PRP vs. CGF

Concentrated Growth Factor (CGF) is a third-generation platelet concentrate that has a denser fibrin matrix and higher growth factor content than PRP and PRF. Few studies have directly compared PRP to CGF in periodontal regeneration. Xu et al. (2019) found that CGF combined with Bio-Oss produced the highest PPD reduction and CAL gain among test groups, outperforming PRP and PRF in terms of overall regenerative outcomes ($P < 0.05$)(56). Alshujaa et al. (2024) demonstrated that autogenous bone grafts provided the best CAL gain, followed by CGF and PRF, while OFD alone showed the least improvement ($P < 0.001$)(57). This suggests that while CGF may offer advantages over PRP and PRF, autogenous grafts remain the gold standard for periodontal regeneration. Contrary to the hypothesized superiority of PRP, these findings further highlight the growing evidence that later-generation platelet concentrates like CGF may be more clinically effective in complex regenerative scenarios.

4.4 Platelet Concentrates in Combination with Biomaterials

The effectiveness of PRP has also been studied in combination with various bone graft materials, such as ABBM, DFDBA, β-Tricalcium Phosphate (β-TCP), and Bovine Porous Bone Mineral (BPBM). Camargo et al. (2009) and Camargo et al. (2005) examined PRP in combination with BPBM and GTR, finding significant improvements in PPD reduction, CAL gain, and RBL fill compared to OFD alone ($P < 0.001$). However, these studies found no statistically significant difference when PRP was compared to BPBM + GTR alone (36,59).

Similarly, Pavani et al. (2021) found that PRF combined with β-TCP resulted in superior radiographic bone fill compared to β-TCP alone ($P < 0.05$), suggesting a synergistic effect of platelet concentrates with bone graft material (50). On the other hand, Naidu et al. (2024) found no significant difference between PRF + DFDBA and DFDBA alone, indicating that the benefits of platelet concentrates may be context-dependent (51).

While PRP's therapeutic effects are notably enhanced when paired with suitable biomaterials, their success remains influenced by defect morphology and the interaction between regenerative components

4.5 Variability in PRP Efficacy

Despite some promising findings, the efficacy of PRP has been inconsistent across research. Several causes contribute to this variation, including:

- **Differences in PRP Preparation Methods**: The concentration of platelets and leukocytes varies depending on centrifugation protocols, influencing growth factor availability (16,24).
- **Patient-Specific Factors**: Systemic conditions such as diabetes or smoking status may affect the regenerative potential of PRP (22).
- **Defect Morphology**: Some studies suggest that PRP is more effective in three-wall intrabony defects compared to one-wall or combination defects (12).

While PRP, PRF, and CGF provide potential benefits in periodontal therapy, their effectiveness appears to depend on preparation methods, defect types, and the presence of additional biomaterials. However, based on the findings of similar studies, a more plausible explanation is that the clinical variability observed with PRP stems from its inconsistent preparation protocols and short-lived release profile compared to second- and third-generation platelet concentrates.

4.6 Advancements in PRF and CGF

While PRP has received substantial research, PRF and CGF are emerging as intriguing alternatives due to their unique benefits. PRF's natural fibrin network allows for sustained growth factor release, which is favourable to wound healing and tissue regeneration. Studies such as those by Patel et al. (2017) and Ajwani et al. (2014) have demonstrated that PRF significantly improves PPD reduction and bone fill compared to OFD alone (47,48). Additionally, iPRF, a liquid form of PRF, has shown even greater regenerative potential in some studies (39).

CGF, on the other hand, has been highlighted for its denser fibrin matrix and superior mechanical properties. Xu et al. (2019) reported that CGF combined with Bio-Oss achieved the greatest improvements in PPD and CAL among platelet concentrates (56). Alshujaa et al. (2024) further confirmed that CGF outperformed PRP and PRF in terms of CAL gain and bone regeneration, making it a valuable option for complex periodontal defects (57). Advances in PRF and CGF have led to more reliable and durable clinical results, establishing these next-generation concentrates as important contributors in the development of biologically driven strategies for periodontal regeneration in the future.

4.7 Limitations

Despite this review's extensive scope, it is important to recognize a few limitations. First, the included randomized controlled trials (RCTs) varied widely in their approaches, especially regarding activation techniques, centrifugation settings, and platelet concentrate preparation protocols. This lack of standardization may have altered clinical results and limited the capacity to draw direct comparisons between trials.

Second, the follow-up periods of the studies ranged from six months to one year, which may not be sufficient to evaluate long-term regenerative outcomes, particularly in relation to bone regeneration stability and functional tissue integration. The relatively short observation periods may underestimate or fail to capture late-stage healing differences among PRP, PRF, and CGF.

Finally, there was heterogeneity in defect types, including the number of residual walls, defect depth, and location, which further complicates the extrapolation of findings to standardized clinical recommendations. These limitations highlight the need for future well-controlled, large-scale studies with uniform methodologies to better evaluate the comparative effectiveness of autologous platelet concentrates in periodontal regeneration.

5. CONCLUSIONS

1) PRP has demonstrated the ability to enhance periodontal results, especially when used with grafting materials. It can improve clinical attachment gain and probing depth decrease. Its efficacy varies from study to study, particularly when applied alone or in less-contained defects. As a result, PRP works better as a complementary approach than as a stand-alone regenerative treatment.

2) When compared, PRF and CGF tend to offer more consistent and longer-lasting regenerative benefits than PRP. PRF supports extended growth factor release, and CGF provides an even denser fibrin matrix and higher concentrations of bioactive molecules, showing the best results in complex defect scenarios. These findings suggest that PRF and CGF are preferable choices for achieving stable, predictable outcomes in periodontal regeneration.

3) Defect shape, biomaterial combinations, preparation techniques, and patient-specific factors including oral hygiene and systemic health all have a significant impact on the effectiveness of platelet concentrates. Understanding these factors enables clinicians to tailor treatments for optimal results and improved long-term prognosis.

6. SUSTAINABILITY

This Final Degree Project promotes healthcare sustainability by offering less invasive, biologically based alternatives to traditional periodontal surgery. The use of autologous platelet concentrates (PRP, PRF, and CGF) enhances environmental and economic sustainability by lowering reliance on synthetic biomaterials and minimizing clinical waste. These therapies make use of the patient's own biological resources, promoting circular practices and efficient resource use in accordance with Sustainable Development Goal 12 (SDG).

Biological regenerative therapies may also save long-term treatment costs by speeding up recovery, reducing the need for retreatment, and allowing for outpatient procedures. This promotes clinical technology innovation and increases the cost-effectiveness of oral healthcare systems, hence addressing SDG 9: Industry, Innovation, and Infrastructure.

From a societal perspective, these regenerative approaches improve clinical results, shorten recovery times, and lessen the need for retreatment, all of which contribute to higher patient quality of life and access to ethical, cost-effective care. SDG 3: Good Health and Well-Being is in line with this.

In summary, this research demonstrates a strong ethical commitment to promoting safer, more natural, and sustainable approaches in periodontal treatment, while encouraging responsible innovation and clinical excellence.

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8. ANNEXES

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2017 WORLD WORKSHOP

WILEY Journal of Clinical Periodontology

A new classification scheme for periodontal and peri-implant diseases and conditions – Introduction and key changes from the 1999 classification

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The proceedings of the workshop were jointly and simultaneously published in the *Journal of Periodontology* and *Journal of Clinical Periodontology*.

Abstract

A classification scheme for periodontal and peri-implant diseases and conditions is necessary for clinicians to properly diagnose and treat patients as well as for scientists to investigate etiology, pathogenesis, natural history, and treatment of the diseases and conditions. This paper summarizes the proceedings of the World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions. The workshop was co-sponsored by the American Academy of Periodontology (AAP) and the European Federation of Periodontology (EFP) and included expert participants from all over the world. Planning for the conference, which was held in Chicago on November 9 to 11, 2017, began in early 2015.

An organizing committee from the AAP and EFP commissioned 19 review papers and four consensus reports covering relevant areas in periodontology and implant dentistry. The authors were charged with updating the 1999 classification of periodontal diseases and conditions[1] and developing a similar scheme for peri-implant diseases and conditions. Reviewers and workgroups were also asked to establish pertinent case definitions and to provide diagnostic criteria to aid clinicians in the use

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REVIEW ARTICLE

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Current concepts in the pathogenesis of periodontitis: from symbiosis to dysbiosis

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ABSTRACT

The primary etiological agent for the initiation and progression of periodontal disease is the dental plaque biofilm which is an organized aggregation of microorganisms residing within a complex intercellular matrix. The non-specific plaque hypothesis was the first attempt to explain the role of the dental biofilm in the pathogenesis of periodontal diseases. However, the introduction of sophisticated diagnostic and laboratory assays has led to the realisation that the development of periodontitis requires more than a mere increase in the biomass of dental plaque. Indeed, multispecies biofilms exhibit complex interactions between the bacteria and the host. In addition, not all resident microorganisms within the biofilm are pathogenic, since beneficial bacteria exist that serve to maintain a symbiotic relationship between the plaque microbiome and the host's immune-inflammatory response, preventing the emergence of pathogenic microorganisms and the development of dysbiosis. This review aims to highlight the development and structure of the dental plaque biofilm and to explore current literature on the transition from a healthy (symbiotic) to a diseased (dysbiotic) biofilm in periodontitis and the associated immune-inflammatory responses that drive periodontal tissue destruction and form mechanistic pathways that impact other systemic non-communicable diseases.

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Dental biofilm; symbiosis; dysbiosis; inflammation; periodontal disease

Introduction

Periodontal disease is a broad term used to encompass diseases and conditions of the periodontal tissues. The two major forms induced by dental plaque biofilm accumulation are gingivitis and periodontitis. Gingivitis is an inflammatory lesion that remains confined to the gingiva, but which may, in susceptible people, progress to a more severe and destructive form, periodontitis [1]]. A causal relationship between periodontitis and systemic diseases has not yet been robustly established, however studies indicate that periodontal pathogens and consequent immune-inflammatory responses to them are independently associated with the pathogenesis of several systemic diseases such as diabetes mellitus, atherosclerotic cardiovascular diseases, chronic obstructive pulmonary diseases, Alzheimer's, chronic kidney disease, rheumatoid arthritis and certain cancers [2–5]. The ulcerated pocket epithelium provides a direct portal of vascular entry for periodontal pathogens, e.g. *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, *Tannerella forsythia*, *Eikenella corrodens*, and *Fusobacterium nucleatum* to the systemic circulation, which may directly or indirectly affect other organ systems [6–8]. A report issued in 2018 estimated the economic burden arising due to periodontal diseases as approximately $154.06 billion in the US and €158.64 billion in Europe [9].

The dental plaque biofilm, alongside other environmental, lifestyle and genetic risk factors, is the main etiological agent responsible for the development and progression of periodontitis. However, since the late 19th century, understanding of this concept has undergone significant advancement, sometimes with conflicting evidence. The specific plaque hypothesis (SPH) emerged which attributed dental caries to specific bacteria in the dental plaque biofilm, mainly *Streptococcus mutans*, *S. sobrinus* and *lactobacilli* [10]. The latter bacteria were observed to be partly indigenous in nature and present in both health and disease, together with the recognition of other bacteria as potential periodontal pathogens which underpinned the SPH. This led researchers to propose the non-specific plaque hypothesis which stated that it was the sheer biomass quantity rather than specific microorganisms that were responsible for the development of periodontitis [11]. In 1994, Marsh suggested that ecological stress was the driver for imbalance in the oral microbiota, encouraging the outgrowth of pathogenic bacteria; this was known as the ecological plaque hypothesis (EPH) [12]. In the late 1990s, pioneering work by Socransky and co-workers

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frontiers in Immunology

REVIEW
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The Nexus Between Periodontal Inflammation and Dysbiosis

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The nexus between periodontal inflammation and the polymicrobial biofilm in the gingival sulcus is critical to understanding the pathobiology of periodontitis. Both play a major role in the etiology and pathogenesis of periodontal diseases and each reinforces the other. However, this nexus is also at the center of a significant conundrum for periodontology. For all mucosal polymicrobial biofilms, the most confounding issue is the paradoxical relationship between inflammation, infection, and disease. Despite significant advances made in both periodontal microbiology and periodontal pathobiology, the issue of which comes first, the inflammatory response or the change to a dysbiotic subgingival microbiota, is still debated. In this paper, we present a model for the pathogenesis of periodontitis based on the central role of inflammation and how this modulates the polymicrobial biofilm within the context of the continuum of health, gingivitis, and periodontitis. We propose a new model termed "Inflammation-Mediated Polymicrobial-Emergence and Dysbiotic-Exacerbation" (IMPEDE), which is designed to integrate into and complement the 2017 World Workshop Classification of Periodontitis.

Keywords: periodontal inflammation, periodontal infection, periodontal pathogen, gingivitis, periodontitis

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INTRODUCTION

Periodontitis is currently considered by the American Academy of Periodontology to be an inflammatory disease initiated by bacteria (1). While this represented a paradigm shift relating to the pathogenesis of periodontitis at the time, it still remains unclear how this relationship plays out during the development of periodontitis. Clearly, one cannot be there without the other. The confounding issue is the relationship between inflammation and disease; which comes first, the immune response or the change in the homeostatic integrity of the mucosal polymicrobial biofilm (2). While remarkable progress has been made in the last 10 years in both the microbiology and immunology of periodontitis, this relationship has not been clarified.

A number of questions remain to be investigated and answered. What drives the shift from the localized and contained inflammatory response of gingivitis to progressive, destructive periodontitis? When and how does the subgingival microbiome become dysbiotic? Is it a spontaneous evolution of maturing biofilms or is it driven by the changing environment mediated by the host response? What is the temporal relationship between the dysbiotic microbiome and the innate and acquired immune response? Is bacterial invasion of tissues an initiator, or consequence, of disease?

In this review, we will critically examine the evidence that addresses these questions in an effort to better understand the interface between inflammation and dysbiosis. Our understanding of the initiation of periodontitis requires reassessment. Management of disease by attempted removal of

The Infrabony Pocket: Classification and Treatment†

by HENRY M. GOLDMAN, D.M.D.* AND D. WALTER COHEN, D.D.S.**

IN recent years, the principal clinical lesion of periodontal disease, the pocket, has been studied clinically, radiographically, and histopathologically. As a result of these investigations it became apparent that the pocket had to be classified on the basis of the location of the bottom of the pocket in its relationship to the alveolar crest. Arising from these studies came the classification of pockets: (1) suprabony or supracrestal and (2) infrabony or subcrestal. The suprabony pocket is defined as a pathological sulcus where the base of the pocket is coronal or occlusal to the alveolar crest, while the infrabony is defined as a pathological sulcus where the bottom of the pocket is apical to the alveolar crest. The suprabony pocket was further subdivided into the gingival or pseudopocket and the periodontal pocket. This classification had merit not only from a teaching standpoint but also on a therapeutic basis.

Much attention has been focused on the infrabony type of pocket in recent publications and this lesion has been described as amenable to either the new attachment procedure or osseous surgery for its eradication. It became obvious to us from our observations of clinical as well as human skull material that a classification of the infrabony pocket was necessary not only for academic purposes but also to serve as a rational basis for the selection of a method of treatment.

The proposed classification of the infrabony pocket is on a morphologic basis and is dependent on the location and number of osseous walls remaining about the pocket. Much of this material studied was from human skulls where the gingivae and other soft tissues were intact. The location of the bottom of the pocket was established, the material radiographed, and then the soft tissue was removed. The remainder of the material was taken from clinical cases under treatment.

The first group of infrabony pockets described have three osseous walls. These trough-like defects are commonly observed in the interdental areas where one finds an intact proximal wall as well as the buccal and lingual walls of the alveolar process. Some of these lesions may be shallow with a broad orifice to the osseous part of the pocket while others may be narrow and deep. Three wall infrabony pockets are occasionally observed on the lingual surfaces of maxillary and mandibular teeth where the lingual plate is intact as well as both proximal walls. Less frequently noted are infrabony pockets located on the buccal surfaces of maxillary and mandibular posterior teeth. It is not uncommon to find them extending around the tooth to involve 2 or sometimes 3 surfaces. When the infrabony pocket is circumferential and involves the four surfaces of the tooth, it actually has four osseous walls (buccal, lingual, mesial, distal). This occurs infrequently.

The determination of the position as well as the number of osseous walls is of concern to the clinician during his examination procedures.

The radiograph can be of great aid in demonstrating the presence of buccal and lingual and proximal walls in a pocket occurring in the interdental area. Placing a radiopaque object such as a gutta percha point, a periodontal probe, or Hirschfeld

†Presented at the Academy of Periodontology Meeting in Miami, Fla. on October 31, 1957.

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Anatomical Considerations in Periodontal Surgery

by

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Kenneth W. Bueltmann, D.D.S., M.S.

A variety of surgical procedures have been devised for the treatment of periodontal disease and associated abnormalities. Such procedures may be accompanied by certain operative hazards related to the presence and location of important anatomic structures. Limits may be imposed on the scope of periodontal therapy by local and individual anatomical features. Effective planning and execution of surgical therapy is based on a clear knowledge of the anatomy of the superficial and deep structures encountered during surgical intervention.

Surgical anatomy may be defined in part as the knowledge of anatomical facts which have local significance in relation to surgical therapy. Primary emphasis is placed on an understanding and awareness of important structures that may be encountered during surgery or which place limits on the nature of the planned surgery, rather than on a detailed and precise knowledge of systematic anatomy.

It is the purpose of this paper to discuss anatomical considerations pertinent to periodontal surgery. A systematic descriptive review of structures that may be encountered by periodontal surgeons will be presented. This will be followed by a detailed description of surgical anatomy in relation to periodontal therapy. Illustrations of important anatomic structures as displayed by conventional periodontal surgical entry procedures will be provided. The significance of such structures in relation to treatment planning, surgical techniques, and the avoidance of operative hazards will be discussed.

Review of the Literature

Very few articles concerning surgical anatomy in relation to periodontal therapy are available in the literature. Rosenberg[1] discussed vestibular alterations in periodontics, including a brief consideration of the muscles of facial expression which might be encountered by the periodontal surgeon. Precautions and hazards in periodontal surgery were described by Bradin.[2] Key anatomical features and their significance were listed, though the bulk of the article was concerned with therapeutic techniques and general patient management. Veal[3] discussed exposure of neurovascular bundles during periodontal surgery, including a clinical photograph illustrating surgical exposure of the mental foramen and nerve.

Heslop[4] discussed surgical anatomy of the jaws in relation to injury, particular diseases, and surgical intervention. Though written for the oral or maxillofacial surgeon, the article contained much useful information for the periodontist.

Articles concerning the pathways by which dental infections may spread are useful in their descriptions of anatomic spaces. Anatomic considerations in diagnosis and treatment of odontogenic infections were listed by Laskin[5] who emphasized the importance of an understanding of regional anatomy in proper diagnosis and treatment planning. He indicated that, from the standpoint of the clinician, certain surgical spaces could be described that were different from the fascial spaces described by anatomists. Spilka[6] described pathways of dental infections, including discussions of pertinent anatomic spaces.

