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Evaluation of platelet-rich fibrin in post-exodontic bone regeneration: systematic review

Abstract

Objective: To analyze the use of platelet-rich fibrin in bone regeneration of postexodontic tooth sockets by means of a systematic review of updated randomized controlled clinical trials.

Materials and methods: the present descriptive, documentary, cross-sectional study was carried out following PRISMA 2020 standards, a search of 25 scientific articles of randomized controlled clinical trials with a minimum of 8 patients who needed dental extractions was carried out, who were divided into two groups, one test group containing platelet-rich fibrin and the other control group without platelet-rich fibrin, articles were collected from databases such as Google Scholar, PubMed, Scielo, Redalyc, Embase, which were within the last 8 years, articles that did not meet the objectives that served for this study were excluded.

Results: Of the 25 articles included in this systematic review, 15 were based on the extraction of bilateral impacted lower third molars, 8 on extractions of teeth due to endodontic failure and coronary fracture and 2 on the extraction of teeth prior to rehabilitation treatment with dental implants. Platelet-rich fibrin improves clinical and imaging conditions in post-exodontic patients, showing in the imaging evaluation after taking radiographs during the control weeks a better healing of soft tissues, a notable difference in bone filling and the formation of new bone.

Conclusion: the use of platelet-rich fibrin is effective in the preservation of the alveolar ridge post-exodontia, maintaining vertical dimensional stability, beneficial also in cellular proliferation which improves bone loss, despite this there is no significant difference in the test sites treated with platelet-rich fibrin compared to control sites treated with physiological healing.

Keywords: platelet-rich fibrin; bone regeneration; blood clot

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Introduction

Currently, one of the most frequent problems in dentistry is the maintenance of the alveolar ridge after the extraction of a dental piece, which can cause problems in oral rehabilitation, which aims to restore the architecture and functionality of the oral cavity. Dental exodontia is the result of several failures to cure advanced dental caries, complex fractures, creation of space for orthodontic treatment and advanced periodontal diseases.[1,2]

During the year 2001 in France, Dr. Joseph Choukroun invented Platelet Rich Fibrin (PRF), this is a platelet concentrate obtained after centrifugation of blood, which is extracted from the same patient, which provides a large set of leukocytes, cytokines and growth factors. It has certain advantages over platelet-rich plasma (PRP) such as: no biochemical intervention of the blood, it is autologous, there is no rejection or allergy, cell proliferation is greater than in PRP, for approximately seven days there is a greater release of growth factors. PRP is not harmful to the organism and easy to prepare, it is biocompatible with the surrounding tissues and relatively cheaper.[2–4]

After an exodontia the alveoli go through a physiological process of bone regeneration, which involves the maturation and migration of bone cells that induces remodeling and resorption of the residual alveolar ridge, these alterations in dimension occur in the first three months post-exodontia.[5–7]

During the last decades different types of options have been used to preserve and maintain the architecture of the alveolar ridge, using bone substitutes and collagen plugs, as well as the use of autologous platelet concentrates where PRF and PRP are found; platelet concentrates are considered the best allies to avoid crossinfection, however, the use of these is limited by the lack of capacity of the treating physician and understanding of the process to be followed.[8,9] In dentistry for the last 30 years, platelet concentrates have been used to stimulate new bone formation and epithelial healing due to the release of growth factors.[10–12]

From platelet-rich plasma to platelet-rich fibrin

During the 1970s platelet-rich plasma was developed, but its popularization occurred in 1980. PRP was introduced by combining collected blood with thrombin and calcium chloride, resulting in platelets trapped in a fibrin network. There are different protocols for the preparation of platelets, traditionally they are isolated by a double speed centrifugation procedure; in the first round red blood cells are separated from the plasma and the leukocyte layer, thereafter, the platelet plug is divided from the platelet poor plasma after a second centrifugation which generates PRP, which has a concentration of growth factors up to 6 to 8 times higher than whole blood.[13–15]

