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Use of platelet-rich fibrin (PRF) in dental surgical procedures

Uso de fibrina rica em plaquetas (PRF) em procedimentos cirúrgicos dentários

Uso de fibrina rica en plaquetas (PRF) en procedimientos quirúrgicos dentales

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Abstract
The aim of this study is to evaluate the use and applicability of Platelet-rich Fibrin (PRF) in surgical procedures of exodontia. The methodology was to perform an integrative literature review that was developed in six phases, in which the guiding question was elaborated by means of the PICo strategy. Thus bibliographic searches were performed in the electronic portals PubMed, LILACS and Cochrane Library, with the keywords Platelet-Rich Fibrin, Extraction and Regeneration, in which 20 articles were selected for the development of this review. he PRF has been increasingly effective in its various applications, especially in soft tissue healing, post-exodontia, contributing to the healing time, morbidity and amount of analgesics needed to reduce pain. Given the above, it is clear that PRF has a high capacity for the stimulation and regeneration of the natural healing process of tissues at extraction sites. Recent findings indicate that PRP can be considered as an efficient, cost-effective and simple therapeutic support for extraction procedures. Furthermore, the use of PRF in surgical procedures for tooth extraction has been shown to be advantageous in terms of tissue healing and bone regeneration, as well as having an expressive role in reducing the risk of delay in the recovery of patients undergoing therapies with oral bisphosphonates. Improvements in the techniques used with PRF can be summed up, as well as further studies and clinical trials with larger samples may confirm the results discussed in this work.
Keywords: Platelet-Rich fibrin; Tooth extraction; Regeneration.

Resumo
O objetivo do presente trabalho foi avaliar a utilização e aplicabilidade da Fibrina Rica em Plaquetas (PRF) em procedimentos cirúrgicos de exodontias. A metodologia destinou-se a efetuar uma revisão literária integrativa, em que a questão norteadora foi elaborada mediante a estratégia PICo. Desta maneira, foram realizadas buscas bibliográficas nos portais eletrônicos PubMed, LILACS e Cochrane Library, utilizando as palavras-chave: Fibrina rica em plaquetas, Extração e Regeneração, no qual foram selecionados 20 artigos para o desenvolvimento desta revisão. O PRF vem se mostrando cada vez mais efetivo em suas mais diversas aplicabilidades, em especial na cicatrização de tecidos moles, pós-exodontia, contribuindo com o tempo de cicatrização, morbidade e quantidade de analgésicos necessários para diminuir a dor. Diante do exposto, torna-se claro que o PRF possui uma alta capacidade para a estimulação e regeneração do processo natural de cura dos tecidos nos locais de extração. Descobertas recentes apontam que o PRF pode ser considerado como um apoio terapêutico eficiente, econômico e simples para os procedimentos de exodontia. Ademais, a utilização da PRF em procedimentos cirúrgicos de exodontia tem demonstrado ser vantajosa em termos de

cicatrização tecidual e regeneração óssea, assim como tem uma expressiva atuação em reduzir o risco de atraso na recuperação dos pacientes em terapias com bisfosfonatos orais. Melhorias nas técnicas utilizadas com o PRF podem ser somatórias, bem como mais estudos e ensaios clínicos com amostras maiores poderão confirmar os resultados discutidos neste trabalho.
Palavras-chave: Fibrina rica em plaquetas; Extração dentária; Regeneração.