Clinical textbooks provide varying degrees of anatomical information. Prichard[7] includes a concise description of normal and pathologic osseous anatomy related to periodontal surgery. Goldman and Cohen[8] briefly consider surgical anatomy in relation to periodontics. Kruger,[9] in his *Textbook of Oral Surgery,* discusses fascial planes and anatomic spaces as pathways for the spread of infection. Anatomical considerations are well illustrated in his descriptions of surgical techniques employed in the correction of hard and soft tissue abnormalities.

Materials and Methods

Basic information concerning systematic anatomy was obtained by a review of standard textbooks of anatomy (Gray,[10] Netter,[11] Pernkopf,[12] Cunningham/Romanes[13]). Similar information concerning surgical anatomy in the head and neck regions was obtained by a review of appropriate textbooks (Hollinshead,[14] Shapiro,[15] Sicher and DuBrul[16]). Material discussed in the preceding review of the literature provided additional background information. Original anatomic drawings were prepared by the authors to illustrate important structural relationships.

Surgical dissections to display anatomic features of significance were performed on fresh and prepared specimens. Surgical entries, utilizing conventional periodontal surgical techniques, were employed wherever possible. Photographic documentation was accomplished with a clinical intraoral camera system.

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Diagnosis and epidemiology of periodontal osseous lesions

Panos N. Papapanou & Maurizio S. Tonetti

Loss of alveolar bone support is one of the characteristic signs of destructive periodontal disease and is generally considered to represent the anatomical sequela to the apical spread of periodontitis. The extent and the severity of alveolar bone loss in the dentition are usually assessed by a combination of radiographic and clinical means and are important adjuncts to the clinician in the diagnosis, treatment planning, and assessment of prognosis of the periodontal patient. The presence of periodontal osseous lesions is clinically significant in many ways. It relates to the associated loss of tooth support, to the site specificity of periodontal destruction, and to the possibility that ecological niches (deep pockets and furcation involvement) associated with some osseous lesions may represent site-specific risk factors or indicators for disease progression.

Etiology

A variety of factors have been associated with the formation of intrabony defects: among these, trauma from occlusion and food impaction have been extensively discussed in the older literature (9, 10). Anatomic factors such as plaque-retaining local elements and the distance between adjacent root surfaces have also been proposed to play a role (47, 50, 52). The latter argument is based on the observation that a close proximity between neighboring roots results in involvement of the whole interdental septum in the inflammatory, resorptive process which, in turn, results in destruction of the entire interdental alveolar bone and precludes the formation of an infrabony defect.

The development of a furcation invasion has been mainly associated with the special anatomical niche that is formed following the exposure of the furcation fornix (51), while the presence of enamel pearls or projections has also been named as predisposing to breakdown (29). Variations in the morphology of multirooted teeth are also of importance in determining at what stage in the periodontal breakdown process a furcation will become involved. The length of the common root trunk, the presence of developmental depressions, the root morphology and the presence of accessory pulp canals have received considerable attention (23).

Irrespective of the number and nature of the contributing factors involved, the formation of an osseous periodontal lesion is today considered to be the result of an apical downgrowth of subgingival plaque with a concomitant resorption of bone within a 2-mm radius from the root surface (17, 50–52). The more remotely located bone structures and the root surface retain their integrity and form the anatomical boundaries of the osseous lesion.

Classification

Since periodontal osseous lesions represent the anatomical sequelae to the apical spread of periodontitis, and in particular to the interplay between site specific progression and the local anatomy, their morphology is determined by a variety of factors which include: location of the causative microorganisms on the root surface, root and root trunk anatomy, thickness of the alveolar bone, root position within the alveolar process, and the steric relationship with adjacent periodontal lesions (that is, proximity with another involved root surface). Each individual defect affecting a specific tooth in the dentition of a certain patient, therefore, presents a unique anatomy. Many attempts, however, have been made to classify periodontal osseous defects. Classifications are generally based upon specific morphological criteria and are aimed at guiding clinicians with their diagnosis, treatment and prognosis. A first level of classification differentiates between suprabony defects, infrabony defects, and interradicular or furcation defects (Fig. 1).

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REVIEW ARTICLE

Periodontal Osseous Defects: A Review

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ABSTRACT

Periodontitis is an inflammatory process affecting the periodontal tissues caused by multi-factorial origin. Among all the characteristic signs of periodontal disease, loss of support from alveolar boneis the one which usually represents theanatomical sequela to the progression of periodontitis apically.The bone loss which is induced by periodontitis occur either single or in different combination forms. The identification of these osseous defects on surgical exposure of bone is clinically challenging as the osseous and it becomes imperative for a clinician to understand these defects and categorize them well to have better therapeutic approaches. Intimate knowledge of all these periodontal osseous defects associated with periodontal disease is essential. So this review is aimed at classification and deep insight which will be helpful for proper diagnosis and treatment of periodontal osseous defects.

Keywords: Alveolar process, Bone resorption, Periodontitis.

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INTRODUCTION

Periodontium is composed of both soft and hard tissues in which alveolar bone is the part which forms and also supports the teeth in both maxilla and mandible. Alveolar bone formation occurs as the eruption of tooth takes place in order to facilitate the osseous attachments to the periodontal ligament and disappears once the tooth is lost.[1]

Alveolar bone has its embryological origin from the initial condensation of ecto-mesenchyme around the early tooth germ. The alveolar process house the teeth and exist as long as teeth are present in it. The sharpey's fibres are embedded in the alveolar bone proper which is the compact bone, compromised of oral and buccal cortical plates and the cancellous bone located between them.[1]

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The bone loss in periodontal disease occurs at local sites, but it is regulated by both systemic and local factors. Bone resorption is probably the most critical factor in periodontal attachment loss leading to eventual tooth loss.[2] Radiographically it is diagnosed by evidence of "bone loss" around the tooth. Normally the crest of alveolar bone is situated between 0.4 to 1.97 mm approximately apically to the cemento-enamel junction (CEJ) of thatparticular tooth.[3]

The bone loss which is induced by periodontitis i.e osseous defects occur either single or in different combination forms. The identification of these osseous defects on surgical bone exposure is clinically challenging as the osseous surgeries are based on this diagnosis. It becomes imperative for a clinician to understand these defects and categorize them well to have better periodontic therapeutic approaches.

Periodontal osseous defects (POD) is an important clinical reality, however, it's classification and description are not being dealt in regular universally accepted text books. Hence, an attempt is made in this review paper to revisit, modify and describe various aspects of POD for the first time in literature.

Incidence and Prevalence

The changes which are observed in the alveolar process architecture may differ in form, distribution and degree within same individual at different sites as well as between individuals.

The prevalence of vertical defect was higher in male patients (14.95%) when compared to female patients (8.2%) and also it was rare in patients with dental awareness (de Toledo et al 2012).[4] Vertical defects are commonly associated with posterior teeth (Baljoon et al.),[5] with the higher prevalence in mandibular posterior teeth (33.8%) (Vrotsos et al., Kasaj et al.).[6,7]

Vertical defects are commonly associated with molars with higher prevalence of crater formation (26.5%), followed by circumferential defects (23.4%) and 3 wall defects (20.08%) (Wu et al.).[8]

Osseous Defects

Definition: Osseous defects are defined as the alterations in the morphology of the alveolar bone (GPT). These occur normally (anatomic variations) and disease induced. As these defects act a crucial role either in initiating or

Relationship Between the Radiographic Periodontal Defect Angle and Healing After Treatment

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THIS STUDY RADIOGRAPHICALLY EVALUATED the correlation between the changes in alveolar bone level occurring in bony defects after periodontal therapy and the corresponding pretreatment defect angles. The defect angle was defined by the bony defect surface and the root surface. The changes were determined from identically exposed and processed radiographs obtained just prior to surgery and 15 to 18 months later.

The defect angle was clearly correlated to the radiographic changes in alveolar bone level. Most defects with an angle less than 45° showed a gain of bone while defects with the largest defect angles showed a loss. In addition, defects on root surfaces without furcations showed better healing than defects associated with furcations.

The results of healing after periodontal therapy have been evaluated clinically in longitudinal studies with different treatment modalities.[1-3] These studies have provided information about the reactions of the periodontal soft tissues, such as the clinical attachment level, and have enhanced the ability to predict the clinical outcomes of such treatments.

Other investigators have radiographically evaluated the changes of the alveolar bone level following either no treatment[4] or active treatment with or without subsequent maintenance therapy.[4-10] Such studies have demonstrated that the bone healing is related to the number of bony walls of the defect,[11] the selection of treatment modality, and the maintenance regimen.

Although it has been established that the clinical management of the patients and that certain clinical defect characteristics are of significance to the tissue response, the associations between radiographic morphological variables and the healing patterns of alveolar bone defects are not yet fully understood. Recent results[12] have shown that interproximal intrabony defects occur in 15% of an adult Swedish population. These findings clearly have emphasized the importance of gaining more information about the effect of treatment of such defects.

It was the aim of the present investigation to evaluate the changes which occur following treatment of bony defects with different radiographic morphology. In particular, it was a goal to determine whether the defect angle was correlated with these bone changes. If so, this would add a valuable tool for predicting the healing potential of bony defects which might be applicable in epidemiological studies as well as clinical practice.

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MATERIALS AND METHODS

Pairs of radiographs covering the premolar and molar regions were obtained from 11 patients who were participating in a clinical study of periodontal treatment at the School of Dentistry, University of Michigan. After scaling and root planing and a reevaluation period for all patients, the treatment consisted of modified Widman flap surgery[13] with no osseous recontouring and complete bone coverage by the repositioned flap. All patients were followed on a regular maintenance program during which time they received prophylaxis every 3 months.

The first radiograph was taken immediately prior to periodontal surgery and served as the baseline reference. The second radiograph was obtained 15 to 18 months later. All radiographs were exposed according to a method which aimed for identical images by using individual bite blocks and identical film developing conditions.[14] The method for recording the morphological parameters of the bony defects, as well as the changes occurring in these areas, has been described in detail.[15] In summary, magnified tracings of the contours of the alveolar bone and the tooth structure were obtained from the pre- and post-treatment radiographs. These tracings were then superimposed and the morphological variables were measured by a microcomputer connected digitizing system.‡

‡ Bit Pad Two tablet, Summagraphics, Fairfield, CT; Sigmascan 3.01 software, Jandel Scientific, Corte Madera, CA; IBM Personal Computer AT.

The angular bony defect as indicator of further alveolar bone loss

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Papapanou PN and Wennström JL: The angular bony defect as indicator of further alveolar bone loss. J Clin Periodontol 1991; 18: 317–322.

Abstract. The aim of the present retrospective study was to evaluate alterations of the alveolar bone level over a 10-year period at tooth sites with "angular" and "even" patterns of bone loss, in subjects who were not exposed to systematic periodontal therapy. A further objective was to evaluate whether the presence of an angular defect can serve as a predictor of additional bone loss. 201 subjects in ages 25–70 years were examined radiographically on 2 occasions 10 years apart. 194 were dentate on the 2nd examination. The radiographic bone height at the mesial and distal aspect of all teeth was assessed by measuring the distance between the cemento-enamel junction and the bone crest. The morphologic pattern of alveolar bone loss at baseline was assessed for each tooth site. Angular defects were classified as degree 1, 2 and 3, according to increasing defect depth. The change in periodontal bone height over the 10-year period was calculated for each site. The results demonstrated an increased frequency of tooth loss among teeth showing presence of an angular bony defect at baseline; whereas 13% of the teeth with an even pattern of bone loss were lost between the 2 examinations, this proportion was 22%, 46% and 68% for teeth with an angular defect of degree 1, degree 2 and degree 3, respectively. Longitudinal bone loss of ≥ 2 mm occurred more often among sites showing an angular defect when compared to sites with an even alveolar bone morphology. Multiple regression analysis revealed a statistically significant increased longitudinal bone loss for tooth sites with angular defects, even though the individual subject's overall past experience of alveolar bone loss and the particular tooth site initial degree of bone loss were taken into account. With an overall incidence of additional bone loss of ≥ 2 mm of 23%, presence of an angular bony defect at baseline predicted longitudinal bone loss with 8% sensitivity, 94% specificity, 28% predictive value for the positive test and 77% predictive value for the negative test. It was concluded that, in absence of systematic periodontal therapy, the presence of an angular bony defect entails an increased risk for further alveolar bone loss.

Key words: dental radiology; periodontal disease; prediction.

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Loss of alveolar bone is one of the characteristic symptoms of destructive periodontal disease. The radiographic pattern of bone loss around teeth affected by the disease has traditionally been described as having an "even" (horizontal) or an "angular" (vertical) appearance. There seems, however, to be no uniform opinion in the literature on the clinical significance of this particular morphologic feature.

Angular bony defects have been associated with trauma from occlusion (Glickman & Smulow 1962, 1965). This association is though not exclusive, since angular bony defects have been also found to occur adjacent to teeth with (i) normal occlusal function (Waerhaug 1979) and (ii) deficient root cementum (Gottlieb 1946, Lindskog & Blomlöf 1983, Blomlöf et al. 1987). Moreover, it has been suggested that the formation of the angular bony defect is a mere result of an asynchronous apical propagation of the subgingival plaque along adjacent approximal root surfaces (Lindhe et al. 1975, Waerhaug 1979). The term "site specificity" which has been used to described this phenomenon (Goodson et al. 1982, Haffajee et al. 1983) has been hypothesized to (i) reflect varying levels of susceptibility to periodontal disease of the involved tooth surfaces (Listgarten 1986, Haffajee & Socransky 1986), or (ii) be a result of different microbial colonization patterns (Evian et al. 1982, Loesche et al. 1985, Newman 1985). Based on clinical observations, it has also been assumed that a number of anatomic factors (e.g., distance between neighboring teeth, morphology and quality of the alveolar bone, concavities/fissures on the root surface) may influence the alveolar bone loss pattern.

None of the relatively scarce long-term longitudinal studies of periodontal disease progression (Lindhe et al. 1983, Buckley & Crowley 1984, Lõe et al. 1986, Lavstedt et al. 1986, Papapanou et al. 1989, Albandar 1990) appear to have attempted an association of the "even" or "angular" pattern of alveolar bone loss with the progression rate of

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Baseline radiographic defect angle of the intrabony defect as a prognostic indicator in regenerative periodontal surgery with enamel matrix derivative

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Tsitoura E, Tucker R, Suvan J, Laurell L, Cortellini P, Tonetti M: Baseline radiographic defect angle of the intrabony defect as a prognostic indicator in regenerative periodontal surgery with enamel matrix derivative: J Clin Periodontol 2004; 31: 643–647. doi: 10.1111/j.1600-051X.2004.00555.x. © Blackwell Munksgaard, 2004.

Abstract

Introduction: The baseline radiographic defect angle has previously been correlated with the clinical outcomes of intrabony defects treated with access flap or guided tissue regeneration. The aim of this study was to investigate whether an association exists between baseline radiographic defect angle and treatment outcome when enamel matrix derivative (EMD) is used in periodontal regenerative surgery.

Materials and Methods: Baseline radiographs were collected from the test group of a previously published clinical trial using a population of 166 patients treated for chronic periodontitis. All intrabony defects were $\geqslant 3$ mm for inclusion in the original study. Either modified or simplified papilla preservation technique was used to access the defect. The roots were conditioned with an EDTA gel and the primary outcome measure was clinical attachment level (CAL) change, 1 year after surgery.

Results: Sixty-seven radiographs were measurable. The probability of obtaining CAL gain >3 mm was 2.46 times higher (95% confidence interval: 1.017–5.970) when the radiographic defect angle was $\leqslant 22^\circ$ than when it was $\geqslant 36^\circ$.

Conclusions: This study showed that there was a significant association between baseline radiographic defect angle and CAL gain at 1 year. The observed increased odds ratio of obtaining CAL gain of $\geqslant 4$ mm after regenerative surgery with EMD is used in narrow ($\leqslant 22^\circ$) intrabony defects, suggests that the baseline radiographic defect angle might be used as a prognostic indicator of treatment outcome.

Key words: clinical trial; enamel matrix derivative; periodontal therapy; prognosis; regeneration

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A correlation between radiographic changes in alveolar bone level (bone fill) occurring in intrabony defects after periodontal access flap surgery and the corresponding pre-treatment defect angles has been described, where greater potential for bone fill was found in defects with small angles (0–45°) compared with wide angles (45–90°, Steffensen & Weber 1989). Tonetti et al. (1993b) showed that, for guided tissue regeneration (GTR), the wider the radiographic defect angle, the lower the regenerated probing attachment level in intrabony defects. In a retrospective three-centre study, it was shown that clinical attachment level (CAL) gain and bone fill were positively correlated to the depth of the intrabony defect and that the less favourable results of one of these three centres were attributed to the fact that this centre had treated significantly wider defects compared with the other two centres (Falk et al. 1997).

Cortellini & Tonetti (1999) studied 242 intrabony defects treated with GTR and found a significant difference in the CAL outcomes when they compared narrow ($<25^\circ$) to wide ($>37^\circ$) defects. They concluded that the radiographic defect angle could represent a useful pre-surgical parameter to determine the potential of CAL gain in intrabony

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PERSPECTIVE

Osseous topography in biologically driven flap design in minimally invasive regenerative therapy: A classification proposal

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Abstract
Minimally invasive periodontal regenerative surgical procedures are a paradigm shift that demands a unique approach encompassing specialized armamentarium, magnification tools, knowledge of handling properties of biomaterials, and specific flap designs. Biologically driven flap design is dictated by optimal soft and hard tissue handling, flap perfusion, and wound stability, all in the pursuit of primary intention healing. The unique architecture of the infrabony defect is a determining factor on incision tracing, boundaries of flap extension, and biomaterial selection. The purpose of this article is to propose a flap design classification based on the osseous topography of infrabony defects during biologically driven minimally invasive surgical periodontal regenerative therapy.

KEYWORDS
biocompatible materials, guided tissue regeneration, regeneration

INTRODUCTION

In an editorial published in the *British Journal of Surgery* in 1990, Fitzpatrick and Wickham[1] concluded that changes occurring in the operating theatres across surgical specialties had one common denominator: ensuring that trauma of surgical access was reduced to a minimum while still achieving the intended therapeutic aims. The field of regenerative periodontal therapy has not been excluded from these revolutionary surgical changes. Since Harrel and Rees[2] illustrated the concept of minimally invasive surgical (MIS) procedures for periodontal regeneration in 1995, different flap designs and suture techniques have been introduced with the purpose of minimizing surgical access, diminishing tissue trauma, enhancing wound closure, providing stability and protection to the blood clot, and avoiding soft tissue recession while facilitating visual and mechanical access to infrabony defects. The MIS technique was subsequently illustrated in several other publications.[3–5]

Flap design has played an important role in the development and application of MIS principles. Takei et al.[6] introduced a papilla preservation technique to protect the interproximal space hosting the infrabony defect by avoiding incisions directly on the col area, thus facilitating primary closure and protecting grafting material placed in the interproximal spaces. The palatal approach proposed by this technique was modified 10 years later when Cortellini et al.[7] described both the modified papilla preservation technique and a few years later, the simplified papilla preservation flap.[8] These novel techniques provided surgical access from the buccal aspect instead. This surgical modality required a well-defined protocol for incision extension and location, soft tissue manipulation, suturing, and wound closure. It is important to recall that non-absorbable and resorbable barriers were being utilized as the standard of care at that time, and due to their size and nature, incision and flap extension had to be more extensive.