In recent years PRF has been catalogued as appropriate for maxillofacial bone regeneration processes; it is considered as the second generation of platelet concentrates because it is obtained after a simplified process which includes the centrifugation of autogenous peripheral blood without biological agents, PRF is composed of a fibrin network in a 4 molecule structure and contains platelets, cytokines, leukocytes and circulating stem cells.[16,17]

Platelet concentrates are classified according to leukocyte and fibrin content:[18]

- Platelet-rich fibrin (PRF).
- Platelet- and leukocyte-rich fibrin (L-PRF).
- Plasma rich in platelets and leukocytes (L-PRP).
- Platelet-rich plasma (PRP).[17]

Benefits of PRF application

This material has been applied in different branches of dentistry such as surgery, dental implantology, periodontics, which are favored by the prevention of gingival dehiscence and gum remodeling. In maxillofacial surgery, PRF favors the action of regeneration and improvement of both hard and soft tissues in a favorable environment for homeostasis, this is an accepted biomaterial, in addition, its potentiation has been evidenced in the reduction of pain, edema and postoperative bleeding.[17]

Materials and methods

The present systematic review was designed outside the protocols of the PRISMA

2020 Declaration; the protocol was registered in PROSPERO, hosted by the National Institute for Health Research, York University, Centre for Reviews and Dissemination, which assigned it the code CRD42023413017

Systematic review question

This review was structured with the PICO strategy,[18] for focused questions, as well as in the literature search:

Population (P): post-tooth extraction patients.

Intervention (I): use of PRF for alveolar preservation.

Comparison (C): spontaneous healing or blood clot.

Outcomes (O): level of bone regeneration.

Search strategy

The search and collection of scientific articles from databases such as: PubMed, Scopus, Embase, Scielo, Redalyc and gray literature was performed, from which 220 articles within the last 8 years of publication (February 2015 to February 2023) were obtained. Controlled vocabulary was used (MesH terms from Pubmed, Emtree terms in Embase). The search strategy was performed using the keywords based on the PICO question section, separated by OR and AND operators. The following keywords were used as keywords: MesH terms: "Extraction, tooth" "Extractions, Tooth", "Tooth, Extractions", "Platelet-Rich Fibrin", "Fibrin, Platelet-Rich", "Blood, Clotting", "Blood, Clottings", "Clotting, Blood", "Coagulation, Blood", "Bone regeneration", "Regeneration, Bone", "Regenerations, Bone" "Osteoconduction". Emtree terms: "Extraction tooth", "Platelet-Rich Fibrin", "Blood clotting", "Bone regeneration". Free terms: "Tooth extraction", "Platelet-rich fibrin", "PRF", "Bone regeneration". Studies were included only in English and Spanish

Inclusion criteria

Randomized controlled clinical trials that analyzed the outcome of PRF in bone tissue regeneration in patients who underwent dental extraction were included in the present systematic review. We included only if the studies consisted of 2 groups, a test group in which PRF was placed and a control group in which PRF was not used, only physiological healing. It was also included if the studies were conducted in at least 10 patients in a split-mouth or parallel design with a reasonable control. In the search for information, articles were not excluded by language or year of publication in order to obtain as much information as possible.

Exclusion criteria

Randomized controlled clinical trials in animals and reporting of methods and/or study design reports of low quality (inadequate according to the Cochrane Tool criteria) were excluded.[19]

Data collection

Articles that did not meet the selection criteria were excluded, the full texts were obtained and the characteristics of the studies were examined to confirm their inclusión (Figure 1).