Resumen
El objetivo de este estudio es evaluar el uso y la aplicabilidad de las plaquetas ricas en fibrina (PRF) en procedimientos quirúrgicos de exodoncia. La metodología tuvo como objetivo realizar una revisión bibliográfica integradora que se desarrolló en seis fases, en la que una pregunta guía fuera desarrollada a través de la estratégia de PICo. Así, se realizaron búsquedas bibliográficas en los portales electrónicos PubMed, LILACS y Cochrane Library, con las palabras clave Platelet-Rich Fibrin, Extraction and Regeneration, en el que se seleccionaron 20 artículos para el desarrollo de esta revisión. La PRF ha sido cada vez más eficaz en sus diversas aplicaciones, especialmente en la cicatrización de los tejidos blandos, después de la exodoncia, contribuyendo a reducir el tiempo de cicatrización, la morbilidad y la cantidad de analgésicos necesarios para reducir el dolor. A la vista de lo anterior, está claro que el PRF tiene una gran capacidad de estimulación y regeneración del proceso natural de curación de los tejidos en los lugares de extracción. Los últimos descubrimientos indican que el PRF puede considerarse como un soporte terapéutico eficaz, económico y sencillo para los procedimientos de exodoncia. Además, el uso de PRF en procedimientos quirúrgicos para la extracción de dientes ha demostrado ser ventajoso en términos de cicatrización de tejidos y regeneración ósea, además de tener un papel expresivo en la reducción del riesgo de retraso en la recuperación de pacientes sometidos a terapias con orales. bisfosfonatos. Se pueden resumir las mejoras en las técnicas utilizadas con PRF, así como estudios y ensayos clínicos posteriores con muestras más grandes pueden confirmar los resultados discutidos en este trabajo.
Palabras clave: Fibrina rica en plaquetas; Extracción dental; Regeneración.

1. Introduction

Since the first description of fibrin-rich platelet (PRF) by Choukron in 2001, this composition has become an important adjuvant in surgical procedures. This biomaterial is an autologous component used for topical use, in which leukocytes, platelets, and growth factors are concentrated, without the interference of any added chemical substances. This fibrin has a complex three-dimensional architecture, which makes this substance act as a scaffold for cells and for new tissue deposits. Possible recommendations for its use in the oral cavity are surgical procedures, which include the preservation of the alveolar ridge after tooth extraction, sinus elevation, third molar exodontias, dental implants, among other procedures (Tambella et al., 2020).

Once it does not need any additives, such as anticoagulants or thrombins, the PRF preparation technique becomes faster, simpler, more economical and biochemically safe. The process of obtaining the PRF involves the collection of blood, of approximately 10 ml, and it should be centrifuged at 2700 rpm (rotations per minute) for 12 minutes, then it is ready to be incorporated into the extractions site (Sharma et al., 2020). After the centrifugation, it is possible to observe three very distinct layers, the first one which is at the bottom of the tube consists of a bunch of a coagulated red blood cells, in the middle layer is where the rigid and elastic PRF clot is found, and the third layer which is composed of a serum supernatant of platelet-poor acellular plasma (Jeyaraj & Chakranarayan, 2018).

The complex dental surgeries, such as impacted third molar extractions, can have repercussions in a postoperative period with possible pain complaints, presence of swelling, limitation in mouth opening and development of alveolar osteitis. In this way, the PRF can be an advantageous alternative for being biocompatible, releasing growth factors in a controlled way, enabling the creation of physiological architecture that benefits the healing process, which directly interferes with the well-being and comfort of patients after surgical procedures. Azangookhiavi, et al., (2020)

In addition to that, many studies which analyze the effect of PRF on alveolar post-extractions procedures have been performed in humans. Most of these studies showed that the use of PRF was clearly beneficial, while in other cases the utility of PRF appeared to be more controversial, with failures to improve the healing process. However, in recent studies, it was not

possible to draw definitive conclusions on the subject (Tambella et al., 2020).

The PRF provides significantly greater bone regeneration compared to normal physiologic wound healing. Furthermore, growth factors in platelet and fibrin concentrate increase the mineralization and bone formation rates in the first six months. A recent study by Kim et al. 2015, used PRF in osteoblasts and measured cellular activities. The results of this study showed the progression of DNA synthesis rate and alkaline phosphatase activities, in which they could conclude that the use of PRF improves bone regeneration capacity (Witek et al., 2019).

The platelet-rich fibrin production protocol aims at the accumulation of platelets and cytokines that are released into a fibrin clot. In the meantime, PRF results from natural and progressive polymerization of the blood during its centrifugation. A network of fibrins is formed that surpasses the characteristics of natural clots (Malhora et al., 2020). Laboratory studies have shown that these platelets release six growth factors, these being platelet-derived growth factor-AB (PDGF-AB), vascular endothelial growth factor (VEGF), transforming growth factor-beta 1 (TGF-β1) insulin-like growth factor, epithelial growth factor, and recombinant human basic fibroblast growth factor, in which TGF-β1, PDGF-AB, and VEGF are the three major growth factors that are released in large amounts.