The evolution of the MIS approach has witnessed the incorporation of the minimally invasive surgical technique (MIST), which limits mesio-distal flap extension and coronal-apical reflection while minimizing trauma and maximizing tissue stability.[9] In an effort to further maximize

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SYSTEMATIC REVIEW

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Periodontal infrabony defects: Systematic review of healing by defect morphology following regenerative surgery

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Abstract

Background: It is thought that infrabony defect morphology affects the outcome of periodontal regenerative surgery. However, this has not been systematically investigated.

Aims: To investigate how well defect morphology is described in papers reporting regenerative therapy of periodontal infrabony defects and to investigate its effect on clinical and radiographic outcomes.

Materials and Methods: A search was conducted in 3 electronic databases for publications reporting clinical and radiographic outcomes of periodontal intra-bony defects after regenerative therapy, divided by defect morphology.

Results: The initial search resulted in 4487 papers, reduced to 143 after first and second screening. Fifteen of these publications were suitable for a fixed-effects meta-analysis. Initial defect depth was found to influence radiographic bone gain 12 months post-surgery, while narrower angles and increased number of walls influenced both radiographic bone gain and clinical attachment level (CAL) gain at 12 months. These associations seemed to occur irrespective of biomaterials used. Risk of bias ranged from low to high.

Conclusion: Deeper defects with narrower angles and increased number of walls exhibit improved CAL and radiographic bone gain at 12 months post-regenerative surgery. More data are needed about other aspects of defect morphology such as extension to buccal/lingual surfaces.

KEYWORDS
intra-bony, osseous defect, periodontitis, regeneration

1 | INTRODUCTION

Classically, periodontal defects have been differentiated based on bone resorption patterns into "supraosseous" ("suprabony") and "infraosseous" ("infrabony") (Goldman & Cohen, 1958). These authors defined suprabony defects as those where the base of the pocket is located coronal to the alveolar crest. On the other hand, infrabony defects are those with apical location of the base of the

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COMMENTARY

A re-evaluation of scaling and root planing

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Abstract

Background: Extensive reviews on the role of scaling and root planing (SRP) in the treatment of periodontitis have been previously published. This commentary will address the importance of subgingival calculus in the progression and treatment of periodontitis and addresses factors that make the execution of a "definitive" SRP a critical part of therapy.

Methods: A search for articles, using keywords relevant to the subject , (e.g., periodontitis, dental scaling, root planing, dental calculus, biofilm, inflammation) was conducted using PubMed, Ovid Medline, Cochrane Reviews and the ADA Center for Evidence Based Dentistry data bases. Additionally, references cited in relevant articles were also considered.

Results: Surfaces of subgingival calculus are covered with a biofilm of metabolically active bacteria. Periodontal inflammation is clearly related to the presence of calculus and biofilm. The primary goal of SRP is removal of subgingival calculus and biofilm deposits to create a biologically compatible root surface and reduce the inflammatory burden. Current evidence suggests that inflammation associated with periodontal infections affects both the immediate oral environment and the patient's systemic health.

Conclusion: SRP is still critical to the treatment of periodontitis. SRP involving deep probing depths ($\geq$ 5 mm) and root surfaces with anatomical and surface irregularities, regardless of the type of instrumentation, requires time, exceptional skill and perseverance, and patient compliance with periodontal maintenance. Sites with persistent nonresponding probing depths and signs of inflammation following a definitive SRP, should be considered for surgical intervention.

KEYWORDS
biofilms, dental calculus, dental scaling, inflammation, periodontitis, root planing

1 | INTRODUCTION

The purpose of this commentary is to reevaluate the impact of root surface accretions and alterations on the pathogenicity of periodontitis, the factors that influence treatment outcomes, and to offer recommendations that will promote optimal long-term success in controlling periodontal disease. The belief that a core of clinical and scientific facts exists independently of interpretation by the clinician is a fallacy. It is common for clinicians to consider the same data and derive different conclusions. What follows is influenced by the authors' combined 100+ years of academic and clinical experience. We present the facts as we know and interpret them and apply them to the clinical practice of scaling and root planing (SRP) as the essential element of non-surgical periodontal therapy.

Original Research

Evaluating the Efficacy of Platelet-Rich Plasma (PRP) in Accelerating Healing and Reducing Complications in Oral Surgery

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Abstract

Background: The process of curing and regaining the integrity of damaged tissues is known as healing. An autologous concentration of platelets embedded in plasma is known as platelet-rich plasma (PRP). **Aim:** This study was conducted to evaluate the role of PRP in the fast healing of wounds and complications in oral surgical procedures. **Materials and Methods:** A total of 60 patients who underwent different oral surgical procedures were included in this study. PRP was placed in the surgical area after surgical procedures and recalled at the 2nd, 4th, and 6th month postoperatively. There was the assessment of soft tissue healing by measuring the probing depth in teeth adjacent to the surgical area and hard tissue healing in the form of alveolar bone density and alveolar bone height. The assessment of postoperative complications was also conducted. **Results:** The decrease in the probing depth at different follow-ups was greater in PRP patients showing better and fast soft tissue healing. The increase in alveolar height and alveolar bone density at different follow-ups was greater in the PRP group showing better and fast hard tissue healing. The frequency of complications, such as trismus and pain, was lesser in patients with PRP. **Conclusion:** The wound healing was at increased rate with reduced complications on using PRP in oral surgical procedures.

Keywords: *Accelerated wound healing, complications, PRP*

Introduction

The process of curing and regaining the integrity of damaged tissues is known as healing. During the process of wound healing, some molecules—typically proteins—are used by cells to communicate with one another. "Cytokines" are proteins that are involved in cellular communication.[1,2] A category of cytokines called growth factors is known to specifically promote cell division. Mammalian blood contains platelets,

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Review

Use of PRP, PRF and CGF in Periodontal Regeneration and Facial Rejuvenation—A Narrative Review

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Simple Summary: Growth factors play a vital role in cell proliferation, migration, differentiation and angiogenesis. Autologous platelet concentrates which contain high levels of growth factors are used in many fields of dentistry. The current review is designed to provide clinical information regarding the use of three autologous platelet concentrates techniques in periodontal regeneration and facial rejuvenation: platelet-rich plasma, platelet-rich fibrin and concentrated growth factor techniques. The aim is to provide the clinician with an up-to-date overview of autologous platelet concentrates evolution over the past decade, clinical indications for use and advantages and limitations of each technique. This article was written in clinical orientation and is designed to provide clinicians with reliable and useful information applicable to their clinical work. Overall, platelet-rich plasma is mainly used in cases of hard and soft tissue procedures, while platelet-rich fibrin is used in gingival recession and treatment of furcation and intrabony defects; concentrated growth factor is mainly used in bone regeneration. In the field of facial rejuvenation, the use of platelet-rich plasma promotes tissue remodeling in aged skin and may be used as an adjuvant treatment to lasers; platelet-rich fibrin holds significant potential for stimulated dermal augmentation, and concentrated growth factor treatment could improve the survival and quality of fat grafts.

Abstract: Growth factors (GFs) play a vital role in cell proliferation, migration, differentiation and angiogenesis. Autologous platelet concentrates (APCs) which contain high levels of GFs make them especially suitable for periodontal regeneration and facial rejuvenation. The main generations of APCs presented are platelet-rich plasma (PRP), platelet-rich fibrin (PRF) and concentrated growth factor (CGF) techniques. The purpose of this review is to provide the clinician with an overview of APCs' evolution over the past decade in order to give reliable and useful information to be used in clinical work. This review summarizes the most interesting and novel articles published between 1997 and 2020. Electronic and manual searches were conducted in the following databases: Pubmed, Scopus, Cochrane Library and Embase. The following keywords were used: growth factors, VEGF, TGF-b1, PRP, PRF, CGF and periodontal regeneration and/or facial rejuvenation. A total of 73 articles were finally included. The review then addresses the uses of the three different techniques in the two disciplines, as well as the advantages and limitations of each technique. Overall, PRP is mainly used in cases of hard and soft tissue procedures, while PRF is used in gingival recession and the treatment of furcation and intrabony defects; CGF is mainly used in bone regeneration.

Keywords: PRP; PRF; CGF; facial rejuvenation; autologous platelet concentrates; periodontal regeneration

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Review

The Platelet Concentrates Therapy: From the Biased Past to the Anticipated Future

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Abstract: The ultimate goal of research on platelet concentrates (PCs) is to develop a more predictable PC therapy. Because platelet-rich plasma (PRP), a representative PC, was identified as a possible therapeutic agent for bone augmentation in the field of oral surgery, PRP and its derivative, platelet-rich fibrin (PRF), have been increasingly applied in a regenerative medicine. However, a rise in the rate of recurrence (e.g., in tendon and ligament injuries) and adverse (or nonsignificant) clinical outcomes associated with PC therapy have raised fundamental questions regarding the validity of the therapy. Thus, rigorous evidence obtained from large, high-quality randomized controlled trials must be presented to the concerned regulatory authorities of individual countries or regions. For the approval of the regulatory authorities, clinicians and research investigators should understand the real nature of PCs and PC therapy (i.e., adjuvant therapy), standardize protocols of preparation (e.g., choice of centrifuges and tubes) and clinical application (e.g., evaluation of recipient conditions), design bias-minimized randomized clinical trials, and recognize superfluous brand competitions that delay sound progress. In this review, we retrospect the recent past of PC research, reconfirm our ultimate goals, and discuss what will need to be done in future.

Keywords: platelet-rich plasma (PRP); platelet-rich fibrin (PRF); platelet concentrates; bone regeneration; randomized controlled trial; standardization; quality assurance

1. Introduction

Since the first study on bone regeneration [1], the aim of platelet concentrate (PC) research has been to establish a basis for the safer, more effective, and more predictable clinical use of PC therapy. Nevertheless, fundamental questions regarding the clinical efficacy of PCs have been raised increasingly over the past two decades, to the point that PC therapy has been called disappointing and a "mirage", "miracle", or "myth" [2]. This may be due to the rapid global spread of PCs without having first established robust evidence. To our knowledge, their clinical use has not yet been endorsed convincingly by either observational or interventional studies.

Nowadays, PC therapies have been widely applied in the fields of oral surgery, orthopedic surgery, plastic surgery, and dermatology, such as treatments for alveolar bone defects, acute injuries of muscles, tendon and ligament injuries, joint injuries, osteoarthritis, skin rejuvenation, scars, inflammation reduction, hair loss, postsurgical repair, and others. If we continue to accept PC therapy "consciously or unconsciously" in its present form, it may soon fall out of use or be remembered in medical history as "a meaningless alternative medicine". Therefore, we must first obtain clear evidence of the functionality

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ORIGINAL ARTICLE

Comparative release of growth factors from PRP, PRF, and advanced-PRF

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Abstract
Objectives The use of platelet concentrates has gained increasing awareness in recent years for regenerative procedures in modern dentistry. The aim of the present study was to compare growth factor release over time from platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and a modernized protocol for PRF, advanced-PRF (A-PRF).
Materials and methods Eighteen blood samples were collected from six donors (3 samples each for PRP, PRF, and A-PRF). Following preparation, samples were incubated in a plate shaker and assessed for growth factor release at 15 min, 60 min, 8 h, 1 day, 3 days, and 10 days. Thereafter, growth factor release of PDGF-AA, PDGF-AB, PDGF-BB, TGFB1, VEGF, EGF, and IGF was quantified using ELISA.
Results The highest reported growth factor released from platelet concentrates was PDGF-AA followed by PDGF-BB, TGFB1, VEGF, and PDGF-AB. In general, following 15–60 min incubation, PRP released significantly higher growth factors when compared to PRF and A-PRF. At later time points up to 10 days, it was routinely found that A-PRF released the highest total growth factors. Furthermore, A-PRF released significantly higher total protein accumulated over a 10-day period when compared to PRP or PRF.
Conclusion The results from the present study indicate that the various platelet concentrates have quite different release kinetics. The advantage of PRP is the release of significantly higher proteins at earlier time points whereas PRF displayed a continual and steady release of growth factors over a 10-day period. Furthermore, in general, it was observed that the new formulation of PRF (A-PRF) released significantly higher total quantities of growth factors when compared to traditional PRF.
Clinical relevance Based on these findings, PRP can be recommended for fast delivery of growth factors whereas A-PRF is better-suited for long-term release.

Keywords Platelet-rich plasma · Platelet-rich fibrin · Choukroun's PRF · Platelet concentrates · Growth factor release

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Introduction

A number of techniques have been utilized in modern dentistry to speed the regeneration of either hard or soft tissues [1–4]. While a great deal of effort in recent years has been focused on the use of biologics as key mediators of tissue regeneration, some of the disadvantages of utilizing recombinant growth factors include high supra-physiological doses as well as high costs associated with their use [5–7]. Nevertheless, the use of growth factors such as recombinant platelet-derived growth factor (PDGF) has been shown to positively increase tissue formation across a wide variety of clinical procedures in both dentistry and medicine [8].

1

Platelet Rich Fibrin: A Second-Generation Platelet Concentrate

Joseph Choukroun and Richard J. Miron

Abstract

Almost two decades have passed since platelet rich fibrin (PRF) was first introduced. Initially, the primary objective was to develop a therapy where platelet concentrates could be introduced into wounds by effectively utilizing the body's natural healing capacity. This was achieved by collecting growth factors derived from blood in a natural way. Platelet rich plasma (PRP) and platelet rich growth factor (PRGF) had been commercialized, yet both contained secondary byproducts that were both unnatural and known inhibitors of wound healing. By removing these anti-coagulants and modifying centrifugation protocols, PRF was introduced some years later with the potential to markedly impact many fields of medicine including dentistry. Many aspects important for tissue regeneration have since been revealed including the important role of fibrin as well as the preferential release of growth factors over longer periods of time from PRF. Furthermore, by introducing a new set of cells into platelet concentrates (namely leukocytes), a marked impact on tissue regeneration and wound healing was observed. Over the past 5 years, further modifications to centrifugation speed and time have additionally improved PRF into a concept now known as the "low-speed centrifugation concept." Investigators began to modify surgical techniques to favorably treat patients with PRF with improved clinical outcomes. Together, many key opinion leaders from around the globe have been gathered to share their experiences and knowledge in many educational courses and seminars in what we now know as platelet rich fibrin. In this first chapter, we highlight the discovery of PRF and the studies leading to its first use in regenerative medicine. We focus specifically on its properties for wound healing and how its presented advantages over previous versions of platelet concentrates have favorably enhanced the regenerative potential of platelet concentrates in dentistry.

Highlights

- Introduction of Platelet Rich Fibrin
- Reasons for its invention two decades ago
- Its variations from the formally known platelet concentrate "platelet rich plasma" or "PRP"
- The first case treated with PRF
- Properties important for wound healing

1.1 Introduction

Wound healing is a complex biological process where many cellular events taking place simultaneously leading to the repair or regeneration of damaged tissues [1–4]. Many attempts have been made in the field of tissue regeneration with the aim of predictably repairing, regenerating, or restoring

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ORIGINAL ARTICLE

Injectable platelet rich fibrin (i-PRF): opportunities in regenerative dentistry?

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Abstract
Objectives Platelet rich plasma (PRP) has been utilized in regenerative dentistry as a supra-physiological concentrate of autologous growth factors capable of stimulating tissue regeneration. Despite this, concerns have been expressed regarding the use of anti-coagulants, agents known to inhibit wound healing. In this study, a liquid formulation of platelet rich fibrin (PRF) termed injectable-PRF (i-PRF) without the use of anti-coagulants was investigated.
Materials and methods Standard PRP and i-PRF (centrifuged at 700 rpm (60G) for 3 min) were compared for growth factor release up to 10 days (8 donor samples). Furthermore, fibroblast biocompatibility at 24 h (live/dead assay); migration at 24 h; proliferation at 1, 3, and 5 days, and expression of PDGF, TGF-β, and collagen1 at 3 and 7 days were investigated.
Results Growth factor release demonstrated that in general PRP had higher early release of growth factors whereas i-PRF showed significantly higher levels of total long-term release of PDGF-AA, PDGF-AB, EGF, and IGF-1 after 10 days. PRP showed higher levels of TGF-β1 and VEGF at 10 days. While both formulations exhibited high biocompatibility and higher fibroblast migration and proliferation when compared to control tissue-culture plastic, i-PRF induced significantly highest migration whereas PRP demonstrated significantly highest cellular proliferation. Furthermore, i-PRF showed significantly highest mRNA levels of TGF-β at 7 days, PDGF at 3 days, and collagen1 expression at both 3 and 7 days when compared to PRP.
Conclusions i-PRF demonstrated the ability to release higher concentrations of various growth factors and induced higher fibroblast migration and expression of PDGF, TGF-β, and collagen1. Future animal research is now necessary to further validate the use of i-PRF as a bioactive agent capable of stimulating tissue regeneration.
Clinical relevance The findings from the present study demonstrate that a potent formulation of liquid platelet concentrates could be obtained without use of anti-coagulants.

Keywords Fibrin · Blood platelets · Regeneration · Wound healing · Fibroblasts · Platelet rich fibrin

Introduction

Platelet concentrations have been utilized in dentistry for over three decades as a regenerative tool capable of releasing supra-physiological doses of growth factors responsible for inducing tissue regeneration derived from autologous sources [1, 2].

Richard J. Miron and Masako Fujioka-Kobayashi contributed equally to this work.

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REVIEW

Use of platelet-rich fibrin for the treatment of periodontal intrabony defects: a systematic review and meta-analysis

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Abstract

Objectives This study aims to compare the treatment outcomes of periodontal intrabony defects by using platelet-rich fibrin (PRF) with other commonly utilized modalities.

Materials and methods The eligibility criteria comprised randomized controlled trials (RCTs) comparing the clinical outcomes of PRF with that of other modalities. Studies were classified into 10 categories as follows: (1) open flap debridement (OFD) alone versus OFD/PRF; (2) OFD/bone graft (OFD/BG) versus OFD/PRF; (3) OFD/BG versus OFD/BG/PRF; (4–6) OFD/barrier membrane (BM), OFD/PRP, or OFD/enamel matrix derivative (EMD) versus OFD/PRF; (7) OFD/EMD versus OFD/EMD/PRF; (8–10) OFD/PRF versus OFD/PRF/metformin, OFD/PRF/bisphosphonates, or OFD/PRF/statins. Weighted means and forest plots were calculated for probing depth (PD), clinical attachment level (CAL), and radiographic bone fill (RBF).

