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SECOND GENERATION PLATELET-RICH FIBRIN

ВТОРА ГЕНЕРАЦИЈА ТРОМБОЦИТНО ЗБОГАТЕН ФИБРИН

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Abstract

Platelet-rich fibrin (PRF) is a second-generation autologous platelet concentrate that has found widespread use in modern oral surgery, primarily due to its regenerative potential and biological safety. It consists of a fibrin matrix enriched with platelets, leukocytes, cytokines, and growth factors, which promote angiogenesis, tissue regeneration, and accelerated wound healing. This literature review aims to assess the current scientific evidence regarding the use of PRF in oral surgical procedures, with an emphasis on its effects on soft and hard tissue healing and the reduction of postoperative complications. In order to meet the set objectives, a comprehensive literature search was conducted using the PubMed and Medline databases, focusing on studies published between 2001 and 2021. The findings indicate that PRF has a variety of clinical applications, including third molar surgery, socket preservation, maxillary sinus lift, implant placement, treatment of oroantral communications, use as biological dressings, and periodontal regenerative procedures. Based on the available literature, it can be noted that PRF contributes to improved clinical outcomes by reducing postoperative pain, swelling, and infection rates, while also improving bone regeneration and soft tissue healing. PRF is considered a safe, cost effective, and minimally invasive adjunct in oral surgery. However, further standardized clinical trials are requiredto optimize its use and confirm long-term outcomes. **Keywords:** PRF, third molar surgery, socket preservation,sinus floor elevation,guided bone regeneration.

Апстракт

Фибринот богат со тромбоцити (PRF) е автологен концентрат на тромбоцити од втора генерација кој наоѓа широка употреба во модерната орална хирургија, првенствено поради неговиот регенеративен потенцијал и биолошка безбедност. Се состои од фибрински матрикс збогатен со тромбоцити, леукоцити, цитокини и фактори на раст, кои ја промовираат ангиогенезата, регенерацијата на ткивата и забрзаното заздравување на раните. Овој преглед на литературата има за цел да ги процени моменталните научни докази во врска со употребата на PRF во оралнохируршките процедури, со акцент на неговите ефекти врз заздравувањето на меките и тврдите ткива иврз намалувањето на постоперативните компликации. За да се исполнат поставените цели, спроведено е сеопфатно истражување на литературата со користење на базите на податоци PubMed и Medline, фокусирајќи се на студии објавени меѓу 2001 и 2021 година. Наодите покажуваат дека PRF има различни клинички апликации, вклучувајќи хирургија на трети молари, зачувување на алвеолата, подигање на максиларниот синус, поставување на импланти, третман на ороантрални комуникации, употреба како биолошки преврски и пародонтални регенеративни процедури. Од литературните податоци, може да се забележи дека PRF придонесува за подобрени клинички исходи со намалување на постоперативната болка, оток и стапки на инфекција, а истовремено ја подобрува регенерацијата на коските и заздравувањето на меките ткива. PRF се смета за безбеден, економичен и минимално инвазивен додаток во оралната хирургија. Сепак, потребни се понатамошни стандардизирани клинички испитувања за да се оптимизира неговата употреба и да се потврдат долгорочните исходи. Клучни зборови: PRF,хирургија на трет молар,презервација на алвеола,подигање на под на синус,водена коскена регенерација.

Introduction

PPRF is a second-generation platelet concentrate. This material has a structure built of a fibrin network that contains a various growth factors and cytokines, which under normal conditions are gradually released during the tissue remodeling and healing process. The biological effects of PRF are predominantly observed in the acceleration of the wound healing process and tissue regeneration, which contributes to its diverse applications in oral surgery[1].

Modern oral surgery is focused on minimally invasive surgical methods and biological strategies that aim to improve the healing process, while minimizing the quantity and quality of postoperative complications, and therefore

the application of PRF is of crucial importance. Unlike PRP, PRF is not obtained in a complex procedure and does not require the use of anticoagulants and biochemical additives, which makes it a biologically safer and more natural substance[2].

PRF is created from whole blood samples without the use of any additional components. Therefore, there is a low risk of side effects. Another advantage is the simplicity of the obtaining process and the ease of the preparation process, which means that the intervention does not involve high costs. PRF in modern dental practice can be used both as a liquid and as a solid matrix[3].