Pubmed:
PI #1 (((Extraction, Tooth) OR Extractions, Tooth) OR Tooth Extractions) AND Platelet-rich fibrin) AND Fibrin, Platelet-Rich) AND Platelet Rich Fibrin).C #1 (Blood clotting) OR Blood Clottings) OR Clotting, Blood) OR Coagulation, Blood).O #3 (Bone regeneration) OR (Regeneration, Bone) OR (Regenerations, Bone) OR (Osteoconduction).
#1AND#2AND#3

Scopus:
PI#1 (TITLE-ABS-KEY (Toot extraction) OR TITLE-ABS-KEY (Extraction tooth) OR TITLE-ABS-KEY (platelet-rich fibrin) OR TITLE-ABS-KEY (PRF) OR TITLE-ABS-KEY (L-PRF))
C#2 (TITLE-ABS-KEY (Blood clot) OR TITLE-ABS-KEY (Wound scarring))
O#3 (TITLE-ABS-KEY (Bone Regeneration) OR TITLE-ABS-KEY (Regenerations, bone) OR TITLE-ABS-KEY (Osteoduction)).
#1AND#2AND#3

Base:
PI #1 "tooth extraction Or Extractions tooth AND Fibrin, Platelet-Rich".C #2 "Blood clottings OR Coagulation, Blood OR Clotting Blood".O #3 "Bone regeneration OR Regeneration, Bone OR Regenerations, Bone".
#1AND#2AND#3

Redalyc:
PI #1 "Extraction tooth" OR "Tooth extraction" OR "Tooth Extractions" AND "Platelet-Rich Fibrin".C #2 "Blood clotting" OR "Blood Clottings" OR "Clotting, Blood" OR "Coagulation, Blood". OR #3 "Bone regeneration" OR "Regeneration, Bone" OR "Osteoconduction".
#1AND#2AND#3

Sky:
PI #1 (*tooth extraction) OR (Extraction, tooth) OR (Tooth Extractions) AND (platelet-rich fibrin) AND (Fibrin, Platelet-Rich).C #2 (blood clot) OR (Coagulation, blood) OR (Blood Clottings) OR (Blood clotting).O #3 (bone regeneration) OR (Regeneration, Bone) OR (Osteoconduction).
#1AND#2AND#3

Gray literature:
Thooth Extraction, Platelet-Rich Fibrin, PRF, L-PRF, Blood Clot.

Abbreviations: PICO strategy:PI: Population, Intervention: Comparison, O: Outcome

Figure 1 Databases and search strategy

The results were:

i. Clinical evaluation of marginal bone regeneration (bone height in the vestibular, lingual and/or palatal region).

ii. Radiographic evaluation in bone regeneration (changes in density or trabecular pattern).

Data analysis

Selection of included and excluded articles was performed using Review Manager (RevMan) software [Computer program]. Version 5.4.1, Cochrane Collaboration, 2020. Excel was used to extract data such as characteristics, variables, results and preparation methods.

Evaluation of the risk of bias

To determine the validity of the studies, they were grouped into 3 categories: low risk of bias, if the inclusion criteria were considered adequate; moderate risk of bias, if 1 or more study criteria were considered unclear; and high risk of bias if 1 or more study criteria were considered inadequate. The results of the risk of bias assessment are presented in Figure 2 & 3. All studies presented a moderate range of risk of bias (Figure 4).