Results From 551 articles identified, 27 RCTs were included. The use of OFD/PRF statistically significantly reduced PD and improved CAL and RBF when compared to OFD. No clinically significant differences were reported when OFD/BG was compared to OFD/PRF. The addition of PRF to OFD/BG led to significant improvements in CAL and RBF. No differences were reported between any of the following groups (OFD/BM, OFD/PRP, and OFD/EMD) when compared to OFD/PRF. No improvements were also reported when PRF was added to OFD/EMD. The addition of all three of the following biomolecules (metformin, bisphosphonates, and statins) to OFD/PRF led to statistically significant improvements of PD, CAL, and RBF.

Conclusions The use of PRF significantly improved clinical outcomes in intrabony defects when compared to OFD alone with similar levels being observed between OFD/BG and OFD/PRF. Future research geared toward better understanding potential ways to enhance the regenerative properties of PRF with various small biomolecules may prove valuable for future clinical applications. Future research investigating PRF at histological level is also needed.

Clinical relevance The use of PRF in conjunction with OFD statistically significantly improved PD, CAL, and RBF values, yielding to comparable outcomes to OFD/BG. The combination of PRF with bone grafts or small biomolecules may offer certain clinical advantages, thus warranting further investigations.

Keywords Intrabony defect · Platelet-rich fibrin · L-PRF · Advanced-PRF

Introduction

Periodontal disease is one of the most prevalent chronic diseases known to man that begins as a superficial inflammatory response of the gingiva (gingivitis) and later progresses to attachment loss with subsequent destruction of the tooth-supporting structures (periodontitis) [1–4]. Results investigating the distribution of the disease from a national survey conducted in the USA found that over 47% of the adult population was affected with 38.5% of the population having either moderate or severe cases (stage III or stage IV) [5]. This finding is most alarming as the disease is characterized with an exponentially more difficult resolution and regeneration once advanced progression has taken place.

Richard J. Miron and Vittorio Moraschini contributed equally to this work.

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Review Article

Platelet concentrates: An elixir of periodontal regeneration

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Abstract

Platelet concentrates (PCs) such as platelet-rich plasma and platelet-rich fibrin (PRF) are commonly used in various surgical procedures in medical as well as dental fields, oral and maxillofacial surgery, plastic surgery and sports medicine. The main motive is to elicit all the components of a blood sample that can be used to promote healing and regeneration. PCs came a long way since their existence in 1954 from titanium-PRF, advanced-PRF and injectable-PRF being introduced newly. These concentrates have been successfully applied in periodontal regenerative procedures and implantology. However, the preparation techniques, methodology, standing time, transfer process, temperature of centrifuge, vibration and other factors tend to produce mixed results. This review is designed to sort out all the confusions by introducing the exact origination of PCs, preparation techniques along with recent trends and clinical applications in periodontology.

Keywords: platelet-rich fibrin, advanced, platelet–rich fibrin, injectable, platelet concentrate, platelet-rich plasma, titanium platelet–rich fibrin

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INTRODUCTION

The main goal of the periodontal therapy is the elimination of the inflammatory process, which leads to progression of periodontal disease and second aim being the regeneration of the lost periodontal structures. Certain biologic occurrences such as cell adhesion, migration, proliferation and differentiation is involved in periodontal regeneration in an organised pattern.[1] Periodontal regenerative procedures comprises soft tissue grafting, bone grafts, root biomodifications, guided tissue regeneration and combinations of these.[2] They are either sourced from the nature or synthesised in the laboratories by certain chemical processing. Regenerative periodontal therapies are able to reconstruct only a fragment of the lost periodontal tissues till date with restricted prospective for achieving absolute periodontal rehabilitation.[3] To achieve complete periodontal tissue regeneration, numerous biomaterials are utilised in addition with autogenous/allogenic/xenogenous/synthetic bone grafts but not a single graft material has been declared as the gold standard in treating periodontal osseous defects.

Periodontal regeneration is the rehabilitation of the lost periodontal structures due to trauma or illnesses to repair the unique structure and characteristic of the periodontium. The main goal is to restore the lost periodontal attachment and bone loss of periodontally compromised tooth, lower depth of the pocket along with gingival recession.

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IMMUNITY & AGEING

REVIEW **Open Access**

Platelet-rich plasma (PRP) in dental and oral surgery: from the wound healing to bone regeneration

Antonino Albanese*, Maria E Licata, Bianca Polizzi and Giuseppina Campisi

Abstract

Platelet-rich plasma (PRP) is a new approach to tissue regeneration and it is becoming a valuable adjunct to promote healing in many procedures in dental and oral surgery, especially in aging patients. PRP derives from the centrifugation of the patient's own blood and it contains growth factors that influence wound healing, thereby playing an important role in tissue repairing mechanisms. The use of PRP in surgical practice could have beneficial outcomes, reducing bleeding and enhancing soft tissue healing and bone regeneration. Studies conducted on humans have yielded promising results regarding the application of PRP to many dental and oral surgical procedures (i.e. tooth extractions, periodontal surgery, implant surgery). The use of PRP has also been proposed in the management of bisphosphonate-related osteonecrosis of the jaw (BRONJ) with the aim of enhancing wound healing and bone maturation. The aims of this narrative review are: i) to describe the different uses of PRP in dental surgery (tooth extractions and periodontal surgery) and oral surgery (soft tissues and bone tissue surgery, implant surgery and BRONJ surgery); and ii) to discuss its efficacy, efficiency and risk/benefit ratio. This review suggests that the use of PRP in the alveolar socket after tooth extractions is certainly capable of improving soft tissue healing and positively influencing bone regeneration but the latter effect seems to decrease a few days after the extraction. PRP has produced better results in periodontal therapy in association with other materials than when it is used alone. Promising results have also been obtained in implant surgery, when PRP was used in isolation as a coating material. The combination of necrotic bone curettage and PRP application seem to be encouraging for the treatment of refractory BRONJ, as it has proven successful outcomes with minimal invasivity. Since PRP is free from potential risks for patients, not difficult to obtain and use, it can be employed as a valid adjunct in many procedures in oral and dental surgery. However, further RCTs are required to support this evidence.

Keywords: PRP, Wound healing, Bone regeneration, Dental surgery, Oral surgery, Tooth extraction, Periodontal surgery, Implant surgery, BRONJ

Introduction

Research in dental and oral surgery often involves materials and procedures which are capable of improving clinical outcomes in terms of percentages of success. The goal of this research was to find a treatment approach which could reduce bleeding, promote effective bone regeneration and rapid soft-tissue healing by employing resources which are easy to use at a modest cost.

Platelet rich plasma (PRP) is a new approach to tissue regeneration: it is widely used in various surgical fields, including head and neck surgery, otolaryngology, cardiovascular surgery, and maxillofacial surgery. Commonly, PRP is used in a gel formulation, which is formed by mixing PRP (derived from the centrifugation of autologous whole blood) with thrombin and calcium chloride. PRP gel includes a high concentration of platelets and a native concentration of fibrinogen [1,2].

During wound healing, platelets are among the first cells to respond at a wound site, being critical to the initiation of this process. Besides their procoagulant effects, platelets form a rich source of important growth factors,

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REVIEW

Application of PRP (platelet-rich plasma) in surgical periodontal therapy: overview

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ABSTRACT

Clinical and morphological manifestation of periodontitis is associated with persistent inflammation of the gingiva, loss of connective tissue attachment, formation of a periodontal pocket and loss of alveolar bone, which indicate variations in a wide range in different individuals. The main purpose of non-surgical therapy for periodontitis is to achieve long-term control of inflammation, and the ultimate goal of therapy is the regeneration of periodontal tissues affected by destruction. The unique anatomy and structure of the entire periodontal complex determine the course of more complex processes related to the restoration of periodontal structures affected by destruction, which include coordination of response by four different types of tissues: epithelial tissue, connective tissue, periodontal ligament and bone. Periodontal regeneration is defined as the regeneration of main tooth-supporting tissues: alveolar bone, periodontal ligament, cementum and attachment. Modern modalities for carrying out the periodontal regeneration include the use of bone substitutes, guided tissue regeneration with barrier membranes, treatments with flaps and a variety of additional components, such as: soft tissue grafts, root biomodifiers and growth factors, the carrier of which is platelet-rich plasma (PRP). This mini-review provides an overview of PRP applied in surgical periodontal therapy. Data of the initial experiences with this method are included, as well as brief references on its usage in the clinical practice. There is no substitute material in the modern literature shown as the gold standard in the treatment of periodontal bone defects.

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KEYWORDS
Periodontitis; periodontal regeneration; growth factors; PRP- platelet-rich plasma; PRF - platelet-rich fibrin

Introduction

Clinical and morphological manifestation of periodontitis is associated with persistent inflammation of the gingiva, loss of connective tissue attachment, formation of a periodontal pocket and loss of alveolar bone, which indicate variations in a wide range in different individuals. The formation of periodontal pockets of variable depth, the attachment loss, as well as horizontal or vertical bone loss are pathognomonic characteristics for diagnosing periodontitis. The main purpose of non-surgical therapy for periodontitis is to achieve long-term control of inflammation and the ultimate goal of therapy is the regeneration of periodontal tissues affected by destruction. Periodontal regeneration is not only associated with obtaining a new connective tissue attachment; it involves, as well, the formation of a new functional cementum with the incorporation of new collagen fibers to that part of the root surface that has lacks periodontal ligament due to periodontitis progression. The unique anatomy and structure of the entire periodontal complex determine the course of more complex processes related to the restoration of periodontal structures affected by destruction, which include coordination of response by four different types of tissues: epithelial tissue, connective tissue, periodontal ligament and bone. Periodontal regeneration is defined as the regeneration of the main tooth-supporting tissues: alveolar bone, periodontal ligament, cementum and attachment [1–3].

Growth factors

As early as 1986, Knighton DR *et al.* [4] examined the ability of platelets to provide additional potential for better healing and regeneration of lost tissue by means of growth factors release from them (Table 1). This thesis was proven by the authors using platelet mass for the treatment of difficult-to-heal skin ulcers [4]. Since then, many authors have considered the

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Original Article

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Dentistry Section

A Comparison of Platelet Count and Enrichment Percentages in the Platelet Rich Plasma (PRP) Obtained Following Preparation by Three Different Methods

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ABSTRACT

Introduction: Platelet rich plasma (PRP) represents an easily accessible and rich source of autologous growth factors. Different manual methods for the preparation of PRP have been suggested. Lacuna in knowledge exists about the efficacy of PRP preparation by these different manual methods.

Aims: This study was performed to determine the effects of centrifugation rate revolutions per minute (RPM) and time on the platelet count and enrichment percentages in the concentrates obtained following the three different manual methods of PRP preparation.

Setting and Design: In vitro experimental study.

Materials and Methods: This was an experimental study in which platelet concentration was assessed in the PRP prepared by three different protocols as suggested by Marx R (method 1), Okuda K (method 2) and Landesberg R (method 3). A total of 60 peripheral blood samples, (n=20 per method) were obtained from healthy volunteers. Baseline platelet count was assessed for all the subjects following which PRP was prepared. The platelet count in the PRP was determined using coulter counter (Sysmex XT 2000i).

Statistical Method: The mean of the platelet count obtained and their enrichment percentage were calculated and intergroup comparison was done (Tukey's HSD test).

Results: The number of platelets and enrichment percentage in PRP prepared by method 1 was higher compared to method 2 and method 3; this difference in platelet concentrates was found to be statistically significant ($p < 0.05$).

Conclusion: The centrifugation rate and time appear to be important parameters, which influence the platelet yield. Method 1 which had lower centrifugation rate and time yielded a greater platelet count and enrichment percentage.

Keywords: Centrifugation, Platelet count, Platelet-rich plasma

INTRODUCTION

Wound healing is the body's ability to repair and replace injured or dead cells. It is an absolute prerequisite for survival and can be divided into four overlapping stages: hemostasis, inflammatory, proliferative, and remodeling [1]. The initial response to tissue injury is inflammation, whereby the goal is to provide rapid hemostasis and begin the sequence of events that leads to regeneration of tissue. Platelets play a key role in wound healing and release various growth factors and cytokines that result in cell migration, proliferation, differentiation, and matrix synthesis [2].

PRP is defined as an "autologous concentration of platelets in a small volume of plasma" and is considered to be a rich source of autologous growth factors [2]. The various growth factors present in PRP are Platelet derived growth factor (PDGF), Transforming growth factor beta (TGF-beta), Vascular endothelial growth factor (VEGF), Epidermal Growth Factor (EGF), Platelet factor 4 (PF-4), Insulin like growth factor-1 (IGF-1), Platelet derived angiogenesis factor (PDAF) [3]. PRP represents a contemporary approach to tissue regeneration and has been found to be a valuable adjunct to promote healing in many oral surgical procedures [4].

The use of PRP in dental surgical procedures could have beneficial outcomes in terms of reduction in bleeding, enhanced soft tissue healing and bone regeneration [5]. Varied methods of preparation of PRP have been reported in the literature. These include commercial systems such as Vivostat ®, PCCS®, Harvest Smart PReP®, Fibrinet ®. Manual methods using laboratory centrifuge have been reported by Marx [6] , Landesberg et al., [7], and Okuda et al., [8]. The clinical effectiveness of each of these methods remains unclear and depends on several variables [9]. The role of centrifugation rate and time on the platelet concentrations achieved in each of the methods has not been evaluated. Thus the objective of this study was to determine the effects of centrifugation rate RPM and time on the platelet numbers in the concentrates obtained following the three different methods of PRP preparation.

MATERIALS AND METHODS

This was an experimental study in which platelet concentration was assessed in the PRP prepared by using three different protocols.

The sample size was calculated based on the data (difference between mean recovery efficiency in percentage of platelet at different centrifugation times) from a recent study by Perez et al., [10]. Based on the true probability of exposure, inclusion of 18 individuals will be able to reject the null hypothesis (centrifugation rate and time have no influence on the platelet enrichment percentage) with the type I error of 5% and power of 80%. The sample size chosen for the study was 20 individuals.

A total of 60 peripheral blood samples required for the study were obtained from the 20 healthy volunteers. The age range of the subjects included in the study was 18–27 years that comprised of 12 males and 8 females. The subjects who were systemically healthy, not presently under any medications and who had no smoking, alcohol consuming habits were included in the study [7]. An informed consent was obtained from all the participants included in the study. The study was in accordance with the ethical standards of the responsible committee and was approved by the institutional Ethics Committee of the university.

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ORIGINAL ARTICLE

Platelet rich fibrin combined with decalcified freeze-dried bone allograft for the treatment of human intrabony periodontal defects: a randomized split mouth clinical trail

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Abstract

Objective. Polypeptide growth factors of platelet rich fibrin (PRF) have the potential to regenerate periodontal tissues. Osteoinductive property of demineralized freeze-dried bone allograft (DFDBA) has been successfully utilized in periodontal regeneration. The aim of the present randomized, split mouth, clinical trial was to determine the additive effects of PRF with a DFDBA in the treatment of human intrabony periodontal defects. ***Materials and methods.*** Sixty interproximal infrabony defects in 30 healthy, non-smoker patients diagnosed with chronic periodontitis were randomly assigned to PRF/DFDBA group or the DFDBA/saline. Clinical [pocket depth (PD), clinical attachment level (CAL) and gingival recession (REC)] and radiographic (bone fill, defect resolution and alveolar crest resorption) measurements were made at baseline and at a 12-month evaluation. ***Results.*** Compared with baseline, 12-month results indicated that both treatment modalities resulted in significant changes in all clinical and radiographic parameters. However, the PRP/DFDBA group exhibited statistically significantly greater changes compared with the DFDBA/saline group in PD (4.15 ± 0.84 vs 3.60 ± 0.51 mm), CAL (3.73 ± 0.74 vs 2.61 ± 0.68 mm), REC (0.47 ± 0.56 vs 1.00 ± 0.61 mm), bone fill (3.50 ± 0.67 vs 2.49 ± 0.64 mm) and defect resolution (3.73 ± 0.63 vs 2.75 ± 0.57 mm). ***Conclusion.*** Observations indicate that a combination of PRF and DFDBA is more effective than DFDBA with saline for the treatment of infrabony periodontal defects.

Key Words: *Chronic periodontitis, intrabony defect, periodontal regeneration, platelet rich fibrin*

Introduction

Various regenerative modalities have been investigated for the management of intrabony periodontal defects, e.g. Bone grafts (BG) and substitutes, guided tissue regeneration, growth factors, enamel matrix derivatives and combined approaches [1]. Decalcified freeze-dried bone allograft (DFDBA) contains bone morphogenetic proteins (BMPs) that aid in mesenchymal cell migration, attachment and osteogenesis; have both osteoinductive as well as osteoconductive activity and the ability to create and maintain the space. DFDBA has been proposed as an effective regenerative material for osseous defects [2–4].

Polypeptide growth factors (PGFs) revealed a potential application in wound healing by promoting periodontal regeneration via cell proliferation, angiogenesis, chemotaxis and differentiation. Autologous blood concentrates constitute a safe and convenient approach to deliver high concentrations of PGFs to periodontal surgical wounds [5,6].

Recent studies examining the effectiveness of PGFs, used alone or in combination with other materials and techniques, have been conducted with autologous platelet-rich plasma (PRP) [7–9], recombinant platelet-derived growth factor [10,11] and platelet rich fibrin (PRF) [12,13]. Among platelet concentrates, PRF belongs to a group of second-generation blood autologous preparations that was originally described by Choukroun et al. [14]. The PRF preparation process creates a gel like matrix that contains high concentrations of non-activated, functional, intact platelets contained within a fibrin matrix that release a relatively constant concentration of growth factors over a period of 7 days [15,16].

Dohan Ehrenfest et al. [17,18] demonstrated that PRF induced a significant and continuous stimulation and proliferation of human primary cultures of

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Review

An overview on platelet concentrates in tissue regeneration in periodontology

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Abstract: Recent research on the use of platelet concentration in medicinal dentistry has enhanced the potential for tissue regeneration. The ability of platelets to enhance tissue regeneration by using different forms of platelet concentration (blood component) such as platelet-rich plasma (PRP), platelet-rich fibrin (PRF), standard platelet-rich fibrin, advanced platelet-rich fibrin, etc. PRP became widely used once its potential for tissue regeneration was discovered; however, the use of anticoagulants restricted the easy use of PRP as compared to PRF; however, after the discovery of PRF because of the easy formulation, it became widely used in medicinal dentistry. The purpose of this review is to elaborate on the importance of platelet concentration in periodontal regeneration.

Keywords: platelets; platelet-rich fibrin; regeneration; concentrate; bone

1. Introduction

The periodontium regenerates continuously through physiological processes. Wear and tear repair is the process of continuously forming new cells and tissues to replace those that mature and die under normal circumstances. Periodontal disorders are chronic inflammatory conditions caused by periodontal microorganisms and the toxins released by them, which cause the destruction of the

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Journal of Clinical Periodontology

Effect of platelet-rich plasma on the healing of intrabony defects treated with an enamel matrix protein derivative and a natural bone mineral

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Döri F, Nikolidakis D, Húszár T, Arweiler NB, Gera I, Sculean A. Effect of platelet-rich plasma on the healing of intrabony defects treated with an enamel matrix protein derivative and a natural bone mineral. J Clin Periodontol 2008; 35: 44–50. doi: 10.1111/j.1600-051X.2007.01161.x.