Evidence from contemporary scientific research shows that PRF contributes to better alveolar bone preservation after tooth extraction and after dental implant placement. Qualitative analyses show that PRF has a significantly increased capacity for bone regeneration, particularlyin alveolar cleft repair cases. Additionally, meta-analytic literature findings from third molar surgical procedures report a lower rate of alveolar osteitis, a common complication in oral surgery[4].

Complications that may occur following oral surgery have catalyzed the development of innovative approaches, such as PRF. In recent years, the topic of PRF has gained significant interest in the field of clinical research.

The main aim of this literature review is to evaluate and present the current scientific evidence regarding the use of platelet-rich fibrin (PRF) in oral surgery, with a particular emphasis on its effects on tissue healing, bone regeneration, and reduction of postoperative complications. This literature review also aims to analyze the clinical efficacy of PRF in various oral surgical procedures, including tooth extraction, implant placement, sinus augmentation, and guided bone regeneration, as well as to present the relevant limitations and disadvantages in the use of this material in the available scientific and professional literature.

To fulfill the objectives of this study, a comprehensive literature search was conducted through the most widelyused medical scientific databases - PubMed and Medline. The following keyword combinations were used in the search: “PRF” AND “third molar surgery” OR “socket preservation” OR “sinus floor elevation” OR “guided bone regeneration” OR “alveolar ridge preservation”. Literature data related to the previously listed keywords, published in the last two decades (2001-2021), were analyzed. Only papers written in English were included in the study.

PRF in Oral Surgery

PRF as a material has a significant role in oral surgery. In the contemporary scientific literature about the use of PRF in oral surgery, the data are predominantly focused on its use in dentoalveolar procedures. It is inevitable to note that research related to the use of PRF in oral surgical procedures has shown mixed results, which will contribute to the hesitation of oral and maxillofacial surgeons to adopt PRF widely.

Contemporary oral surgical practice encompasses a wide range of procedures in which PRF can be used, such as:

- mandibular third molar surgery,
- socket preservation after tooth extraction,
- maxillary sinus augmentation,
- application of biological dressings,
- placement of dental implants,
- treatment of osteonecrosis of the jaw,
- closure of oroantral communications, and
- various periodontal surgical procedures.

Third molar extraction

Third molar tooth extraction is a frequently performed oral surgical procedure that can result in numerous complications leading to patient discomfort. The most common potential postoperative complications include: trismus, pain and severe swelling, which are usually more common in relation to the occurrence of infections, alveolar osteitis and sensory disturbances[5,6].

PRF can be applied after the extraction of third molars in order to improve the wound healing process, reduce postoperative pain and swelling and reduce the risk of alveolar osteitis[7]. For this purpose, especially to reduce adverse postoperative outcomes in patients related to the occurrence of swelling, trismus and pain, the literature describes the positive effect of using PRF clot to fill the defect after third molar extraction[8]. It must also be noted that some systematic literature reviews have indicated that patients treated with PRF have a reduced incidence of alveolar osteitis and lower levels of postoperative pain after third molar surgery[4,9-11].

Perhaps the most significant conclusion is the one that was drawn by Ribeiro et al.[12] who reported that the use of PRF is crucial in minimizing postoperative discomfort, edema, alveolar osteitis rate, and infections after surgical removal of third molars, compared with patients who did not use PRF.

Socket preservation

In contemporary literature, Platelet-rich fibrin (PRF) has been widely investigated as a biological adjunct for socket preservation after tooth extraction. PRF is widely known to serve as a fibrin-based scaffold that allows for the continuous release of vital growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF), thereby facilitating angiogenesis

and osteogenic activity during the early stages of wound healing[13].

This material has been used to promote the soft tissue healing process, reduce post-extraction alveolar bone loss, and improve the quality of the regenerative ridge in preparation for future implant placement[14].

Systematic reviews suggest that PRF may help reduce post-extraction alveolar bone resorption, although its clinical efficacy may vary based on defect morphology, surgical technique, and patient-related factors[15-17]. It must also be noted that there is considerable heterogeneity in the literature, predominantly due to variations in study design, preparation protocols, and centrifugation methods, making direct comparisons of results difficult.

Numerous clinical studies have shown that the application of PRF in extraction sockets leads to better and faster soft tissue closure and more effective preservation of alveolar ridge dimensions compared to natural healing alone. In addition, its use is associated with less postoperative pain and discomfort, as well as faster maturation of the healing socket[18,19].