The odontologic surgery benefits significantly from the available biomaterials, in which the evolution and applicability of PRF is evident since its first use in 2001. In this assumption, changes in the preparation of the PRF can lead to the development of advanced platelet-rich fibrin (A-PRF), which can be acquired by decreasing the force in the centrifugation process (Clark et al., 2018). Therefore, the fibrin-rich platelet lysate (L-PRF) is also widely used in surgical procedures, as there are studies that highlight that the addition of titanium (T-PRF) can be summed up in these issues, as it has similar osteoinductive properties. bone and preserve tissue volume (Ustaoglu; et al., 2019).

Thus, the aim of the present work was to evaluate the use and applicability of platelets rich in fibrin (PRF) in surgical procedures of extractions.

2. Methodology

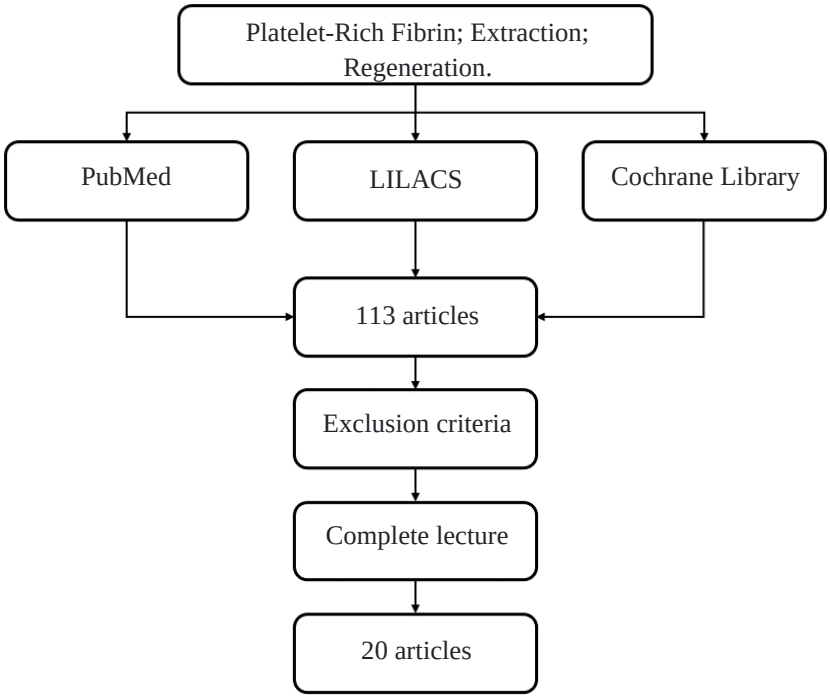
This study is an integrative literature review developed in six phases, which were: a) development of the research question; b) definition of the databases and the inclusion criteria used; c) definition of the information to be extracted from the studies taken from the databases; d) evaluation of included studies; e) interpretation of results; f) presentation of the synthesis of knowledge (Whittemore & Knafl, 2005).

The research question was posed according to the Population Context of Interest (PICo) strategy (Lockwood et al., 2017). Thus, the following structure was considered: P - platelet-rich fibrin (L-PRF), I - Extraction and Co - Regeneration. Thus, the following question was formulated: "Can the use of fibrin-rich platelets be useful and effective in surgical exodontic procedures?"

The literature searches were performed in July 2022, using the PubMed, Cochrane Library and LILACS databases. Two groups of independent investigators, composed of two members in each group respectively, performed the searches and selection of studies, where they formulated the steps and performed them separately, in order to identify any divergences in the results obtained.

The inclusion criteria of the present study were: primary studies that inform the use of PRF as an alternative treatment for regeneration, published between 2017 and 2022. The exclusion criteria were: Theses, editorials, monographs, dissertations, review articles, electronically incomplete articles and those that did not answer the guiding question. As it is an integrative literature review, the present study was not submitted to the Ethics Committee, however, the authors' ideas about the publications used in the development of this study remained. To compose this review, we used the electronic portals: PubMed, LILACS and Cochrane Library, with the descriptors: Platelet-Rich Fibrin, Extraction and Regeneration (Figure 1).