Abstract

Background: Regenerative periodontal surgery utilizing a combination of an enamel matrix protein derivative (EMD) and a natural bone mineral (NBM) and platelet-rich plasma (PRP) has been shown to enhance the outcomes of regenerative surgery significantly. At present, it is unknown whether root conditioning with EMD, followed by defect fill with a combination of NBM+PRP may additionally enhance the clinical results obtained with EMD+NBM.

Aim: To compare clinically the treatment of deep intrabony defects with either EMD+NBM+PRP or EMD+NBM.

Material and Methods: Twenty-six patients suffering from advanced chronic periodontitis, and each of whom displayed one advanced intrabony defect were randomly treated with either EMD+NBM+PRP (test) or EMD+NBM (control). The following clinical parameters were evaluated at baseline and at 1 year after treatment: plaque index (PI), gingival index (GI), bleeding on probing (BOP), probing depth (PD), gingival recession (GR) and clinical attachment level (CAL). The primary outcome variable was CAL.

Results: Healing was uneventful in all patients. At 1 year after therapy, the test sites showed a reduction in mean PD from 8.8 $\pm$ 1.9 mm to 3.1 $\pm$ 0.9 mm ($p<0.001$) and a change in mean CAL from 10.8 $\pm$ 2.0 mm to 6.0 $\pm$ 1.5 mm ($p<0.001$). In the control group the mean PD was reduced from 8.8 $\pm$ 2.0 mm to 2.8 $\pm$ 1.6 mm ($p<0.001$) and the mean CAL changed from 10.5 $\pm$ 1.6 mm to 5.5 $\pm$ 1.4 mm ($p<0.001$). CAL gains of $\geqslant$4 mm were measured in 77% (i.e. in 10 out of 13 defects) of the cases treated with EMD+NBM+PRP and in 100% (i.e. in all 13 defects) treated with EMD+NBM. No statistically significant differences in any of the investigated parameters were observed between the two groups.

Conclusions: Within its limits, the present study has shown that (i) 1 year after regenerative surgery, both treatments resulted in statistically significant PD reductions and CAL gains and (ii) the use of PRP failed to enhance the results obtained with EMD+NBM.

Key words: controlled clinical trial; enamel matrix protein derivative; intrabony defects; natural bone mineral; platelet-rich plasma; regenerative periodontal therapy

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Regenerative periodontal therapy aims at the restitution of the tooth's supporting periodontal tissues [i.e. new periodontal ligament (PDL), new cementum with inserting connective tissue fibres and new bone] that have been lost due to periodontal disease (Karring et al. 2003). In human intrabony defects, periodontal regeneration has been demonstrated following treatment with an enamel matrix protein derivative (EMD), guided tissue regeneration

Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)
TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne
on behalf of the RoB2 Development Group

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The PRISMA 2020 statement: an updated guideline for reporting systematic reviews

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The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement, published in 2009, was designed to help systematic reviewers transparently report why the review was done, what the authors did, and what they found. Over the past decade, advances in systematic review methodology and terminology have necessitated an update to the guideline. The PRISMA 2020 statement replaces the 2009 statement and includes new reporting guidance that reflects advances in methods to identify, select, appraise, and synthesise studies. The structure and presentation of the items have been modified to facilitate implementation. In this article, we present the PRISMA 2020 27-item checklist, an expanded checklist that details reporting recommendations for each item, the PRISMA 2020 abstract checklist, and the revised flow diagrams for original and updated reviews.

SUMMARY POINTS

To ensure a systematic review is valuable to users, authors should prepare a transparent, complete, and accurate account of why the review was done, what they did, and what they found

The PRISMA 2020 statement provides updated reporting guidance for systematic reviews that reflects advances in methods to identify, select, appraise, and synthesise studies

The PRISMA 2020 statement consists of a 27-item checklist, an expanded checklist that details reporting recommendations for each item, the PRISMA 2020 abstract checklist, and revised flow diagrams for original and updated reviews

We anticipate that the PRISMA 2020 statement will benefit authors, editors, and peer reviewers of systematic reviews, and different users of reviews, including guideline developers, policy makers, healthcare providers, patients, and other stakeholders

Systematic reviews serve many critical roles. They can provide syntheses of the state of knowledge in a field, from which future research priorities can be identified; they can address questions that otherwise could not be answered by individual studies; they can identify problems in primary research that should be rectified in future studies; and they can generate or evaluate theories about how or why phenomena occur. Systematic reviews therefore generate various types of knowledge for different users of reviews (such as patients, healthcare providers, researchers, and policy makers).[1 2] To ensure a systematic review is valuable to users, authors should prepare a transparent, complete, and accurate account of why the review was done, what they did (such as how studies were identified and selected) and what they found (such as characteristics of contributing studies and results of meta-analyses). Up-to-date reporting guidance facilitates authors achieving this.[3]

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement published in 2009 (hereafter referred to as PRISMA 2009)[4-10] is a reporting guideline designed to address poor reporting of systematic reviews.[11] The PRISMA 2009 statement comprised a checklist of 27 items recommended for reporting in systematic reviews and an "explanation and elaboration" paper[12-16] providing additional reporting guidance for each item, along with exemplars of reporting. The recommendations have been widely endorsed and adopted, as evidenced by its co-publication in multiple journals, citation in over 60 000 reports (Scopus, August 2020), endorsement from almost 200 journals and systematic review organisations, and adoption in various disciplines. Evidence from observational studies suggests that use of the PRISMA 2009 statement is associated with more complete reporting of systematic reviews,[17-20] although more could be done to improve adherence to the guideline.[21]

Many innovations in the conduct of systematic reviews have occurred since publication of the PRISMA 2009 statement. For example, technological advances have enabled the use of natural language processing and machine learning to identify relevant evidence,[22-24] methods have been proposed to

Effect of Platelet-Rich Plasma on the Healing of Intrabony Defects Treated With an Anorganic Bovine Bone Mineral and Expanded Polytetrafluoroethylene Membranes

Ferenc Döri,* Tamás Huszár,† Dimitris Nikolidakis,‡ Nicole B. Arweiler,§ István Gera,* and Anton Sculean‡

Background: Regenerative periodontal therapy with a combination of platelet-rich plasma (PRP) + an anorganic bovine bone mineral (ABBM) + guided tissue regeneration (GTR) has been shown to result in significantly higher probing depth reductions and clinical attachment level gains compared to treatment with open flap debridement (OFD) alone, ABBM alone, or GTR alone. However, there are no data evaluating to what extent the use of PRP may additionally enhance the clinical outcome of the therapy compared to treatment with ABBM + GTR. This study aimed to clinically evaluate the effect of PRP on the healing of deep intrabony defects treated with ABBM and GTR by means of a non-resorbable expanded polytetrafluoroethylene (ePTFE) membrane.

Methods: Twenty-four patients with advanced chronic periodontal disease and displaying one intrabony defect were randomly treated with a combination of either PRP + ABBM + GTR or ABBM + GTR. The following clinical parameters were evaluated at baseline and at 1 year after treatment: plaque index (PI), gingival index (GI), bleeding on probing (BOP), probing depth (PD), gingival recession (GR), and clinical attachment level (CAL). The primary outcome variable was CAL.

Results: No differences in any of the studied parameters were observed at baseline between the two groups. Healing was uneventful in all patients. At 1 year after therapy, the sites treated with PRP + ABBM + GTR showed a reduction in mean PD from 8.6 ± 1.7 mm to 3.1 ± 1.3 mm (P <0.001) and a change in mean CAL from 10.3 ± 1.4 mm to 5.7 ± 1.6 mm (P <0.001). In the group treated with ABBM + GTR, mean PD was reduced from 8.8 ± 1.7 mm to 3.1 ± 1.0 mm (P <0.001), and the mean CAL changed from 10.4 ± 2.6 mm to 5.9 ± 1.8 mm (P <0.001). In both groups, all sites gained ≥3 mm of CAL. CAL gains ≥4 mm were measured in 83% (i.e., in 10 of 12 defects) of the cases treated with PRP + ABBM + GTR and in 92% (i.e., in 11 of 12 defects) treated with ABBM + GTR. No statistically significant differences in any of the studied parameters were observed between the two groups at 1-year reevaluation.

Conclusion: Within its limits, the present study has shown that, at 1 year after regenerative therapy in periodontal intrabony defects, optimal clinical results were obtained with ABBM + GTR with a non-resorbable barrier, with or without the addition of PRP. *J Periodontol 2007;78:983-990.*

KEY WORDS

Membranes; platelet-rich plasma; polytetrafluoroethylene; randomized controlled clinical trials.

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Treatment of Periodontal Intrabony Defects With Demineralized Freeze-Dried Bone Allograft in Combination With Platelet-Rich Plasma: A Comparative Clinical Trial

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Background: The aim of the present randomized, double-masked, clinical trial was to compare platelet-rich plasma (PRP) combined with a demineralized freeze-dried bone allograft (DFDBA) to DFDBA mixed with a saline solution in the treatment of human intrabony defects.

Methods: Sixty interproximal intrabony osseous defects in 60 healthy, non-smoking subjects diagnosed with chronic periodontitis were treated in this study. Thirty subjects each were randomly assigned to the test group (PRP + DFDBA) or the control group (DFDBA + saline). Clinical and radiographic measurements were made at baseline and at the 12-month evaluation.

Results: Compared to baseline, the 12-month results indicated that both treatment modalities resulted in significant changes in all clinical parameters (gingival index, bleeding on probing, probing depth, clinical attachment level, and gingival recession; $P<0.001$) and radiographic parameters (hard tissue fill and bone depth reduction; $P<0.001$). However, the test group exhibited statistically significantly greater changes compared to the control group in probing depth reduction (4.3 ± 1.7 mm versus 2.6 ± 2.2 mm; $P<0.05$) and clinical attachment gain (3.5 ± 2.1 mm versus 2.3 ± 2.4 mm; $P<0.001$).

Conclusions: Treatment with a combination of PRP and DFDBA led to a significantly greater clinical improvement in intrabony periodontal defects compared to DFDBA with saline. No statistically significant differences were observed in the hard tissue response between the two treatment groups, which confirmed that PRP had no effect on hard tissue fill or gain in new hard tissue formation. *J Periodontol 2008;79:802-810.*

KEY WORDS

Allograft; bone; periodontitis; platelet-rich plasma.

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Untreated periodontal disease leads to tooth loss through destruction of the attachment apparatus and tooth-supporting structures. The goals of periodontal therapy include the arrest of periodontal disease progression and regeneration of structures lost to disease where appropriate.[1]

Autogenous grafts,[2-4] demineralized freeze-dried bone allografts (DFDBAs),[5,6] biologic mediators alone[7] or with DFDBAs,[8-10] and bovine bone xenografts[11-13] have demonstrated regenerative potential. DFDBAs have repeatedly demonstrated significant improvements in soft and hard clinical tissue parameters for the treatment of intraosseous periodontal defects.[14,15] Substances present in the demineralized bone graft material, bone morphogenic proteins, stimulate local cell cycles to produce new bone.[16] The freeze-drying process destroys cells while maintaining cellular morphology and chemical integrity. These two factors, in conjunction with other materials, enhance periodontal regeneration and/or bone fill.[17-19]

Recently, the attention of periodontal researchers and clinicians has

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Journal of Clinical Periodontology

Effect of platelet-rich plasma on the healing of intra-bony defects treated with a natural bone mineral and a collagen membrane

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Dőri F, Huszár T, Nikolidakis D, Arweiler NB, Gera I, Sculean A. Effect of platelet-rich plasma on the healing of intra-bony defects treated with a natural bone mineral and a collagen membrane. J Clin Periodontal 2007; 34: 254–261. doi: 10.1111/j.1600-051X.2006.01044.x.

Abstract

Background: Regenerative periodontal therapy with a combination of platelet-rich plasma (PRP)+a natural bone mineral (NBM)+guided tissue regeneration (GTR) has been shown to result in significantly higher probing depth reductions and clinical attachment-level gains compared with treatment with open flap debridement alone. However, at present, it is unknown to what extent the use of PRP may additionally enhance the clinical outcome of the therapy compared with treatment with NBM+GTR.

Aim: To clinically compare treatment of deep intra-bony defects with NBM+PRP+GTR with NBM+GTR.

Material and Methods: Thirty patients suffering from advanced periodontal disease, and each of whom displayed one advanced intra-bony defect were randomly treated with a combination of either NBM+PRP+collagen membrane (GTR) or NBM+GTR. The following clinical parameters were evaluated at baseline and at 1 year after treatment: plaque index, gingival index, bleeding on probing, probing depth (PD), gingival recession and clinical attachment level (CAL). CAL changes were used as the primary outcome variable.

Results: No differences in any of the investigated parameters were observed at baseline between the two groups. Healing was uneventful in all patients. At 1 year after therapy, the sites treated with NBM+PRP+GTR showed a reduction in mean PD from 8.9 ± 2.3 mm to 3.4 ± 2.0 mm ($p<0.001$) and a change in mean CAL from 10.9 ± 2.2 mm to 6.4 ± 1.8 mm ($p<0.001$). In the group treated with NBM+GTR, the mean PD was reduced from 8.9 ± 2.5 mm to 3.4 ± 2.3 mm ($p<0.001$), and the mean CAL changed from 11.1 ± 2.5 mm to 6.5 ± 2.3 mm ($p<0.001$). In both groups, all sites gained at least 3 mm of CAL. CAL gains of $\geqslant 4$ mm were measured in 80% (i.e. in 12 out of 15 defects) of the cases treated with NBM+PRP+GTR and in 87% (i.e. in 13 out of 15 defects) treated with NBM+GTR. No statistically significant differences in any of the investigated parameters were observed between the two groups.

Conclusions: Within its limits, the present study has shown that (i) at 1 year after regenerative surgery with both NBM+PRP+GTR and NBM+GTR, significant PD reductions and CAL gains were found, and (ii) the use of PRP has failed to improve the results obtained with NBM+GTR.

Key words: collagen membrane; intra-bony defects; natural bone mineral; platelet-rich plasma; randomized controlled clinical trial

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Original Research Article

Comparative clinical and radiographic evaluation of autogenous bone grafts and demineralized freeze dried bone xenograft (Osseograft) combined with PRP in the treatment of human periodontal intra-osseous defects – 6 months study

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Abstract

Aim and objectives: The aim of the present study was to compare autogenous bone graft (Group - 1) and xenograft combined with PRP (Group - 2). The clinical and radiographic healing was evaluated after a period of six months in periodontal intra bony defects.

Material and methods: A split mouth design was followed, where two sites in the contra lateral quadrants with probing pocket depth of ≥ 5 mm with radiographic evidence of bone loss at baseline were chosen. Patients were grouped as **Group - 1:** 7 intra bony defects treated with autogenous

Original Article

Use of Platelet Rich Plasma in the Management of Periodontal Intra-Osseous Defects: A Clinical Study

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Abstract

Background: Periodontal disease is characterized by the presence of gingival inflammation, periodontal pocket formation, loss of connective tissue attachment, and alveolar bone around the affected tooth. Alveolar bone support and attachment apparatus regeneration has been achieved through various processes and have given elusive results. An expedient and cost-effective approach to obtain autologous platelet-derived growth factor (PDGF) and transforming growth factor (TGF)-β is the use of platelet-rich plasma (PRP). PRP is obtained by sequestrating and concentrating platelets by gradient density centrifugation.

Aims: The current study was aimed at evaluating the regenerative potential of platelet-rich plasma in comparison with open flap debridement.

Settings and Designs: This study was a randomized controlled clinical trial conducted in the Department of Periodontics and Oral Implantology, KIDS, Bhubaneswar, Odisha.

Materials and Methods: Twenty periodontal infrabony defects in 10 patients; 6 males and 4 females of age between 25–45 years were included in this study and were followed up for a period of 6 months.

Statistical Analysis: Both the groups showed a mean plaque index of 2.10 and 2.50 at baseline, 1.75 and 2.05 at 3 months, and 1.28 and 1.53 at the end of 6 months. The mean reduction of 0.35 and 0.45 at three months and 0.82 and 0.97 at six months was achieved, which was statistically significant. ($P < 0.001$). When comparison was done between the two groups it was not found to be statistically significant ($P < 0.05$). In each of the group there was definitive reduction in plaque score over a period of time.

Results and Conclusion: There was no statistically significant difference in the treatment outcome between open flap debridement and PRP alone. Platelet-rich plasma application holds promise and needs further exploration.

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Keywords: *Angular bone defects, periodontal regeneration, periodontitis, platelet-rich plasma PRP*

Introduction

Periodontal disease is one of the most prevalent afflictions worldwide and is the major cause of tooth morbidity and mortality. The disease is characterized by the presence of gingival inflammation, periodontal pocket formation, loss of connective tissue attachment, and alveolar bone around the affected tooth. Alveolar bone support and attachment apparatus regeneration has been achieved through various processes and has given elusive results.[1] This goal can be accomplished using regenerative surgical procedure such as root biomodification, use of bone replacement grafts, guided tissue regeneration (GTR), and growth factors.[1,2]

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Effect of Platelet-Rich Plasma on the Healing of Intrabony Defects Treated With Beta Tricalcium Phosphate and Expanded Polytetrafluoroethylene Membranes

Ferenc Döri,* Tamás Huszár,† Dimitris Nikolidakis,‡ Dora Tihanyi,* Attila Horváth,* Nicole B. Arweiler,§ István Gera,* and Anton Sculean‡

Background: Regenerative periodontal therapy using platelet-rich plasma (PRP) and different types of bone substitutes with or without guided tissue regeneration (GTR) has been proposed as a modality to enhance the outcome of regenerative surgery. However, there are limited data from controlled clinical studies evaluating the effect of PRP on the healing of deep intrabony defects treated with a combination of bone substitutes and GTR. The aim of this study was to clinically evaluate the effect of PRP on the healing of deep intrabony defects treated with beta tricalcium phosphate (β-TCP) and GTR by means of a non-bioresorbable expanded polytetrafluoroethylene membrane.

Methods: Twenty-eight subjects with advanced chronic periodontal disease and displaying one intrabony defect were treated randomly with a combination of PRP + β-TCP + GTR or β-TCP + GTR. Plaque index, gingival index, bleeding on probing, probing depth (PD), gingival recession, and clinical attachment level (CAL) were evaluated at baseline and at 1 year after treatment. CAL was the primary outcome variable.