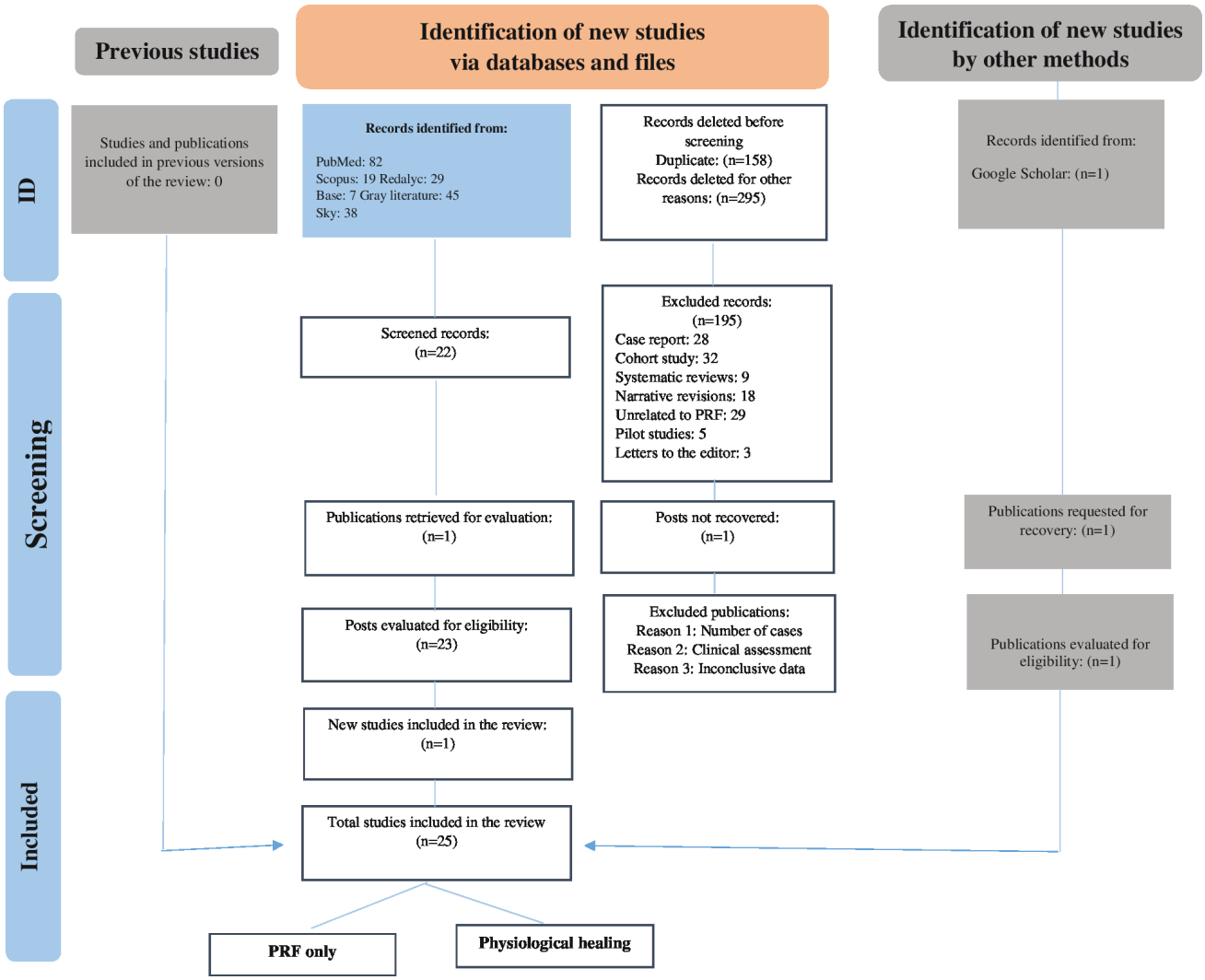

Figure 2 Flowchart of the article selection process. PRISM 2020

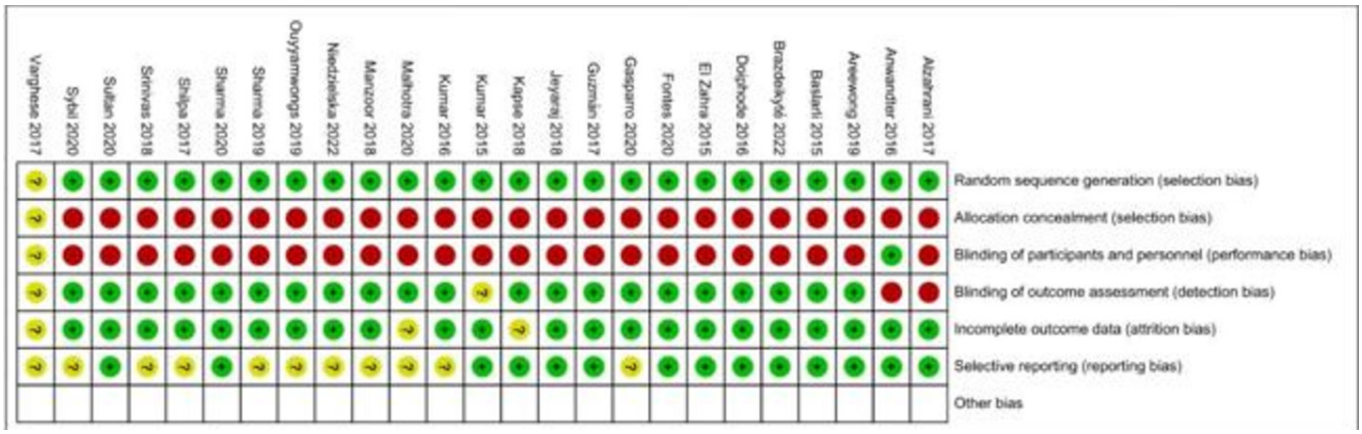

Figure 3 Risk of individual RCT studies

Citation: Molina Barahona RM, Morales-Navarro D, González Campoverde LA et al. Evaluation of platelet-rich fibrin in post-exodontic bone regeneration: systematic review. *Int J Mol Biol Open Access*. 2023;6(1):32–45. DOI: 10.15406/ijmboa.2023.06.00150

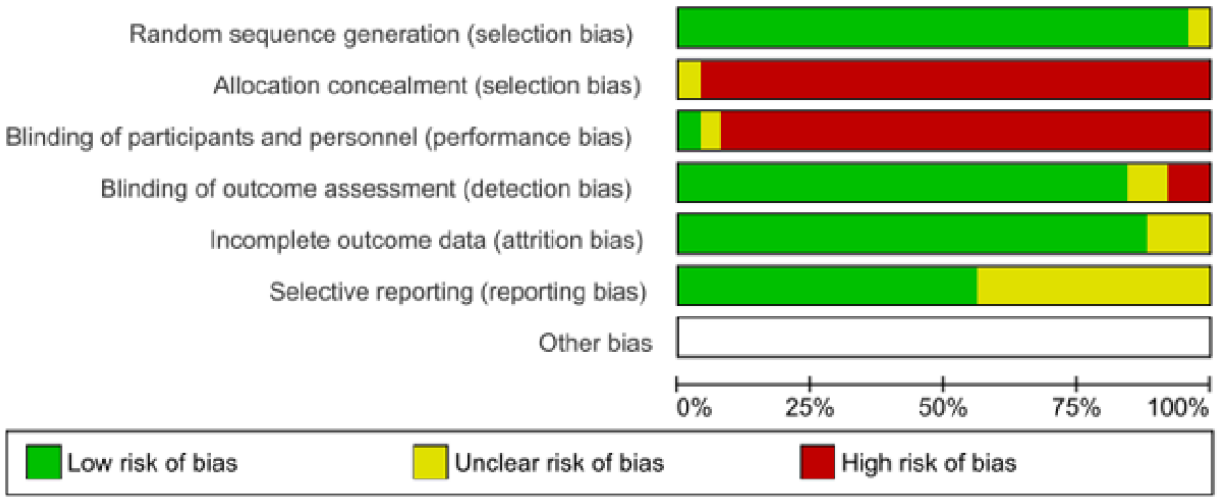

Figure 4 Total risk of bias of included studies

Results

The selection of 220 randomized controlled trial articles excluded 110 because they did not meet the necessary requirements for this study, the complete reading of the articles excluded 85, leaving 25 articles selected for data extraction analysis.

Of the studies analyzed 15 were related to the extraction of bilateral impacted lower third molars, the results showed significant changes in the percentage of bone filler in the test group (PRF) than in the control group (without PRF), (P<0.05). 2 studies.[21,22] were related to extraction of teeth prior to rehabilitation with dental implants, the results of the studies showed no significant differences for bone filling both clinically and radiographically (P> 0.9; P< 0.5), respectively. 8 studies[20–24,27,36–40] were related to tooth extraction due to endodontic failure and coronary fracture, where the results showed that the loss of alveolar ridge width in the test group was less than in the control group (-0.97mm, -1.92mm), respectively.