Figure 1 – Flowchart of the search strategy.



Source: Authors (2022).

3. Results and Discussion

The bibliographic survey of this work addressed the period of work research from 2017 to 2022, a total of 113 publications were found, which after applying the inclusion and exclusion criteria, 20 articles were chosen to compose this review, with samples ranging from 6 to 102 patients, which are distributed as follows: seventeen (85%) in MEDLINE/PubMed and three (15%) in the Cochrane Library. In terms of study design, seven (35%) are randomized clinical trials, six (30%) are prospective studies, two (10%) are randomized controlled trials, two (10%) are randomized controlled clinical trials and one (5%) in vivo study. Table 1 shows the 20 selected publications, according to authors, year of publication, objective, type of study, sample and main findings.

Table 1 - Summary of selected primary studies.

AUTHOR/YEAR	OBJECTIVE	METHODOLOGY	SAMPLE	MAIN FINDINGS
Azangookhiavi et al. (2020)	Compare the clinical application of lyophilized bone allografts and fibrin-rich platelets for post-extraction alveolar ridge preservation.	Randomized controlled clinical trial.	32 patients.	The results showed acceptable efficacy for PRF without graft materials in preserving the alveolar ridge. The PRF was denoted as economical and easy to prepare.
Malhotra et al. (2020)	Evaluate the PRF as a biomaterial for bone regeneration and wound healing.	Controlled, single-blind, split-mouth prospective study.	50 patients.	This study showed that PRF can accelerate bone healing and physiological tissue after impacted lower third molar extractions.
Mourão et al. (2020)	Evaluate the postoperative effect of leukocyte and	Prospective, parallel-arm, randomized study.	32 patients.	The results showed that L-PRF reduces postoperative pain and discomfort and

	platelet-rich fibrin (L-PRF) in improving epithelialization and decreasig alveolar pain.			that its use should be considered whenever there is a need to improve socket healing.
Tambella et al. (2020)	Rate and compare the wound healing and alveolar bone regeneration in sockets after tooth extraction with and without application of PRF in dogs.	*In vivo* randomized controlled study.	12 dogs.	The results suggest that PRF could be able to stimulate the natural process of tissue healing and regeneration of post-extraction sockets in dogs with spontaneous periodontal disease (PD).
Sharma et al. (2020)	Evaluate the influence of PRF in soft tissue healing and bone regeneration.	Prospective split-mouth study.	30 patients.	The present study proved that PRF is significantly better at promoting soft tissue healing and bone tissue regeneration. It also showed that the alveolus graft with PRF seems to be a minimally invasive technique, with simple preparation and great cost-benefit.
Sybil et al. (2020)	Appraise the efficacy of PRF in soft tissue healing and bone tissue (through periapical radiographs) after lower third molar extraction.	Prospective split-mouth study.	25 patients.	There was a significant improvement in the symptoms of pain, swelling and tenderness. There was also a statistically significant improvement in sulcus bleeding index, plaque index and probing depth. While the clinical attachment level and bone height were not influenced by the use of PRF.
Witek et al. (2020)	Evaluate the effect of L-PRF/PLGA composite grafts in bone regeneration.	*In vivo* study.	6 sheeps.	The study indicated that L-PRF exudate has an impact on bone regeneration when incorporated with the PLGA scaffold in a large translation model. More studies are needed for confirmation.
Afat, Akdogan and Gönül, (2019)	Appraise the hypothesis that PRF alone, and especially when combined with hyaluronic acid, will accelerate healing and reduce the incidence of postoperative complications.	Prospective randomized clinical trial.	60 patients.	The findings suggest that PRF when combined with hyaluronic acid may improve soft tissue healing, as well as may be advantageous in preventing alveolar osteitis and postoperative infection of impacted third molars.
Areewong, Chantaramungko and Khongkhunthian (2019)	The aim of this study was to compare the rate of bone neoformation between the use of PRF as a socket preservation material and normal wound healing, through histomorphometric analysis.	Randomized controlled study.	33 patients.	Findings suggest that the use of PRF in ARP does not statistically significantly increase new bone formation after tooth extraction compared to normal wound healing.
Ritto et al. (2019)	Evaluate the use of leukocyte and platelet-rich fibrin (L-PRF) in bone	Randomized clinical trial.	20 patients.	Due to its good biological effects, low cost and easy preparation, the L-PRF can be considered a reliable treatment