Results: No differences in any of the investigated parameters were observed at baseline between the two groups. Healing was uneventful in all subjects. At 1 year after therapy, the sites treated with PRP + β-TCP + GTR showed a reduction in mean PD from 9.1 ± 0.6 mm to 3.3 ± 0.5 mm ($P<0.001$) and a change in mean CAL from 10.1 ± 1.3 mm to 5.7 ± 1.1 mm ($P<0.001$). In the group treated with β-TCP + GTR, mean PD was reduced from 9.0 ± 0.8 mm to 3.6 ± 0.9 mm ($P<0.001$), and the mean CAL changed from 9.9 ± 1.0 mm to 5.9 ± 1.2 mm ($P<0.001$). In both groups, all sites gained ≥3 mm of CAL. CAL gains ≥4 mm were noted in 86% (12 of 14 defects) of the cases treated with PRP + β-TCP + GTR and in 79% (11 of 14 defects) of those treated with β-TCP + GTR. No statistically significant differences in any of the investigated parameters were observed between the two groups at the 1-year reevaluation.

Conclusion: At 1 year after surgery, both therapies resulted in significant PD reductions and CAL gains. *J Periodontol 2008;79:660-669.*

KEY WORDS

Beta tricalcium phosphate; defects; platelet-rich plasma; polytetrafluoroethylene; randomized controlled clinical trials; therapy.

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Regenerative periodontal therapy aims at the reconstruction of the tooth-supporting apparatus (i.e., root cementum, periodontal ligament, and alveolar bone), which has been lost because of periodontitis or trauma.[1] During the last decade, polypeptide growth factors have been demonstrated to promote the proliferation and differentiation of cells involved in periodontal wound healing.[2] Findings from animal studies[3-8] provided histologic evidence of periodontal regeneration following the short-term application of polypeptide growth factors, such as platelet-derived growth factor (PDGF) and insulin-like growth factor (IGF). Recent data from controlled clinical studies[9,10] showed that reconstructive periodontal surgery

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A Surgical Reentry Study on the Influence of Platelet-Rich Plasma in Enhancing the Regenerative Effects of Bovine Porous Bone Mineral and Guided Tissue Regeneration in the Treatment of Intrabony Defects in Humans

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Background: The purpose of this study was to evaluate the additional benefits provided by the incorporation of platelet-rich plasma (PRP) into a regenerative protocol consisting of bovine porous bone mineral (BPBM) and guided tissue regeneration (GTR) in the treatment of intrabony defects in humans.

Methods: Twenty-three paired intrabony defects were surgically treated using a split-mouth design. Defects were treated with BPBM/GTR/PRP (experimental group) or with BPBM/GTR (control group). The clinical parameters evaluated included changes in probing depth, clinical attachment level, and defect fill as revealed by reentry surgeries at 6 months.

Results: Preoperative probing depths, attachment levels, and transoperative bone measurements were similar for the two groups. Post-surgical measurements taken at 6 months revealed that both treatment modalities resulted in a significant decrease in probing depth, gain in clinical attachment, and bone fill of the defects compared to baseline. Postoperative differences observed between the two groups were 0.72 ± 0.36 mm at buccal sites and 0.90 ± 0.32 mm at lingual sites for probing depth, 0.82 ± 0.41 mm at buccal sites and 0.78 ± 0.38 at lingual sites for gain in clinical attachment, and 0.85 ± 0.36 mm at buccal sites and 0.94 ± 0.42 mm at lingual sites for defect fill, all favoring the experimental sites. However, none of the differences were statistically significant.

Conclusion: Within the limitations related to using a small sample size, PRP did not significantly augment the effects of BPBM and GTR in promoting the clinical resolution of intrabony defects. *J Periodontol 2009;80:915-923.*

KEY WORDS

Guided tissue regeneration; periodontal regeneration; platelet-rich plasma.

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Periodontal regeneration involves the formation of alveolar bone, cementum, and a new functional periodontal ligament.[1] For periodontal regeneration to occur, a number of biologic events, including cell migration, adherence, multiplication, and differentiation, need to occur in a well-orchestrated sequence. Therefore, therapeutic modalities that aim at facilitating periodontal tissue cells to behave in a way that is conducive to regenerate the periodontium have potential application in patient care.

Polypeptide growth factors (PGFs) are biologic mediators that have the ability to regulate cell multiplication, migration, and differentiation. Therefore, PGFs have potential applications in periodontal regeneration. Several PGFs have been identified in human periodontal tissues by immunohistochemistry and in situ hybridization.[2] Moreover, these PGFs were shown to promote cell growth and differentiation in vitro and periodontal regeneration in animals.[3-12] Human studies on the effects of PGFs on periodontal

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ORIGINAL ARTICLE

Use of platelet-rich plasma in periodontal surgery—a prospective randomised double blind clinical trial

L. Harnack · R. H. Boedeker · I. Kurtulus · S. Boehm · J. Gonzales · J. Meyle

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Abstract The aim of this prospective controlled randomized clinical trial was to evaluate the additional effect of platelet-rich plasma (PRP) in attachment gain. Twenty-two patients showing contralateral intrabony defects were included. Defects were randomized to β-TCP (Cerasorb®) in combination with PRP (test) or alone (control). Probing pocket depth (PPD), clinical attachment level (CAL), and relative AL (RAL) were assessed at the first, initial, re-evaluation (or basis examinations) and 6 months after surgery. Defect dimensions were recorded at baseline surgery (day 0) and during re-entry surgery (after 6 months), with vertical depth of the defect as primary outcome variable. An early healing index (EHI) was assessed 3 days, 1, 2 and 4 weeks after surgery. Both treatments led to clinical improvements. The median reduction of open vertical depth was 1.9 mm (interquartile intervals, 0.75 and 2.5 mm) at test sites, compared with 2.6 mm (1.8 and 3.5 mm) at control sites (p=0.19, Wilcoxon). The median reductions of PPD and CAL at the four sites in close proximity to the defect in the interproximal area at test sites were 0.8 and 0.28 mm, and at control sites 0.4 and 0.13 mm, respectively. The EHI showed a reduction from grade 3 after 3 days to grade 1 after 4 weeks. PRP did not improve the results achieved with β-TCP in the treatment of intrabony defects.

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Keywords Platelet-rich plasma · Periodontal surgery · Early healing · β-Tricalcium phosphate · Wound healing

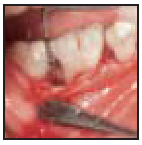
Introduction

Traditional synthetic bone grafts are ceramics of hydroxyapatite (HA; $Ca_{10}(PO_4)_6(OH)_2$), tricalcium phosphate ($Ca_3(PO_4)_2$) or combinations of the two. α- and β-tricalcium phosphate (TCP), although chemically identical, have different physiological characteristics [14, 15, 32]. The β-form is the most stable with a calcium-to-phosphate atomic ratio of 1.5 [18]. Porous β-TCP synthetic cancellous bone resembles human cancellous bone in structure and composition. Generally, β-TCPs contain approximately 39% calcium and 20% phosphorus by weight, similar to natural mineral content in bone [24]. TCP has been evaluated in spinal fusion with results comparable to those with autogenous bone [12].

These materials are considered to be resorbable, since the rate of biodegradation is higher when compared with HA [9, 10]. When used alone for grafting, these synthetic grafting materials function as osteoconductive scaffold for new bone growth and as bridges to the host bone. The scaffold is then removed by a combination of dissolution and phagocytosis (cell-mediated resorption) [16, 17, 25, 35].

β-TCP Cerasorb® (Curasan AG, Kleinostheim, Germany) is a pure phase β-TCP. This material has been used in the treatment of osseous defects in animals and humans [2, 34, 36, 37, 39]. It has been used as synthetic bone substitute in orthopedics and dentistry without adverse events since many years [2, 5, 11, 13, 20, 36, 37]. β-TCP has been used in sinus floor augmentation treatments [44, 49]. The effect on bone regeneration was evaluated in hollow titanium cylinders implanted in the posterior jaws of

Platelet-Rich Plasma Combined with Decalcified Freeze-Dried Bone Allograft for the Treatment of Noncontained Human Intrabony Periodontal Defects: A Randomized Controlled Split-Mouth Study



Ashish Agarwal, MDS[1]
Narindra Dev Gupta, MDS[2]

The aim of the present randomized split-mouth clinical trial was to compare platelet-rich plasma (PRP) combined with a demineralized freeze-dried bone allograft (DFDBA) to DFDBA with a saline solution in the treatment of noncontained human periodontal intrabony defects. Forty-eight noncontained interproximal intrabony defects in 24 healthy nonsmoking patients diagnosed with chronic periodontitis were randomly assigned to the test group (PRP/DFDBA) or the control group (DFDBA/saline). Clinical (probing pocket depth, clinical attachment level [CAL], and gingival recession [REC]) and radiographic (bone fill, defect resolution, and alveolar crest resorption) measurements were made at baseline and at a 12-month evaluation. Compared with baseline, 12-month results indicated that both treatment modalities resulted in significant changes in all clinical and radiographic parameters. However, the test group exhibited statistically significantly greater changes compared with the control group in CAL (3.15 ± 0.50 versus 2.40 ± 0.61 mm), REC (0.54 ± 0.59 versus 1.23 ± 0.47 mm), bone fill (3.02 ± 0.50 versus 2.37 ± 0.47 mm), and defect resolution (3.29 ± 0.53 versus 2.69 ± 0.38 mm). Findings indicate that a combination of PRP and DFDBA is more effective than DFDBA with saline for the treatment of noncontained intrabony defects. (Int J Periodontics Restorative Dent 2014;34:705–711. doi: 10.11607/prd.1766)

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Various types of bone grafts, guided tissue regeneration (GTR), and combined approaches have been utilized for regenerative periodontal treatment in intrabony defects.[1,2,3] Decalcified freeze-dried bone allografts (DFDBA) have repeatedly demonstrated significant improvement in clinical and radiographic parameters in the treatment of intrabony defects.[2,3] Osteoinductive bone morphogenetic proteins (BMPs), present in DFDBA, stimulate local cell cycles for new bone production.[2]

Polypeptide growth factors such as platelet-derived growth factors (PDGF) and transforming growth factor β (TGF-β) have been shown to exert a favorable effect on periodontal regeneration processes, including mitogenesis, angiogenesis, and up-regulation of other growth factors, and serve as a scaffold for cellular migration and adhesion, collagen synthesis, and bone regeneration.[4–7]

PDGF and TGF-β are abundant in alpha granules of platelets.[4–6] Specific sequestration and concentration of platelets in plasma to produce platelet-rich plasma (PRP) and subsequent application of this preparation at wound healing sites

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COMPARISON BETWEEN PRP VS IPRF AS AN ADJUNCT THERAPY IN INFRA-BONY POCKET TREATMENT

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ABSTRACT

Objective: The aim of the present study was to adjunct the healing of intra bony periodontal deep pockets using minimal invasive technique and materials (injectable platelet rich fibrin-I PRF-). **Subjects & Method:** A total of 70 medically healthy adult subjects with chronic periodontitis in a randomized controlled clinical trial were divided into 3 groups; PRP group, iPRF group & control group. PRP preparation: Two Acid citric dextrose (ACD) 8.5 ml tubes of whole blood were centrifuged at 2000 rpm for 7 min at room temperature using Heraeus Megafuge 16R centrifuge. IPRF preparation: Two tubes (without anticoagulant) of 10 ml of whole blood were centrifuged at 700 rpm for 3 min at room temperature using Heraeus Megafuge 16R centrifuge. **Results:** Postoperative evaluation: I-PRF group showed the highest reduction of probing depth from baseline, while PRP group came second followed by the control group which had the lowest reduction in probing depth. **Conclusion:** the repeated injection of i- PRF showing a stronger and more durable effect, since it has number of growth factors which are responsible for tissue regeneration capable of inducing fibroblast behavior.

KEY WORDS: PRP, iPRF, CAL, Probing Index

INTRODUCTION

Periodontitis is a multifactorial inflammatory illness characterized by progressive loss of the tooth-supporting apparatus and is linked to dysbiotic plaque biofilms. Clinical attachment loss (CAL), alveolar bone loss, and pocket development are all symptoms of periodontitis[1]. The first phase of periodontal treatment mainly aimed at removing local factors through scaling and root planing (SRP), there by assisting in the resolution of inflammation. However, this treatment decreases probing pocket depth due to shrinkage or development of long junctional epithelium but not often forms a new attachment. At this point, healing outcome looks to be adequate but is susceptible to future disease progression [2]. Periodontal healing is a organized procedure which includes three phases: inflammation, fibroblastic-granulation ,matrix formation, and remodeling. It involves a biochemical chain of reactions, cellular organization and synthesis of extracellular matrix[3]. Platelets play a vital role in haemostasis and

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Comparative Evaluation of Autologous Platelet-Rich Fibrin and Platelet-Rich Plasma in the Treatment of 3-Wall Intrabony Defects in Chronic Periodontitis: A Randomized Controlled Clinical Trial

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Background: The topical use of platelet concentrates is recent, and its efficiency remains controversial. The present study aims to explore the clinical and radiographic effectiveness of autologous platelet-rich fibrin (PRF) and platelet-rich plasma (PRP) in the treatment of intrabony defects in patients with chronic periodontitis.

Methods: Ninety intrabony defects were treated with either autologous PRF with open-flap debridement or autologous PRP with open-flap debridement or open-flap debridement alone. Clinical and radiologic parameters, such as probing depth (PD), clinical attachment level (CAL), intrabony defect depth, and percentage defect fill, were recorded at baseline and 9 months postoperatively.

Results: Mean PD reduction and CAL gain were greater in PRF (3.77 ± 1.19 and 3.17 ± 1.29 mm) and PRP (3.77 ± 1.07 and 2.93 ± 1.08 mm) groups than the control group (2.97 ± 0.93 and 2.83 ± 0.91 mm). Furthermore, significantly greater percentage of mean bone fill was found in the PRF (55.41% ± 11.39%) and PRP (56.85% ± 14.01%) groups compared with the control (1.56% ± 15.12%) group.

Conclusions: Within the limit of the present study, there was similar PD reduction, CAL gain, and bone fill at sites treated with PRF or PRP with conventional open-flap debridement. Because PRF is less time consuming and less technique sensitive, it may seem a better treatment option than PRP. However, long-term, multicenter randomized, controlled clinical trials will be required to know their clinical and radiographic effects on bone regeneration. *J Periodontol 2012;83: 1499-1507.*

KEY WORDS

Clinical trial; chronic periodontitis; dental; platelet-rich plasma; radiography; regeneration.

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Periodontitis is an infectious disease that causes destruction of the tooth-attachment apparatus. Untreated periodontitis results in progressive attachment loss that may eventually lead to early tooth loss.[1] There are a broad range of treatment options available, but only some may be regarded as truly regenerative procedures. Regeneration is defined as the reproduction or reconstitution of a lost or injured part of the body in such a way that the architecture and function of the lost or injured tissues are completely restored.[2] The aim of regenerative periodontal therapy is to restore the structure and function of the periodontium. Periodontal regeneration requires an orchestrated sequence of biologic events, such as cell migration, adherence, growth, and differentiation, to have the potential to increase the success and predictability of periodontal regenerative procedures.[3] According to a position paper from the American Academy of Periodontology, periodontal regenerative procedures include soft tissue grafts, bone replacement grafts, root biomodifications, guided tissue regeneration (GTR),

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A Reentry Study on the Use of Bovine Porous Bone Mineral, GTR, and Platelet-Rich Plasma in the Regenerative Treatment of Intrabony Defects in Humans

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This study compared the clinical effectiveness of a combination therapy consisting of bovine porous bone mineral (BPBM), guided tissue regeneration (GTR), and platelet-rich plasma (PRP) in the regeneration of periodontal intrabony defects in humans. Twenty-eight paired intrabony defects were surgically treated using a split-mouth design. Defects were treated with BPBM, GTR, and PRP (experimental), or with open-flap debridement (control). Clinical parameters evaluated included changes in attachment level, pocket depth, and defect fill as revealed by reentry at 6 months. Preoperative pocket depths, attachment levels, and transoperative bone measurements were similar for the two groups. Postsurgical measurements taken at 6 months revealed that both treatment modalities significantly decreased pocket depth and increased clinical attachment and defect fill compared to baseline. The differences between the experimental and control groups were 2.22 ± 0.39 mm on buccal and 2.12 ± 0.34 mm on lingual sites for pocket depth, 3.05 ± 0.51 mm on buccal and 2.88 ± 0.46 mm on lingual sites for gain in clinical attachment, and 3.46 ± 0.96 mm on buccal and 3.42 ± 0.02 mm on lingual sites for defect fill. These differences between groups were statistically significant in favor of the experimental defects. The combined therapy was also clinically more effective than open-flap debridement. The superiority of the experimental group could not be attributed solely to the surgical intervention and was likely a result of the BPBM/GTR/PRP application. Combining BPBM, GTR, and PRP was an effective modality of regenerative treatment for intrabony defects in patients with advanced periodontitis.

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Regeneration of the periodontium includes the restoration of bone, cementum, and periodontal ligament.[1] Successful periodontal regeneration is similar to the development of an organ because it requires a series of orchestrated biologic events, including cell mitogenesis, chemotaxis, adhesion, and differentiation, which will result in the formation of the functional periodontal unit. Because of its multifactorial nature, techniques directed at enhancing various relevant biologic phenomena in periodontal regeneration have a greater potential to result in more favorable clinical outcomes than those that address a single event.

Bovine porous bone mineral (BPBM) is one of the graft materials used in periodontal regenerative procedures. It is prepared by protein extraction of bovine bone that results in a trabecular structure of hydroxyapatite similar to human cancellous bone and has the ability to enhance bone formation. The combination of BPBM and guided tissue regeneration (GTR) has been shown to be an effective

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BMC Oral Health

RESEARCH ARTICLE

Open Access

Efficacy of a new-generation platelet-rich fibrin in the treatment of periodontal intrabony defects: a randomized clinical trial

Boróka Klára Csifó-Nagy*, Eleonóra Sólyom, Vera Lili Bognár, Annamária Nevelits and Ferenc Dőri

Abstract

Background: The aim of the study was to clinically evaluate the healing of intrabony defects after treatment with a new generation of platelet-rich fibrin (A-PRF+) respect to enamel matrix derivative (EMD).

Methods: Thirty (30) intrabony defects of 18 patients (9 males, 9 females) were randomly treated with A-PRF+ (test, $n=15$) or EMD (control, $n=15$). The following clinical parameters were recorded at baseline and 6 months after surgery: pocket depth (PD), gingival recession (GR) and clinical attachment level (CAL). After debridement the intrabony defects were filled with A-PRF+ in the test group, respectively with EMD in the control group, and fixed with sutures to ensure wound closure and stability.

Results: Both treatment methods resulted in statistically significant PD reductions, respectively CAL gains six months post-operatively. No statistically significant differences were found between the two groups as the mean CAL gain was 2.33 ± 1.58 mm in the A-PRF+ group, respectively 2.60 ± 1.18 mm in the EMD group ($p < 0.001$).

Conclusion: Within the limits of this study the new-generation platelet-rich fibrin seems to be as clinically effective as EMD during surgical treatment of intrabony defects. Treatment with A-PRF+ or EMD resulted in reliable clinical outcomes. The use of A-PRF+ as a human autologous product can give a positive impact on periodontal healing.

Clinical Relevance A-PRF+ may be suitable for the treatment of intrabony periodontal defects.

Trial registration number (TRN) NCT04404374 (ClinicalTrials.gov ID).