Table 1 shows the characteristics of the included studies, which indicate that the use of PRF increases the speed of wound healing in the post-exodontic sockets clinically; radiographic analysis also shows a decrease in alveolar resorption and a greater increase in bone filling (Table 2). The improvement in the use of PRF also lies in the way it is obtained because it is much easier to obtain, faster and does not represent a significant expense (Table 2).

Table 1 Details of included studies; intervention, control and time applied to them

Author	No. of patients	No. of pieces		Intervention		Control weeks
		Proof	Control	Proof	Control	
Anwandter Andreas, et al.[19]	18	9	9	PRF	Blood clot	1 day, 4 months.
Kanokporn Areewong, et al.[20]	33	18	18	PRF	Blood clot	2 months
Ozgur Baslari, et al.[21]	twenty	10 (patients)	10 (patients)	PRF	Blood clot	1 and 3 months
Valdoné Brazdeikyté, et al.[22]	43	22	twenty-one	PRF	Blood clot	1 day, 1 month
Amol Doiphode, et al.[23]	30	15 (patients)	15 (patients)	PRF	Blood clot	2, 4 and 6 months
El Zahra Fatma El Bagoury, et al.[24]	twenty	twenty	twenty	PRF	Blood clot	1 week, 3 and 6 months
Lucas Caldas Fontes Martins, et al.[25]	fifteen	10	5	PRF	Blood clot	6 months
Roberta Gasparro, et al.[26]	18	18	18	PRF	Blood clot	2, 4 weeks, 3, 6 months
Galo Guzmán, et al.[27]	30	30	30	PRF	Blood clot	1, 8 weeks
Priya Esther Jeyaraj, et al.[28]	60	30	30	PRF	Blood clot	8 weeks
Sheetal Kapse, et al.[29]	30	30	30	PRF	Blood clot	8, 16 weeks
Nilima Kumar, et al.[30]	31	16	fifteen	PRF	Blood clot	3 months
Amrendra Kumar, et al.[31]	fifteen	fifteen	fifteen	PRF	Blood clot	1, 2 and 6 months
Aayush Malhotra, et al.[32]	fifty	fifty	fifty	PRF	Blood clot	1, 2 and 4 months
Manzoor Mohammad, et al.[33]	30	30	30	PRF	Blood clot	4, 12 weeks
Iwona Niedzielska, et al.[34]	fifty	fifty	fifty	PRF	Blood clot	6 months
Warisara Ouyyamwongs, et al.[35]	12	twenty	twenty	PRF	Blood clot	2, 4,6 7 8 weeks
Rahul Sharma, et al.[36]	60	60	60	PRF	Blood clot	1, 4 and 8 weeks
Ankit Sharmaa, et al.[37]	30	30	30	PRF	Blood clot	16 weeks
BS Shilpa et al.[38]	7	7	N/E	PRF	N/E	3 months
Baratam Srinivas, et al.[39]	30	30	30	PRF	Blood clot	3 months
Tipu Sultan, et al.[40]	10	5	5	PRF-CS	PRF-X	5 months
Deborah Sybil, et al.[41]	25	25	25	PRF	Blood clot	3 and 6 months
Mathew P.Varghese, et al.[42]	30	30	30	PRF	Blood clot	1, 4 and 16 weeks

Citation: Molina Barahona RM, Morales-Navarro D, González Campoverde LA et al. Evaluation of platelet-rich fibrin in post-exodontic bone regeneration: systematic review. *Int J Mol Biol Open Access.* 2023;6(1):32–45. DOI: 10.15406/ijmboa.2023.06.00150

Table 2 Details of included studies; reason for extraction, evaluation method, results of the intervention, effect of platelet concentrate