	healing after third molar extraction.			option to stimulate cell proliferation, but further studies with larger samples and standardization of evaluation methods are still needed.
Ustaoglu et al. (2019)	Analyze the characteristics of early healing of soft tissues and Fractal Dimension (FD) of extraction sockets preserved by leukocyte-rich fibrin (L-PRF) and titanium prepared platelet-rich fibrin (T-PRF).	Randomized controlled clinical trial.	57 patients.	The results showed a significantly lower rate in the control group than in the L-PRF and TPRF groups at week 1. In week 2, both test groups showed a 100% CWE rate compared to only 40.7% in the control group. The VAS (Visual Analogue Scale) pain score was significantly higher in the control group than in the L-PRF and T-PRF groups on day 1.
Asmael, Jamil, and Hassan (2018)	The aim of this study was to evaluate the potential of platelet-rich fibrin (PRF) in improve soft tissue healing after tooth extraction and to assess its effectiveness in reducing the prevalence of dry sockets among smokers.	Randomized clinical trial.	20 patients.	The results of this study showed that PRF improved the quality of soft tissue healing of the extraction socket in smoking patients, but showed no significant difference regarding pain reduction, dry socket prevention and socket closure. Future clinical trials are needed to clearly identify the effectiveness of PRF in this regard.
Clark et al. (2018)	Conduct the first randomized controlled clinical trial evaluating four different ridge preservation approaches, including A-PRF alone or in combination with lyophilized bone allograft (FDBA), FDBA alone or without graft (blood clot).	Randomized controlled clinical trial.	40 patients.	Results demonstrated that A-PRF is a suitable biomaterial for ridge preservation, A-PRF produced significantly more vital bone compared to FDBA, while preserving ridge dimensions similarly to FDBA and better than clot blood. Thus, the findings suggest broader applications of A-PRF.
Daugela, Grimuta, Sakavicius, Jonaitis and Juodzbalys (2018)	To appraise the influence of leukocyte- and platelet-rich fibrin (L-PRF) on impacted mandibular third molar (IMTM) extraction wound healing, postoperative patient discomfort, and incidence of alveolar osteitis.	Split-mouth randomized clinical trial.	30 patients.	L-PRF treated sites resulted in improvements and decreased pain in the first postoperative week. A significant reduction in facial swelling was recorded on the first and third postoperative days in L-PRF sites versus controls, with the non-significant difference ceasing on the seventh day.
Jeyaraj et al. (2018)	To evaluate soft tissue healing and bone regeneration in sockets after extraction of impacted third molars with and without PRF.	Randomized prospective study.	60 patients.	After postoperative comparison between the two groups, it was found that the study group in which autologous PRF was incorporated into the surgical site exhibited rapid and uncomplicated soft tissue healing, as well as reossification and bone filling of the extraction socket faster and with reduced morbidity.

Kapse et al. (2018)	To evaluate the effectiveness of PRF in the healing of impacted lower third molar extraction sockets.	Randomized clinical trial.	30 patients.	The findings showed that the use of autologous PRF helps in earlier and better wound healing in a controlled manner.
Unsal e Basar (2018)	To assess whether the incidence of alveolar osteitis (AO) after extraction of partially erupted third molars differs when platelet-rich fibrin (PRF) is administered into the alveolar socket and to assess the influence of PRF on postoperative pain levels and depth. of the periodontal probe.	Randomized clinical trial.	50 patients.	In total, 8% of patients in the PRF group and 18% of patients in the control group were diagnosed with OA. None of the smokers in the PRF group and 37.5% of the smokers in the control group were diagnosed with OA. Mean postoperative pain levels were always lower in the PRF group than in the control group at all times.
Asaka et al. (2017)	To appraise the efficacy of platelet-rich fibrin (PRF) as a wound healing accelerator in patients undergoing oral bisphosphonate therapy and requiring dental extractions.	Experimental study.	102 patients.	There were no intraoperative complications in any of the patients exposed to initiation of osteonecrosis of the jaw (MRONJ) medication. Delayed recovery was seen in 9 of 73 control patients (12%), while 29 patients with PRF exhibited complete epithelialization from taking within 1 month.
Asutay et al (2017)	The aim of the present study was to evaluate whether the use of platelet-rich fibrin (PRF) decreased the levels of pain, swelling and trismus in the postoperative period of third molar surgery.	Randomized clinical trial.	30 patients.	The results of this study suggest that PRF was not observed to have a positive effect on postoperative discomfort, therefore, even so, PRF is assumed to have positive effects on healing and recovery processes.
Varghese, Manuel and Kumar (2017)	Investigate the potential of platelet-rich fibrin for bone regeneration and soft tissue healing in impaction sockets of lower third molars.	*In vivo* prospective study.	30 patients.	There was evidence of improved bone regeneration and tissue healing in response to PRF.