Keywords: Intrabony defects, Periodontal healing, Advanced platelet-rich fibrin, Enamel matrix derivative

Background

The main goal of the comprehensive periodontal treatment is to eliminate inflammation and to prevent further destruction of the periodontium, as well as to achieve sustainable condition in the long-term [1]. Over the past decades, significant efforts have been made to develop both materials and surgical techniques that can predictably contribute to periodontal regeneration [2]. Nowadays, regenerative periodontal therapy can restore only a part of the original tissue to some extent, while complete periodontal restoration remains idealistic [3]. Enamel matrix derivative (EMD) was introduced to enhance periodontal regeneration by mimicking the formation of periodontal attachment tissues more than 20 years ago. They play an important role as chemical barriers and biological mediators in periodontal regeneration and healing [4]. Advances in cell and molecular biology have contributed to an increased understanding of wound healing. There is evidence that polypeptide growth and differentiation factors (GDF's) can support wound healing and regeneration by regulating chemotaxis, differentiation, proliferation of

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Original Article

Efficacy of platelet rich fibrin in the treatment of human intrabony defects with or without bone graft: A randomized controlled trial

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Abstract

Aim: To evaluate the efficacy of platelet rich fibrin (PRF) with or without bone graft [demineralized bone matrix (DBM) graft] in the treatment of intrabony defects based on clinical and radiographic parameters. **Materials and Methods:** Thirty six intrabony defects in 36 patients were randomly divided into three different groups and were treated with group A (PRF with DBM) or group B (PRF alone) or group C [open flap debridement (OFD)]. Clinical parameters such as plaque index (PI), gingival index (GI), probing depth (PD), relative attachment level (RAL), and gingival recession (GR) were assessed at baseline and 9 months postoperatively; radiographic parameters such as linear bone growth (LBG) and percentage in bone fill (%BF) were calculated by using the image analysis software. Comparisons of groups were analyzed using Kruskal–Wallis analysis of variance test. Pair-wise comparison of groups was done by Mann–Whitney U test. **Results:** Mean PD reduction and RAL gain were greater in group A (4.25 ± 1.48, 3.92 ± 0.90) and group B (3.82 ± 0.75, 3.27 ± 0.65) than control (3.00 ± 1.21, 2.25 ± 0.62). Furthermore, statistically significant improvement in LBG and %BF was found in group A (3.47 ± 0.53, 61.53 ± 4.54) compared to group B (2.55 ± 0.61, 49.60 ± 14.08) and group C (1.21 ± 0.80, 24.69 ± 15.59). **Conclusions:** The study demonstrated that PRF improves clinical and radiological parameters compared to OFD alone in intrabony defects. Addition of DBM enhances the effects of PRF in RAL gain and radiographic defect fill.

Key words: *Chronic periodontitis, clinical trial, periodontal attachment loss, platelet-derived growth factor, regeneration*

INTRODUCTION

Various biomaterials have been used for the treatment of intrabony defects and have demonstrated variable results.[1] Recently, biological modifiers demonstrated their ability to stimulate cells which are located in periodontal defects and resulted in proliferation and differentiation of periodontal ligament cells.[2] Platelets are considered as a natural source of these growth

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PLOS ONE

RESEARCH ARTICLE

The effect of titanium-platelet rich fibrin on periodontal intrabony defects: A randomized controlled split-mouth clinical study

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Abstract

This study aimed to determine the contribution of titanium prepared platelet-rich fibrin (T-PRF) with open flap debridement (OFD) on clinical, biochemical and radiographic measurements of periodontal regeneration. Twenty periodontitis patients with bilateral intrabony defects and stage III grade A periodontitis were included in the study. A total of 40 defects were randomly selected for OFD alone (control group, n = 20) or combined OFD+ T-PRF (test group, n = 20). Clinical and radiographic parameters (at baseline and nine months after surgery), and growth factor levels in gingival crevicular fluid (at baseline and at two, four, six, and twelve weeks after surgical treatment) were also evaluated. Considering the clinical parameters, alterations in probing pocket depth, gingival marginal level and clinical endpoint in the test regions treated with T-PRF significantly improved ($P<0.05$). Fibroblast growth factor-2 and platelet-derived growth factor-BB levels between the two groups in the second and fourth weeks were also significantly different ($P<0.05$). Furthermore, the receptor activator of nuclear factor κB ligand/osteoprotegerin ratio between the groups was significantly different in the second, fourth, sixth, and twelfth weeks ($P<0.05$). The bone-filling rate was also significantly greater in the test group than in the control group ($P<0.001$). Compared with OFD alone, combining T-PRF with the procedure was more successful with regards to clinical, radiographic, and biochemical measurements of periodontal regeneration.

Introduction

Periodontitis is a multifactorial inflammatory disease that destroys the soft and hard tissues surrounding a tooth [1]. A common goal of any periodontal treatment is improving this inflammation, reducing the probing pocket depth (PPD), and increasing the clinical attachment level (CAL). Treating intraosseous defects and regenerating lost hard tissue is challenging in periodontology, and the effectiveness of nonsurgical and surgical periodontal treatments is evaluated based on the positive effects on bone levels [2]. When treating periodontal defects, current practice includes open flap debridement (OFD) either alone or in

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RESEARCH

Injectable platelet-rich fibrin with demineralized freeze-dried bone allograft compared to demineralized freeze-dried bone allograft in intrabony defects of patients with stage-III periodontitis: a randomized controlled clinical trial

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Abstract

Aim The current randomized controlled clinical trial assessed the effect of injectable platelet-rich fibrin (I-PRF) combined with demineralized freeze-dried bone allograft (DFDBA) compared to DFDBA alone in the management of intrabony defects of stage-III periodontitis patients.

Methodology Following sample size calculation, twenty stage-III periodontitis patients with ≥ 5 mm clinical attachment level (CAL)-loss and ≥ 3 mm intrabony defects were randomized into test (I-PRF + DFDBA; $n = 10$) and control (DFDBA; $n = 10$) groups. CAL (primary outcome), periodontal probing depth (PPD), gingival recession depth (GRD), full-mouth plaque scores (FMPS), full-mouth bleeding scores (FMBS), radiographic linear defect depth (RLDD), and bone fill (secondary outcomes) were examined at baseline, 3, 6, and 9 months post-surgically.

Results I-PRF + DFDBA and DFDBA independently demonstrated significant intragroup CAL-gain, PPD-, and RLDD-reduction at 3, 6, and 9 months ($p < 0.05$), with no significant intergroup differences observed ($p > 0.05$). CAL-gain (mean ± SD) of 2.40 ± 0.70 mm and 2.50 ± 0.85 mm and PPD-reduction of 3.50 ± 1.18 mm and 2.80 ± 0.42 mm were demonstrated for I-PRF + DFDBA and DFDBA at 9 months respectively. Both groups showed significant intragroup RLDD improvement, with a RLDD of 3.58 ± 0.66 mm and 3.89 ± 1.57 mm for I-PRF + DFDBA and DFDBA at 9 months respectively. Stepwise linear regression analysis revealed that baseline RLDD and bone fill at 9 months were significant predictors of CAL ($p < 0.05$).

Conclusion Within the present study's limitations, DFDBA with or without I-PRF resulted in significant improvement in clinical and radiographic periodontal parameters in the surgical treatment of periodontal intrabony defects of stage-III periodontitis patients. Addition of I-PRF to DFDBA does not appear to significantly enhance the DFDBA's reparative/regenerative outcomes.

Clinical relevance Within the current study's limitations, routinely adding I-PRF to DFDBA cannot be recommended to significantly improve DFDBA's treatment outcomes in intrabony defects.

Keywords Platelet rich-fibrin · Allograft · Periodontal · Regeneration · Intrabony · Periodontitis

Mashaal Mohammed Alshoiby and Karim Mohamed Fawzy El-Sayed contributed equally to this work.

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Introduction

Periodontitis is a chronic inflammatory disorder, associated with dysbiotic plaque biofilms, resulting untreated in progressive destruction of the tooth-supporting apparatus and intrabony periodontal defects [1]. Such defects present risk factors for further disease progression, and their therapy improves teeth prognosis [2]. In this context, a number of periodontal approaches were advocated, employing barrier membranes, enamel matrix derivatives, bone grafts, or growth factor concentrates [3].

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HUMAN RANDOMIZED CONTROLLED TRIAL

Treatment of periodontal intrabony defects using bovine porous bone mineral and guided tissue regeneration with/without platelet-rich fibrin: A randomized controlled clinical trial

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Abstract

Background: To investigate the regenerative effect of adjunctive use of guided tissue regeneration (GTR), bovine porous bone mineral (BPBM), and platelet-rich fibrin (PRF) in intrabony defects.

Methods: Fourteen participants were enrolled, and for each patient their left and right two sides were randomized to the test group or control group. Only the worst intrabony defect on each side was analyzed. The test group received GTR, BPBM, and PRF, whereas the control group received only GTR and BPBM. The PRF used in the trial was fluid PRF, which combined with the BPBM to form a BPBM-PRF complex. The patients were followed up by clinical and radiographic evaluation for 24 months after surgery.

Results: Probing depth (PD) in the test group was significantly less than that in the control group at 12 and 24 months after surgery, and the mean difference was ≈ 0.5 to 0.7 mm. Clinical attachment level (CAL) gain in the test group was ≈ 0.9 mm higher than that in the control group at 6 months after surgery, and the difference reached 1.0 to 1.1 mm 12 and 24 months after surgery. None of the other clinical or radiographic parameters differed significantly between the two groups at any time-point after the surgery.

Conclusion: Compared with GTR and BPBM, the combination of GTR and BPBM-PRF complex is more effective clinically, and results in better clinical outcomes.

KEYWORDS

guided tissue regeneration; periodontal; platelet-rich fibrin; randomized controlled trials

1 | INTRODUCTION

The aim of periodontal treatment is the restoration of periodontal function and esthetics by eliminating periodontal inflammation and controlling of predisposing factors.[1] If indicated, the regeneration of periodontal tissues is an important additional aim of periodontal therapy.[2] Guided tissue regeneration (GTR) is an important method for the achievement of periodontal regeneration.[2] In GTR, the space between the membrane and the root is important for

Platelet-Rich Fibrin in Regeneration of Intrabony Defects: A Randomized Controlled Trial

Gauresh Kumar Patel,* Shivali S. Gaekwad,* Sheela Kumar Gujjari,* and Veerendra Kumar S.C.*

Background: Platelet-rich fibrin (PRF) is an autologous non-transfusional hemo-component with a high concentration of platelets. It incorporates leukocytes, platelets, and growth factors within the dense fibrin matrix and can be used as healing biomaterial. This study assesses the adjunctive use of PRF in regenerative management of intrabony defects in comparison with open flap debridement (OFD).

Methods: Twenty-six bilateral defects (13 per group) in 13 patients were randomized as either PRF (test group) or OFD alone (control group) sites. Probing depth (PD), clinical attachment level (CAL), and bone PD were recorded. Reduction in defect depth and percentage of bone fill was assessed radiographically. Primary outcomes assessed were changes in PD, CAL, and percentage of bone fill, and they were assessed at 6, 9, and 12 months. Secondary outcome was assessment of wound healing using a wound healing index (WHI).

Results: The PRF group showed significant improvement in clinical parameters compared with the control group at 6, 9, and 12 months. The PRF group showed a bone fill of 45.18% ± 7.57%, which was statistically significant compared with 21.6% ± 9.3% seen in the control group at the end of the study period. The PRF group also showed significant soft tissue healing and reduction in PD. WHI also showed significant advantages for the PRF group.

Conclusion: The adjunctive use of PRF to conventional OFD may be potentially used in the treatment of intrabony defects. *J Periodontol 2017;88:1192-1199.*

KEY WORDS

Chronic periodontitis; clinical attachment level; growth factors; regeneration; probing depth; wound healing.

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Periodontitis is a progressive inflammatory disease that causes destruction of the periodontal ligament and alveolar bone with pocket formation.[1] Periodontal therapy aims to control disease activity and regenerate periodontal structures.[2] In periodontium, regeneration involves the reconstitution of new alveolar bone, cementum, and periodontal ligament.[3]

Predictable regeneration requires use of barrier membranes and bone grafts of various types. Endogenous regenerative technology is an attempt at in situ periodontal regeneration using patient-derived growth factors (GFs), fibrin scaffolds, and platelet concentrates to assist recruitment of progenitor/stem cells from neighboring tissues.[4]

Choukroun's platelet-rich fibrin (PRF) involves the production of a leukocyte and PRF clot by simple natural coagulation process without biochemical modification of the collected blood.[5] Platelets contain platelet-derived GF AB, transforming GF β-1, and vascular endothelial GF (VEGF). These GFs stimulate cell proliferation, matrix remodeling, and angiogenesis.[5]

Use of PRF in mandibular Class II furcation defects has shown faster healing and bone fill.[6] Gingival recession treated with PRF membrane resulted in greater gingival thickness and complete root coverage.[7,8] PRF is used in sinus lift procedures and cystic cavity and socket augmentation procedures.[9] Thus, PRF used adjunctively in surgical periodontal

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Original Research

Comparative Evaluation of Platelet-Rich Fibrin Biomaterial and Open Flap Debridement in the Treatment of Two and Three Wall Intrabony Defects

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Abstract:

Background: Platelet-rich concentrates are the most widely used regenerative biomaterials. Stimulation and acceleration of soft and hard tissue healing are due to local and continuous delivery of growth factors and proteins, mimicking the needs of the physiological wound healing and reparative tissue processes. This article aims to evaluate the clinical efficacy of open flap debridement (OFD) with or without platelet-rich fibrin (PRF) in the treatment of intrabony defects.

Materials and Methods: Twenty subjects with forty intrabony defects were treated with either autologous PRF with open-flap debridement (test, n = 20) or open-flap debridement alone (control, n = 20). Soft tissue parameters included: Plaque index, sulcus bleeding index, probing depth, relative attachment level and gingival marginal level (GML). The hard tissue parameters included-distances from: Cement enamel junction to the base of the defect (CEJ-BOD): Alveolar crest to the base of the defect (AC-BOD): And CEJ to AC. The parameters were recorded at baseline and at 9 months postoperatively calculated using standardized radiographs by image-analysis software.

Results: Statistically significant (0.005*) intragroup improvements were seen with all the hard and soft parameters in both test and control groups, except for GML. Statistically significant improvements were seen with the mean defect fill (CEJ-BOD and AC-BOD) (P = 0.003*) when intergroup comparisons were made.

Conclusions: Adjunctive use of PRF with OFD significantly improves defect fill when compared to OFD alone. PRF has consistently been showing regenerative potential; it is simple, easy and inexpensive biomaterial compared with bone grafts.

Key Words: Intrabony defect, open flap debridement, periodontal grafts, platelet rich fibrin, reconstructive osseous surgery

Introduction

The definitive goal of regenerative periodontal therapy aims at the reconstruction/regeneration of the tooth supporting apparatus, which has been lost because of periodontitis or trauma.[1] Periodontal regeneration is defined as the complete restoration of lost tissues to their original architecture and function by recapitulating the crucial wound-healing events associated with their development.[2]

Among the broad range of available treatment options, only a few may be regarded as truly regenerative. A material or technique must histologically demonstrate that periodontal tissue regeneration (new attachment) is formed on a previously diseased/destroyed root surface, in order to be considered a regenerative modality.[3] In the last two decades, various biomaterials[4-9] have been developed and experimented for periodontal tissue regeneration based on their endogenous regenerative capacity, but there is no graft material that is considered as the gold standard.[10]

Platelet-rich fibrin (PRF), an autologous fibrin material as described by Choukroun *et al.* belongs to the second-generation platelet concentrate with cicatricial properties.[11] The preparation of this material as described by Choukroun is a simplified and an inexpensive (The preparation does not require any anticoagulants, bovine thrombin or any other gelling agent) procedure.[12] It consists of an intimate assembly of cytokines, glycanic chains, and structural glycoproteins enmeshed within a slow releasing fibrin network.[12] This leads to more efficient cell migration and proliferation. This unique structure may act as a carrier for cells that are

Original Article

Injectable platelet-rich fibrin polymerized with hydroxyapatite bone graft for the treatment of three-wall intrabony defects: A randomized control clinical trial

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Abstract:

Background: The study was aimed to compare and evaluate the clinical and radiographic outcomes of injectable platelet-rich fibrin (i-PRF) polymerized with hydroxyapatite (HA) bone graft and HA bone graft alone for treating three-wall intrabony defects (IBDs). **Materials and Methods:** The trial was planned as a randomized, prospective clinico-radiographic study with inclusion of 34 three-wall IBDs in patients with stage III periodontitis. IBDs were assigned randomly to one of the groups, i.e., Group I – experimental (i-PRF + HA) and Group II – control (HA alone). At baseline and 6 and 9-month intervals, both the clinical and radiographic measurements were taken and baseline and 9-month data were tabulated and imported into SPSS 22 software. Student unpaired and paired t-tests were used to find significant differences ($p<0.05$). **Results:** Both the groups showed substantial changes in all clinical and radiographic measures on comparison from baseline values. On intergroup comparison, the i-PRF + HA group reported significantly higher original defect resolution and original defect fill as compared to the HA group. **Conclusion:** i-PRF polymerized with HA graft has shown better results as compared to HA graft alone in three-wall IBDs and therefore can be used as a better possible alternative for the treatment of three-wall IBDs.

Key words:

Alveolar bone defect, bone graft, injectable platelet-rich fibrin, intrabony defect, periodontal pocket, regeneration

INTRODUCTION

Periodontitis is a pervasive disease, which causes the destruction of the periodontium, and it also affects the normal function of the oral cavity and quality of life.[1] Various previous studies as well systematic reviews state that in patients suffering from periodontitis, scaling and root planing (SRP) procedure leads to significant improvement in the clinical parameters. However, in deep periodontal pockets and also due to the presence of tissue-invading pathogens, SRP fails to show successful results and thus periodontal infection may recur.[2-4] Due to this limitation in periodontitis patients with deep pockets, surgical periodontal therapy is undertaken. Furthermore, various adjuncts such as bone grafts and bone substitutes, guided tissue regeneration, and various combination of other therapies are being used for the regeneration of the lost periodontium.[5-7] For the regeneration of lost alveolar bone during the periodontal disease process, various bone grafts and bone substitutes are available and are being used regularly with successful results.[8] Hydroxyapatite (HA) bone graft is a biocompatible material, which helps in bone formation through osteoconductive mechanisms, eventuating in clinically acceptable responses.[9,10]

From their evolution since the late 1990s, platelet concentrates have gained considerable attention due to their autologous nature as well as potential to get favorable regenerative outcomes.[11,12] The journey of platelet concentrates has come far from platelet-rich plasma (PRP), followed by the focus on the next generation of platelet concentrates,

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Original Article

Evaluation of platelet-rich fibrin and tricalcium phosphate bone graft in bone fill of intrabony defects using cone-beam computed tomography: A randomized clinical trial

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Abstract:

Background: Platelet-rich fibrin (PRF) is the second-generation platelet concentrate first described by Choukron *et al.* It incorporates leukocytes, platelets, and growth factors within dense fibrin matrix, can be used in periodontal regeneration alone or in combination with bone grafts. **Aim:** This study assesses bone fill in intrabony defects, following the use of β tricalcium phosphate (TCP) bone graft with and without PRF. **Materials and Methods:** Thirty sites with intrabony defects in periodontitis patients were selected, randomly allotted into three groups: Group A open flap debridement (OFD), Group B OFD with β TCP with PRF, and Group C β TCP. Clinical parameters such as plaque index, gingival index, sulcus bleeding index, and PPD recorded at baseline and 6 months. Radiographic parameters include cementoenamel junction (CEJ) to base of defect, CEJ to alveolar crest, depth of defect, and bone fill assessed using the cone-beam computed tomography (CBCT). The comparison between the test group and control group in terms of clinical and radiographical parameters was assessed using the independent sample *t*-test. **Results:** Significant reduction in probing depth measurements, defect fill observed in both β TCP with PRF and β TCP alone groups compared to OFD. However, intergroup comparison assessed using the independent sample *t*-test found to be statistically nonsignificant ($P < 0.05$ is considered significant). **Conclusion:** All three treatment strategies resulted in significant reduction in probing depth and bone fill at 6 months. Bone fill achieved in β TCP with PRF was more compared to β TCP alone and OFD at 6 months follow-up. CBCT can be accurately used to assess the morphology of intrabony defect and also in evaluating bone fill.