Author	Dental piece - reason for extraction	Variables	Evaluation method	PRF result in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue.	Result of physiological healing and/or biomaterials in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue	Statistical significance YES/NO	Effect of platelet concentrate reported in the study
Ahmed Abdullah Alzahrani, et al.	Extraction of a tooth due to root fracture, reserved periodontal prognosis, failure of endodontic treatment, advanced caries	Alveolar ridge width, bone regeneration	Clinical and radiographic evaluation (periapical)	PRF:1,4 and 8 weeks: Alveolar ridge width: 1 week: 11.70±2.37 4 weeks: 11.33±2.30 8 weeks: 10.97±2.33 Bone fill: 1 week: 68.82±1.07% 4 weeks: 74.03±1.22% 8 weeks: 80.35±2.61%	Blood clot:1,4 and 8 weeks: Alveolar ridge width 1 week: 13.01±3.00 mm. 4 weeks: 12.04±2.50 mm. 8 weeks: 11.54±2.42 mm Bone fill: 1 week: 74.05±1.66% 4 weeks: 81.54±3.33% 8 weeks: 88.81±1.53%	YEAH: 1 -4 week: p=0.012 1- 8 weeks: p=0.036 NO: 4-8 weeks: 0.37	The loss of alveolar ridge width in the PRF group (-0.97mm - 8.58%) was significantly lower compared to the control group (-1.92 - 13.54%) at 4 and 8 weeks. ; PRF increases the efficiency of cell proliferation therefore decreases long-term bone loss
Anwandter Andreas, et al.[19]	Exodontia prior to dental implants	Clinical and radiographic dimensional changes of the alveolar ridge	Clinical and radiographic evaluation	Mean horizontal resorption of 1.18±2.4 mm (p = 0.8) at the crest, 1.25±2.0 mm (p = 0.57) and 0.83±2.0 mm (p = 0.78) at 2 mm and 4 mm apical to the crest.	N/E	NO. p= 0.99	No significant differences were observed for bone fill. between jaws, neither clinically (0.03±4.4 mm, p= 0.9, CI: -4.46 to 4.39) nor radiographically (-0.06±3.84 mm, p= 0.7 , CI: -4.31 to 3.04).
Kanokporn Areewong, et al.[20]	Exodontia prior to dental implants	Formation of new bone and wound healing.	Clinical and radiographic evaluation	PRF: 31.33±18%.	Clot: 26.33±19.63%.	There were no statistically significant differences in the proportion between the PRF and control groups (P = 0.431).	The use of PRF in PRA does not statistically significantly improve new bone formation after tooth extraction compared to normal wound healing (P > 0.05).

Table 2 Continued.....

Author	Dental piece - reason for extraction	Variables	Evaluation method	PRF result in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue.	Result of physiological healing and/or biomaterials in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue	Statistical significance YES/NO	Effect of platelet concentrate reported in the study
Ozgur Baslari, et al.[21]	Extraction of impacted bilateral mandibular third molars	Soft tissue and bone healing	Radiographic evaluation (panoramic, bone scans)	PRF:1 and 3 months:1 month: 4,713 month: 4.1	1 and 3 months:1 month: 4.63 month: 3.96	No: Mean bone gray value scores in extraction areas with or without PRF were similar, with no statistically significant differences, at both postoperative visits.	The mean increase in technetium-99m methylene diphosphonate uptake as an indication of improved bone healing did not differ significantly between PRF-treated and non-PRF-treated sockets 30 and 90 days postoperatively.
Valdoné Brazdeikyté, et al.[22]	Extraction of mandibular molars	Soft tissue and bone healing	Clinical, radiographic evaluation (tomograms)	PRF: 8.4mm	Clot: 7.9 mm	Significantly reduced PRF (P: 0.04	PRGF and PRF did not have a significant effect on the dimensions of the primary bone tissues formed in the socket.
Amol Doiphode, et al.[23]	Extraction of impacted bilateral mandibular third molars	Probing depth, soft tissue healing, bone density	Clinical, radiographic evaluation	Alveolar bone height:Preoperative: 3.64±1.89 mm2 month: 3.37±1.72 mm4 month: 1.80±0.84 mm6 month: 1.57±0.62 mmBone density:Preoperative: 149.47±10.90 mm2 month: 120.60±8.42 mm4 month: 133.74±9.30 mm6 month : 141.4±11.41mm	Alveolar bone height:Preoperative: 3.10±2.09 mm2 month: 3.10±2.09 mm4 month: 2.97±2.11 mm6 month: 2.77±2.24 mmBone density:Preoperative: 144.33±13.76 mm2 month: 75.87±8.38 mm4 month: 99.94±14.91 mm6 month : 127.80±11.87mm	There was no significant difference between the mean bone values	PRF has shown good results, it can be incorporated as an adjunct to promote wound healing and bone regeneration in extraction sites of human mandibular third molars
El Zahra Fatma El Bagoury, et al.[24]	Extraction of impacted lower third molar	Bone height, probing depth	Clinical and radiographic evaluation	Preoperative: 12.90±2.22 mmWeek 1: 12.60±2.14 mmMonth 3: 12.33±2.11 mmMonth 6: 12.47±2.07 mm	Preoperative: 12.58±2.39 mmWeek 1: 11.98±2.10 mmMonth 3: 11.49±2.13 mmMonth 6: 11.36±2.05 mm	Shows differences in bone height between the study and control sides. R, study side = 17.6 mm; L, control side = 15.3 mm.	PRF is considered a cheap and readily available material for clinical use that allows postoperative healing of soft and hard tissues.