Source: Authors (2022).

Surgical procedures of exodontia may become necessary due to various reasons, among which can be highlighted traumatic dental injuries, extensive caries that cannot be treated in more conservative ways, as well as severe periodontal disease. Post-exodontic alveolar healing leads to ridge resorption in height and width, which can hinder the aesthetic and functional results of posterior prosthetic rehabilitations. In this way, the current dental view has improved with alveolar preservation procedures, which are procedures with the use of biomaterials administered inside the alveolus after extraction to try to reduce the bone and soft tissue changes resulting from tooth loss (Ustaoglu et al., 2019).

In this context, platelet-rich fibrin (PRF) has been widely investigated for being a rich source of autogenous growth factors, as it encompasses platelets, leukocytes and cytokines in a strong fibrinolytic network. The material under discussion has biocompatibility with living tissue, confers advantageous applicability in the dental sciences, and can be acquired viably

and easily. Growth factors are released slowly with the use of PRF, during the period of 7 to 14 days, an aspect that can influence the healing periods in surgeries (Azangookhiavi et al., 2020).

In studying the tricks and repercussions of leukocyte- and platelet-rich fibrin (L-PRF), Daugela et al. (2018), conducted a split-mouth randomized clinical trial with 34 patients, 30 of whom followed through to completion. The trial proceeded with bilateral tooth extractions on lower third molars that were impacted, so one side received L-PRF and the other served as a regular blood clot control. When following the patients from 1 to 14 days after exodontia, the results showed no alveolar osteitis in the alveoli where the L-PRF was administered, but 4 cases of alveolar osteitis were observed in the control portions. Improved soft tissue healing, reduced postoperative pain, and reduced edema were observed with L-PRF administration. The authors pointed out that within the limitations of the study, the benefits of L-PRF were remarkable.

In contrast, when studying the multifactors of PRP, specifically with regard to healing after mandibular third molar extractions, a clinical trial that elected 30 patients aged between 18 and 40 years, which were divided equally into 2 groups, group A - test, which received PRP post-exodontia and group B - control, received the suture without the prior application of PRP in the alveolus. Follow-up radiographic and clinical data showed that postoperative pain and swelling were lower in group A compared to group B. Furthermore, radiographs taken at weeks 8 and 16 after surgery made it possible to analyze the presence of early bone healing (Kapse et al., 2018).

Similarly, Varghese et al. (2017), investigated the potential of platelet-rich fibrin for bone regeneration and soft tissue healing in lower third molar impaction alveoli. This prospective study included healthy patients aged 18-35 years, where the control site received the suture primarily and the test site had autologous PRF gel added to the socket prior to synthesis. On the days following the exodontic procedure, digital periapical radiographs were taken, and with the aid of HL Image++ software, the results from weeks 1, 4, and 16 were compared. However, the imaging evidence led to the conclusion that the control sites had less bone formation than the PRP-treated alveoli. In addition, there was evidence of improved soft tissue regeneration in response to PRF, the authors highlighted that further investigations with larger sample numbers will be imperative to oral surgery.