In conclusion, it can be noted that PRF can be considered a cost-effective, autologous biomaterial that enhances biological healing processes in socket preservation procedures.

Maxillary Sinus Augmentation

Platelet-rich fibrin (PRF) is a significant biologically active adjunct in maxillary sinus augmentation procedures, particularly with the goal of enhancing bone regeneration and improving clinical outcomes[20]. In sinus lift surgery, PRF can be applied either alone or in combination with bone graft materials to promote faster healing, enhance graft stability, and improve bone formation within the elevated sinus cavity[21].

Clinical studies and systematic reviews have shown that the addition of PRF to sinus augmentation procedures can enhance new bone formation and reduce healing time compared to traditional grafting techniques alone[4,18,22,23].

As previously noted, PRF acts as an autologous fibrin matrix that releases growth factors such as PDGF, TGF-β, and VEGF, thereby stimulating angiogenesis and osteogenesis in the grafted sinus area. This biological activity is particularly vital in the maxillary sinus, where bone regeneration is often limited due to poor vascularity and inadequate underlying bone volume[24,25].

Finally, it must be noted that PRF is associated with increased graft stability, fewer postoperative complications, and improved soft tissue healing at the site of the intervention.

Application of biological dressings

Platelet-rich fibrin (PRF) can be used as biological dressings predominantly due to its autologous origin, ease of preparation and regenerative potential. This potential is since PRF forms a dense fibrin matrix enriched with platelets, leukocytes and a wide range of growth factors, including transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF). This matrix acts as a natural substrate that supports cell migration, proliferation and differentiation, while providing a continuous release of bioactive molecules over time[26,27].

Its fibrin architecture not only stabilizes the wound site, but also improves angiogenesis and soft tissue healing by facilitating neovascularization[28]. In addition, the presence of leukocytes in PRF contributes to its antimicrobial and immunomodulatory effects, further supporting tissue regeneration[24].

When applied as a biological dressing, PRF creates a protective barrier over surgical or traumatic wounds, promoting hemostasis and reducing the risk of infection. These properties make PRF particularly valuable in oral and maxillofacial surgery, including extraction sockets, periodontal defects, soft tissue grafting, and maxillary sinus augmentation procedures[3].

Clinical studies have shown that the application of PRF results in reduced postoperative pain, accelerated epithelialization, and improved wound healing outcomes[29,30]. Compared to conventional dressings, PRF offers the advantage of being completely biocompatible and additive-free, thus minimizing the risk of adverse reactions[31].

Based on the literature data, it can be concluded that PRF is increasingly considered a safe and effective biological dressing in regenerative dentistry and implantology.

Placement of dental implants

Platelet-rich fibrin (PRF) has emerged as a significant advance in dental implantology. The success of dental implants largely depends on the osseointegration process. PRFcontributes to osseointegration by enhancing the initial healing events at the implant site[32]. The fibrin matrix acts as a scaffold that supports the migration and proliferation of surrounding cells, while the sustained release of growth factors stimulates osteoblast activity and angiogenesis[24].

In addition to cell migration and proliferation, PRF enhances neovascularization, leading to an improved supply of oxygen and nutrients to the regenerating tissues. Such increased vascularization not only accelerates bone regeneration, but also reduces the risk of implant failure[33].

PRF can be applied immediately after implant placement, with PRF being placed in extraction sockets to promote faster healing and preserve the alveolar bone dimensions. PRF can also be used in socket preservation techniques, helping to minimize bone resorption after extraction[34].

PRF can be used alone, but it can also be used in combination with bone graft materials to improve graft stability and integration. Its fibrin network facilitates the incorporation of graft particles and supports the formation of new bone[22].

PRF also has beneficial effects on the soft tissues around implants. The presence of leukocytes and cytokines leads to a reduction in inflammation and an improved immune response, promoting adequate conditions for wound healing. Improved soft tissue healing is particularly important in aesthetic areas, where the quality and stability of the peri-implant mucosa significantly affect the final outcome[35].

Importantly, PRF can reduce postoperative complications. Clinical studies have shown that the use of PRF is associated with reduced postoperative pain, risk of infection, and swelling. The presence of leukocytes significantly influences the healing process predominantly due to antimicrobial and immunomodulatory effects. Along with rapid wound closure and tissue regeneration, the likelihood of complications such as delayed healing or implant exposure is reduced[18,36,37].