Key words:

Cone-beam computed tomography, intrabony defects, platelet-rich fibrin, β tricalcium phosphate

INTRODUCTION

Periodontitis is a disease of the periodontium characterized by the irreversible loss of connective tissue attachment and supporting alveolar bone.[1] Loss of attachment due to periodontal disease can be regenerated with definitive periodontal therapy. Intraosseous periodontal defects of varying morphology may have a varying regenerative potential depending on the extent of the source of the cells of periodontium.[2]

The periodontal regeneration requires an orchestrated sequence of biological factors and techniques for its successful outcome.[3-4] The combination of various regenerative biologic agents and techniques has attracted the interest of researchers in the field of reconstructive periodontal surgery. Autogenous bone grafting is considered the gold standard for grafting, although it has limitations.[5]

Traditional synthetic bone grafts are ceramics of hydroxyapatite, tricalcium phosphate (TCP) or combination of two which are resorbable materials.[6] Among the tested bone substitutes, β TCP showed significantly higher percentage of bone fill at 24 weeks of healing.[7] It is well tolerated and has no adverse affects such as allergic reactions.[8]

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Original paper

Comparative study of demineralized freeze-dried bone allograft and its combination with platelet-rich fibrin in the treatment of intrabony defects: A randomized clinical trial

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of the article

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Abstract

Background. The clinical and radiographic efficacy of bone grafts and biomaterials, such as platelet-rich plasma and platelet-rich fibrin (PRF), for reconstructing lost periodontal structures has been well documented. However, there is limited data regarding the presence of demineralized freeze-dried bone allograft (DFDBA) in an environment with abundant growth factors provided by platelet concentrates.

Objectives. The aim of the study was to compare the clinical and radiographic effectiveness of DFDBA with PRF versus DFDBA alone in the treatment of intrabony defects.

Material and methods. Twenty-four intrabony defects in contralateral sites were randomly assigned to either the DFDBA group or the DFDBA combined with PRF group. Clinical parameters, including the plaque index (PI), the gingival index (GI), probing pocket depth (PPD), relative attachment level (RAL), and radiographic bone fill (RBF), were measured at baseline, and at 6 and 9 months. Paired and unpaired *t*-tests were used for intra- and intergroup comparisons.

Results. Both the PI and the GI showed statistically significant improvements from baseline to 9 months. However, the intergroup comparisons did not reveal any significant differences ($p < 0.05$) between the groups with regard to clinical and radiographic measurements from baseline to 9 months.

Conclusions. Platelet-rich fibrin in combination with DFDBA did not show any additional benefit in terms of reconstructive output in the treatment of intrabony defects compared to the use of DFDBA alone.

Keywords: plaque index, gingival index, probing pocket depth, relative attachment level, radiographic bone fill

Evaluation of intrabony defects treated with platelet-rich fibrin or autogenous bone graft: A comparative analysis

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ABSTRACT

Objective: The primary objective of this study was to compare clinically and radiographically the efficacy of autologous platelet rich fibrin (PRF) and autogenous bone graft (ABG) obtained using bone scrapper in the treatment of intrabony periodontal defects. **Materials and Methods:** Thirty-eight intrabony defects (IBDs) were treated with either open flap debridement (OFD) with PRF or OFD with ABG. Clinical parameters were recorded at baseline and 6 months postoperatively. The defect-fill and defect resolution at baseline and 6 months were calculated radiographically (intraoral periapical radiographs [IOPA] and orthopantomogram [OPG]). **Results:** Significant probing pocket depth (PPD) reduction, clinical attachment level (CAL) gain, defect fill and defect resolution at both PRF and ABG treated sites with OFD was observed. However, inter-group comparison was non-significant ($P > 0.05$). The bivariate correlation results revealed that any of the two radiographic techniques (IOPA and OPG) can be used for analysis of the regenerative therapy in IBDs. **Conclusion:** The use of either PRF or ABG were effective in the treatment of three wall IBDs with an uneventful healing of the sites.

Key words: Autogenous bone graft, blood platelets, chronic periodontitis, wound healing

INTRODUCTION

Owing to their osteogenetic potential, autogenous bone grafts (ABGs) have been widely used in periodontics for the treatment of intrabony defects (IBDs) and can be harvested from either extraoral or intraoral donor sites. Among the various methods of harvesting intraoral ABG, use of bone scraper is less aggressive. Further, the autogenous graft material is obtained from the adjacent areas of actual graft site, thus avoiding second intra or extra oral surgical sites and attendant morbidities. This autogenous cortical bone graft mixed with blood is sufficient to augment localized osseous defects.[1]

Second-generation platelet concentrate, platelet rich fibrin (PRF), developed in France by Choukroun *et al.*[2] in 2001, is a fibrin-matrix in which platelet, cytokines and cells are entrapped that are released after a certain time and can serve as resorbable membrane. PRF is considered to be a healthy biomaterial, and was initially used in oral implantology by its promoters, and presently, its application has been advocated in various disciplines of dentistry.[3] The present study was conducted to compare and evaluate autologous PRF and ABG obtained using the bone scrapper in the treatment of intrabony periodontal defects clinically and radiographically.

MATERIALS AND METHODS

The present randomized clinical study was conducted between December 2010 and June 2013. Ethical clearance was obtained from institutional ethical committee.

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Original Article

Clinical and radiographic evaluation of nanocrystalline hydroxyapatite with or without platelet-rich fibrin membrane in the treatment of periodontal intrabony defects

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Abstract:

Background: Nano-sized ceramics may represent a promising class of bone graft substitutes due to their improved osseointegrative properties. Nanocrystalline hydroxyapatite (NcHA) binds to bone and stimulate bone healing by stimulation of osteoblast activity. Platelet-rich fibrin (PRF), an intimate assembly of cytokines, glycan chains, and structural glycoproteins enmeshed within a slowly polymerized fibrin network, has the potential to accelerate soft and hard tissue healing. The present study aims to explore the clinical and radiographical outcome of NcHA bone graft with or without PRF, in the treatment of intrabony periodontal defects. **Materials and Methods:** In a split-mouth study design, 20 patients having two almost identical intrabony defects with clinical probing depth of at least 6 mm were selected for the study. Selected sites were randomly divided into two groups. In Group I, mucoperiosteal flap elevation followed by the placement of NcHA was done. In Group II, mucoperiosteal flap elevation, followed by the placement of NcHA with PRF was done. Clinical and radiographic parameters were recorded at baseline and at 6-month postoperatively. **Results:** Both treatment groups showed a significant probing pocket depth (PPD) reduction, clinical attachment gain, increase bone density 6-month after surgery compared with baseline. However, there was a significantly greater PPD reduction and clinical attachment gain when PRF was added to NcHA. **Conclusion:** The NcHA bone graft in combination with PRF demonstrated clinical advantages beyond that achieved by the NcHA alone.

Key words:

Nanocrystalline hydroxyapatite, periodontal regeneration, platelet-rich fibrin

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INTRODUCTION

The ultimate goal of periodontal therapy is the regeneration of periodontal tissues that have been destroyed due to periodontal disease. Periodontal regeneration is the reconstruction of the lost tissues as evidenced histologically in the formation of new cementum, new alveolar bone, and functionally oriented periodontal ligament. Different modalities have been proposed to obtain regeneration of periodontal tissues employing various bone grafts, bone substitute materials, guided tissue regeneration (GTR), combination of bone grafts or bone substitutes with GTR and growth factors.[1-4]

Hydroxyapatites (HAs) represent a family of bone grafting materials with a high degree of biocompatibility that is largely attributable to its presence in natural calcified tissue.[7] Preliminary experimental studies have shown that nano-sized ceramics may represent a promising class of bone graft substitutes due to their improved osseointegrative properties.[8,9] Accordingly, a synthetic nanocrystalline hydroxyapatite (NcHA) bone graft has been introduced for augmentation procedures in intrabony defects. Advantages of NcHA material are osteoconductivity, bioresorbablity, and close contact. A special feature of nanostructured materials is an extremely high number of molecules on the surface of the material. When the NcHA was used as a bone graft substitute, rapid healing of critical size defects was observed in animal experiments and in human applications.[10] NcHA binds to bone and stimulate bone healing by stimulation of osteoblast activity.[11] NcHA has been used for the treatment of metaphyseal fractures in orthopedic surgery,[12] ridge augmentation,[13] and peri-implantitis lesions.[14]

Platelet-rich plasma (PRF) is an autologous concentration of platelets in plasma.[15,16] PRP has been used to enhance the clinical outcome obtained by using bone grafts with and without GTR in the treatment of intrabony defects. PRF, a second-generation platelet concentrate has been introduced by Choukroun *et al.* in 2001 that has several advantages over PRP.[17]

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Original Article

Clinical and radiographic evaluation of platelet-rich fibrin as an adjunct to bone grafting demineralized freeze-dried bone allograft in intrabony defects

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Abstract:

Background: Several bone graft materials are popularized in the treatment of intrabony defects. Demineralized freeze-dried bone allograft (DFDBA) is widely used in the treatment of intrabony defects. Platelet-rich fibrin (PRF) is autologous blood preparation which helps in wound healing and regeneration. Hence, this study focuses on evaluation of PRF, DFDBA, and their combination in the regeneration of intrabony defects. **Materials and Methods:** A total of 39 sites with intrabony defects were randomly assigned into three groups: (Group I - Open flap debridement, Group II - DFDBA alone, and Group III- DFDBA + PRF). Parameters such as probing pocket depth (PPD), relative attachment level (RAL), and radiographic bone fill were measured at baseline, 3 months, and 6 months. Intragroup comparison at various study intervals was made using one-way ANOVA test. Intergroup comparison was made using Tukey's multiple *post hoc* test. **Results:** Reduction in the PPD and greater difference in RAL was observed over the study period in all the three groups with greater reduction in DFDBA + PRF group. Reduction in the radiographic defect depths was observed over the study period in all the three groups with the greatest reduction of 38.99% in the DFDBA + PRF group. However, no statistically significant difference was reported by DFDBA versus DFDBA + PRF group. **Conclusion:** Combination of DFDBA and PRF improved the clinical and radiographic parameters compared to PRF and DFDBA alone. PRF was combined with DFDBA to produce a synergistic effect for treating intrabony defects in chronic periodontitis patients.

Key words:

Demineralized freeze-dried bone allograft, intrabony defects, periodontal surgery, platelet-rich fibrin

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INTRODUCTION

Chronic periodontitis is an infectious disease, resulting in inflammation within the supporting tissues of the teeth which lead to periodontal pocket deepening, loss of attachment and bone. The osseous defects occurring as a result of periodontitis can be treated employing various regeneration methods. Periodontal reconstruction surgery uses a combination of a variety of biologic agents and methods,[1] which enhance the success of regeneration by helping in cell migration, adherence, growth, and differentiation.[2] Autogenous bone, bone substitutes play vital role in regeneration.[3] The autogenous bone grafting, though considered "gold standard" in bone grafting procedures has certain limitations such as, limited availability and complications pertaining to donor site. Such limitations with regard to the autogenous bone grafts encouraged the use of bone graft substitutes in periodontal regeneration.[1] Demineralized freeze-dried bone allograft (DFDBA) is an allograft that exhibits osteoinductive property because of bone morphogenetic proteins (BMPs-2, 4, 7).[4] Platelet-rich fibrin (PRF) is an autologous platelet concentrate possessing higher amounts of growth factors (GFs) that aid in regeneration.[1] It consists of different GFs, leukocytic cells, and their cytokines (interleukins-1,6,4 and tumor necrosis factor-α). Studies reported that PRF as

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Future Science OA

The effect of concentrated growth factors in the treatment of periodontal intrabony defects

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Aim: To investigate the effect of concentrated growth factors (CGFs) in human intrabony defect treatment. **Methods:** Thirty-one intrabony defects were randomly treated with CGFs + bovine porous bone mineral (BPBM) or BPBM alone. Probing depth, clinical attachment level and hard tissue fill were evaluated at baseline and 1 year post surgery. **Results:** No differences in any of the investigated parameters were observed at baseline. At 1 year post therapy, both groups showed significant improvement in clinical parameters ($p < 0.001$). CGFs + BPBM was more effective than BPBM alone at decreasing probing depth (4.2 ± 1.3 mm vs 3.0 ± 1.6 mm) and clinical attachment level gain (3.7 ± 1.3 mm vs 2.4 ± 1.1 mm; $p \leq 0.05$). A favorable increase of hard tissue fill was noted in CGFs + BPBM group compared with BPBM group ($p > 0.05$). The contents of growth factors in CGFs were statistically higher than those in platelet poor plasma ($p < 0.001$). **Conclusion:** Addition of CGFs significantly improved clinical effectiveness of BPBM for intrabony defect treatment.

Lay abstract: Concentrated growth factors (CGFs) are a new generation of platelets concentrates, which contain abundant growth factors. We assumed that CGFs might promote periodontal (gum) regeneration. In the present study, we used CGFs in the treatment of periodontal intrabony defects. The results at 1 year post surgery indicated that the addition of CGFs significantly improved the clinical effectiveness of bone graft alone. More research is needed to better understand this effect.

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Keywords: bovine porous bone mineral • concentrated growth factors • periodontal intrabony defects • periodontal regeneration

Periodontitis is an inflammatory disease that leads to the loss of tooth-supporting tissues. Tissue loss caused by periodontal disease is typically treated by a variety of regenerative treatment modalities, including bone grafts, guided tissue regeneration (GTR) and growth factors, to reform the tooth's supporting tissues [1–5].

However, a common problem of GTR therapy is the high variability and low predictability of healing outcomes, even as complete and predictable reconstruction of periodontal tissues is difficult to obtain with any therapeutic plan [6,7]. Specifically, the degree of healing depends on both the local characteristics of the intrabony defects and the regenerative potential of the residual periodontal tissues [4,8,9].

Polypeptide growth factors are one of the fundamental elements in tissue engineering, which have shown an important role in the growth and differentiation of cells involved in periodontal wound healing [10,11]. Recombinant forms of growth factors may have positive effects in experimental studies but are not practical for clinical application owing to complexity of application and their high costs.

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One-Year Results Evaluating the Effects of Concentrated Growth Factors on the Healing of Intrabony Defects Treated with or without Bone Substitute in Chronic Periodontitis

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Statistical Analysis C
Data Interpretation D
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Background: The restoration of damaged periodontium, especially one-wall intrabony defects, is a major challenge for clinicians. Concentrated growth factors (CGF) are a 100% autologous fibrin with multiple concentrated growth factors. The rigid fibrin structure of CGF makes it possible to preserve or reconstruct the initial bone volume. The aim of this study was to evaluate the clinical healing patterns after surgical application of CGF with and without a Bio-Oss graft in one-wall infrabony defects.

Material/Methods: We randomly divided 120 one-wall intrabony defects in 54 patients into 4 groups: flap surgery alone (Group 1), flap surgery with autologous CGF (Group 2), flap surgery with Bio-Oss (Group 3), and flap surgery with CGF+Bio-Oss (Group 4). Clinical parameters such as probing depth (PD) and clinical attachment level (CAL) change were recorded at baseline and at 6 and 12 months postoperatively.

Results: At 12 months postoperatively, Group 2 showed significant improvement in clinical parameters over Group 1 ($P<0.05$) and the results were significantly greater in Groups 3 and 4 compared to the other groups ($P<0.05$). Although no significant difference was noted between Groups 3 and 4 in clinical parameters ($P>0.05$) compared to Group 3, the mean change of CAL at 6–12 months in Group 4 was not significant ($P>0.05$).

Conclusions: CGF reduced periodontal intrabony defects depth and, when mixed with Bio-Oss, CGF showed better results in the early period and the effect was more stable.

MeSH Keywords: Chronic Periodontitis • Receptors, Growth Factor • Therapeutics

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ORIGINAL ARTICLE

Clinical and radiographic evaluation of the use of PRF, CGF, and autogenous bone in the treatment of periodontal intrabony defects: Treatment of periodontal defect by using autologous products

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Abstract

Background: The purpose of this randomized clinical study was to clinically evaluate and compare the efficiencies of platelet-rich fibrin (PRF), concentrated growth factor (CGF) and autogenous bone graft (ABG) in the treatment of intrabony pockets and to assess the alveolar bone gain (AB gain) radiographically (panoramic and CBCT images).

Methods: Eighty intrabony pockets were divided into four groups: ojnly open flap debridement (OFD), OFD+PRF, OFD+CGF and OFD+ABG; each group consisted of 20 defects. Plaque index (PI), gingival index (GI), probing depth (PD), clinical attachment level (CAL), and tooth mobility (TM) by using Periotest M device were evaluated. Radiographic images were also taken to evaluate the AB gain. PRF was produced using a protocol of 2,700 RPM for 12 min and the relative centrifugal force (RCF) was evaluated. CGF was prepared as follows: 2 min 2700 rpm, 4 min 2400 rpm, 4 min 2700 rpm, 3 min 3000 rpm.

Results: The study results revealed a similar improvement in PI and GI values in all groups ($p > 0.05$). There was a statistically significant decrease in PD and CAL in favor of ABG group at day 180 in comparison with other groups ($p = 0.001$). There was also a statistically significant decrease in TM and alveolar bone height loss (ABHL), whereby the AB gain gradually increased among the groups with the best group being ABG, followed by CGF, PRF, and control groups, respectively ($p = 0.001$).

Conclusions: The study results support the treatment of periodontal intrabony pockets using OFD in combination with ABG, CGF, and PRF, as ABG showed the best results followed by CGF and PRF.

KEYWORDS
periodontal pocket, periodontitis, platelet-rich fibrin, regeneration