As Asutay et al. (2017), divergently highlighted in their study by stating that by mid-2017 the literature contained few papers on the effect of PRF on pain, trismus, and edema in third molar surgery. The results of this clinical research showed that PRF had no significant positive effect on postoperative pain, swelling, and trismus after surgical removal of impacted mandibular third molars. The study included a total of thirty patients, 6 men and 24 women with a mean age of 20 to 32 years (range: 18-29 years). The division was made into 16 sites (eight controls, eight studies). Was observed that there's no significant differences between control group and the study group, in terms of pain, edema and trismus. Otherwise, the postoperative complication of alveolitis was observed in three patients in the control group and one in the study group.

Surgeries on impacted third molars are frequent, have great prominence in scientific research because they are procedures that require safe dental management and provide a good rehabilitation. Moreover, possible complications such as prolonged or delayed bleeding and infections may be mainly related to the quality of the clot and the patient's ability to recover, such factors when predominant may negatively influence the trust towards the dentist. Prospective clinical studies have shown that a good alternative is to unite the actions of a hyaluronic acid-based sponge with two layers of PRF to improve soft tissue healing and prevent postoperative complications. However, it is emphasized that clinical trials with a longer follow-up and with samples that exceed 60 patients may provide more accurate results (Afat et al., 2018).

Additionally, Clark et al. (2018) point out that modifications to the PRF preparation procedure by using lower G forces to achieve greater release of growth factors may result in A-PRF, i.e., advanced fibrin-rich platelet. The results of this study demonstrated that A-PRF produced significantly more vital bone than freeze-dried bone allograft, while preserving alveolar ridge dimensions on par with allograft and better than natural clot without additives. Therefore, the findings highlight

that future studies should investigate beyond the osteogenic potential of A-PRF, so that its evaluation in more extensive ridge augmentations and regenerative capacity will be important for surgery.

Also noteworthy, which has been explored, is its performance in smoking patients, since nicotine absorbed by the oral mucosa acts as a vasoconstrictor component, so that the negative pressure created during inhalation of smoke causes the removal of clot from the alveolus, consequently, smoking is considered a risk factor for the presence of alveolar osteitis (OA). In this design, the reduction in the incidence of OA in smoking patients who received PRF administration after exodontia may be justified by the composition that PRF adds, with cytokines, platelets, leukocytes and cell migration inducers, as well as this biomaterial for having a special structure, supports the formation of clots and prevents mechanical displacement that occurs more easily due to smoking habit (Unsal & Erbasar, 2018).

According, Asmael et al. (2018), PRF leveraged the quality of healing and soft tissue regeneration in the first week after exodontia in smoking patients, however showed no difference in pain reduction, but had prevention of inflammation and alveolus closure. At the same time, the statistical analysis for percentage of epithelialization at the 2nd and 3rd week after extraction was not significant. Twenty male patients, smokers, with a mean age of 44 years, ranging from 18 to 72 years, participated in this clinical study. The sum of extraction was 40. The amount of cigarettes consumed by the patients per day ranged from 6 to 120 cigarettes, with a mean of 47.3. The complication rate for both groups was: bleeding 0%, infection 0%, bone sequestration 0%, acutely infected alveolus 0%, acutely inflamed alveolus 0%. However, the rate of alveolitis in the control group was 5%, while it was 0% in the test group (group that previously received PRF).

Malhotra et al. (2020), carried out a comparative evaluation of PRF in relation to pain, swelling, periodontal pocket depth, bone density and bone height. The prospective study was performed with the inclusion of fifty patients and the total of one hundred third molars, in which the division was made equally into two groups, being n=50- control group (normal healing), n=50-test group (addition of PRF). The results revealed that the test sites that received PRF, showed better periodontal healing distal to the second molar and in the issue of periodontal pocket. Furthermore, the radiographs showed that the level of bone formation was more significant with the addition of PRF than in the control sites, in which there was no intervention. The findings were not so much based on the aspects of pain and swelling, but were convergent in stating that the PRF was helpful in bone healing after the extraction of the third molars studied and in the assumption of acceleration of physiological scar tissue.