However, it must be stated that, although many studies report positive results, there is still variability in clinical outcomes and standardized protocols are needed to optimize its use. In the future, the integration of PRF with new technologies, such as biomaterials and growth factor delivery systems, may open up new possibilities in implant dentistry.

Closure of oroantral communications

Oroantral communications most often occur during extraction of maxillary posterior teeth due to the close anatomical contact of the roots of these teeth and the floor of the maxillary sinuses. Untreated oroantral communications can transform into oroantral fistulas. Oroantral communications and fistulas inevitably lead to chronic maxillary sinusitis, as a significant complication[38].

The treatment of oroantral communications depends on numerous factors such asthe presence of infection, the size of the defect and the duration of the communication[39]. Treatment in everyday dental practice is predominantly through conventional techniques, although in recent years, PRF has been increasingly used for this purpose. This is primarily due to the fact that PRF represents a minimally invasive and biologically active alternative for the therapy of oroantral communications.

In the treatment of oroantral communications with PRF, this material acts as a biological membrane and filler, while simultaneously having a positive effect on the healing of both soft tissues and bones. The fibrin matrix provided by this material also acts on blood clotting, which closes the communication, and the matrix acts as a basis in which the regeneration of epithelial and connective tissues occurs[40].

A modern clinical study comparing the effects of PRF with a buccal flap showed comparable closure success rates (approximately 90%), with the use of PRF also significantly improving and accelerating wound healing, minimal displacement of the mucogingival layer, and of course reduced postoperative pain[41].

Finally, it must be noted that most studies confirm that PRF in the treatment of oroantral communications is often used as an adjunct, and notas a soletreatment method.

Regenerative periodontal procedures

Regenerative periodontal techniques using PRF are becoming increasingly common among clinicians. As previously mentioned, the slow polymerization process of PRF leads to the formation of a strong fibrin network that allows release of growth factors over time; enhanced angiogenesis; increased fibroblast proliferation; and adequate modulation of the inflammatory response[42]. These fundamental advantages allow for effective healing and periodontal regeneration. Adequate regeneration is still a challenge, especially in complex periodontal cases such as those with infrabony defects, gingival recession, and furcation involvement[43].

The fibrin matrix deposited in periodontal defects allows for the migration and proliferation of cellular structures. In turn, the presence of growth factors stimulates the proliferation and differentiation of fibroblasts, osteoblasts, periodontal ligament cells and pluripotent cells[44]. These methods also affect the formation of the extracellular matrix by initiating collagen synthesis. It also leads to the formation of new blood vessels, which increases the supply of oxygen and nutrients and thus reduces the concentration of cytokines that stimulate the immune response of the host cells[45].

In periodontal surgery, PRF has been successfully used in the treatment of intrabony defects, furcation defects, gingival recession defects, socket preservation, and guided tissue regeneration procedures[14,46]. Clinical studies and systematic reviews have demonstrated that the adjunctive use of PRF may lead to significantly greater probing pocket depth reduction, clinical attachment level gain, and radiographic bone fill compared with conventional surgical therapy alone[47,48]. Furthermore, PRF has been associated with improved soft tissue healing, reduced postoperative discomfort, and enhanced patient-reported outcomes[47,49].

Recent systematic reviews and meta-analyses have confirmed the positive effects of PRF on periodontal regeneration, particularly in the treatment of infrabony and furcation defects, either alone or in combination with bone graft materials[47-49]. Nevertheless, differences in centrifugation protocols, preparation methods, and study designs con-

tinue to contribute to variability in clinical outcomes. Therefore, additional well-designed randomized controlled trials with long-term follow-up are necessary to establish standardized clinical protocols and optimize the use of PRF in periodontal surgery.

Finally, we can conclude that PRF with its ability to improve the healing of both soft and hard tissues, as well as reduced postoperative morbidity, can easily improve therapeutic outcomes. Hence, PRF can be a significant addition to periodontal surgical interventions due to its regenerative potential and biological compatibility.

Conclusion

Platelet-rich fibrin (PRF) is an autologous, safe, and cost-effective biomaterial that significantly improves the healing process of both soft and hard tissues in oral surgical procedures. Its application has been shown to achieve improved clinical outcomes, including accelerated wound healing, improved bone regeneration, and reduced postoperative complications such as pain, swelling, and infection. However, variability in clinical protocols and outcomes highlights the need for further standardized, high-quality studies to optimize its use and confirm long-term efficacy.

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