The prospective split-mouth study conducted by Sharma et al. (2020) aimed to evaluate tissue regeneration at 3, 7 and 14 days postoperatively and also to evaluate bone regeneration through panoramic radiographs, which were taken immediately after exodontia and after 4 months, using the software Radiant DICOM Viewer (version 4.0.3) to calculate the bone density of the alveolus. The study included 30 healthy patients between 18 and 45 years of age, all of whom needed bilateral mandibular molar exodontia, except third molars, where only one of the alveoli was filled with PRF, randomly chosen through a computer program. It was observed that PRF alveolus grafting is a minimally invasive technique, with simple preparation, low risk, and satisfactory clinical results. After the evaluation of the data obtained, it was concluded that PRF is significantly better in promoting soft tissue healing, however, it did not have such an expressive result in bone tissue regeneration. The same type of study was performed by Sybil et al. (2020) and it was found that the side that received PRP had a significant improvement in pain and tenderness symptoms, precisely due to its clinical potential to increase angiogenesis, which aids in improving healing and pain symptoms. However, corroborating with the study by Sharma et al. (2020), it was again confirmed that the use of PRF was not effective in healing bone tissue.

In contrast, the prospective study conducted by Jeyaraj and Chakranarayan (2018), evidenced that PRF was not only effective in terms of reducing pain, swelling, and trismus, but also promoted much faster reossification and bone filling of the alveolus, coupled with optimal soft tissue healing, without any types of complications. To substantiate this, 60 patients

requiring extraction of unerupted third molars were selected, divided into two equal groups of 30 people, in which the control group that did not receive the PRF membrane in the socket, presented bone filling of the lower socket, with a higher frequency of complications such as edema, pain and trismus, associated with a higher morbidity compared to the study group, which received the PRF.

Areewong et al. (2019), revealed in a randomized clinical trial that the mean ratios of new bone formation between males and females in each group (control group and test group) were calculated. Bone neoformation in the PRF (test) group was 28.84 ± 20% in males and 33.82 ± 16.05% in females. Simultaneously, the control group showed that bone neoformation in males was 28.71 ± 23.88% and 25.14 ± 18.21% in females. The area of new bone formation was calculated by comparing with the total bone area. The results are reported as a percentage proportion. New bone formation was found in 28 old alveoli, while the remaining eight alveoli were found without new bone formation in the center of the alveoli (three cases in the PRF group, five cases in the control group). The mean rates of new bone formation were 31.33 ± 18% in the PRF group and 26.33 ± 19.63% in the control group, respectively. Thus, with the limitations present in this study, it was possible to conclude that there was no difference with the use of PRP in preserving the alveolus.

The study by Ritto et al. (2020), selected 17 patients aged 16-29 years. It was also concluded that the use of L-PRF resulted in pain reduction, there was no statistically significant difference between the means. The use of L-PRF does not yet have a clear standard protocol per surgical procedure, and all studies included in a systematic review used only an L-PRF clot or membrane to fill the alveolus. It is believed that L-PRF has a dose-dependent effect and it is not possible to know if one membrane would be sufficient to stimulate the migration of osteoblasts and endothelial cells. The application of L-PRF improved bone density and bone healing in the test group, but there was no statistical difference related to pain or soft tissue between the two groups. Therefore, based on the results presented, it can be concluded that the use of L-PRF in extraction was beneficial for bone healing. Consolidating the effectiveness of L-PRF, the study of Mourão et al. (2020), pointed out a higher consumption of analgesics in the control group, linked to a greater pain symptomatology, compared to the test group.

Therefore, based on the results in the current literature, further studies, with larger sample size and long-term follow-up as parameters, are needed to confirm the predictability of this procedure and standardization of the preparation form that provide better clinical results when combined with PRF.

4. Conclusion

In light of the above, it is clear that PRF has a high capacity for the stimulation and regeneration of the natural healing process of tissues at extraction sites. Recent findings indicate that PRP can be considered as an efficient, economical and simple therapeutic support for exodontic procedures. Additionally, the performance of fibrin-rich platelet in surgical procedures has shown to be advantageous, since the addition of the discussed biomaterial is promising in decreasing the incidence of alveolar osteitis.

Nevertheless, PRF may reduce the risk of delayed recovery for patients on oral bisphosphonate therapy. Furthermore, improvements in the techniques used in the use of PRF can and should be improved in the coming years through the addition of various healing cytokines. However, further studies are needed to confirm these results and larger trials are needed to evaluate the advantages of PRF compared to other procedures commonly used by dental surgeons.

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