Table 2 Continued.....

Author	Dental piece - reason for extraction	Variables	Evaluation method	PRF result in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue.	Result of physiological healing and/or biomaterials in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue	Statistical significance YES/NO	Effect of platelet concentrate reported in the study
Lucas Caldas Fontes Martins, et al.[25]	Upper anterior tooth extraction	Mineralized tissue	Clinical and radiographic evaluation	54.20±4.31%	40.60±5.98%	No. P=: 0.0528.	It indicates that the clinical use of bone marrow aspirate concentrate, when used with platelet-rich fibrin as a vehicle, in fresh extraction sockets, could have some potential to increase mineralization.
Roberta Gasparro, et al.[26]	Extraction of the impacted mandibular third molar	Clinical attachment loss	Clinical evaluation. Radiographic evaluation	PRF: 6 months 0.69±0.46	6 months 0.79±0.34	No: 0.47±0.41mm to 0.60±0.46mm	PRF shows better results in CAL gain and PS reduction compared to control sites
Galo Guzmán, et al.[27]	Exodontia of lower third molars	Soft tissue and bone healing	Clinical evaluation, radiographic evaluation	PRF: 60 days 163.86 UH	60 days 159.31 UH	Yes: 60 days (P<0.015)	Healing of the gingival tissue wound. Healing of bone tissue
Priya Esther Jeyaraj, et al.[28]	Extraction of mandibular third molars	Pain, swelling, lockjaw, periodontal health, bone healing	Clinical and radiographic evaluation			Yes: P = 0.001d	The incorporation of PRF within the extraction sockets of impacted third molars proved to be beneficial to patients, resulting in faster postoperative recovery with fewer complications, such as postoperative swelling and edema, pain, and lockjaw; better overall post-operative results in terms of faster soft tissue healing as well as earlier bone regeneration.

Table 2 Continued.....

Author	Dental piece - reason for extraction	Variables	Evaluation method	PRF result in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue.	Result of physiological healing and/or biomaterials in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue	Statistical significance YES/NO	Effect of platelet concentrate reported in the study
Sheetal Kapse, et al.[29]	Bilateral impacted third molars	Pain, edema. Bone regeneration (lamina dura, bone density and trabecular pattern)	Clinical evaluation (VAS, edema) and radiographic (periapical)	PRF:8 and 16 weeks Lamina dura: 8 weeks: 1.23±0.10 16 weeks: 1.80±0.07 Bone density: 8 weeks: 1.23±0.09 16 weeks: 1.83±0.07 Trabecular pattern 8 weeks: 1.20±0.11 16 weeks: 1.87±0.06	Blood clot:8 and 16 weeks Lamina dura: 8 weeks: 0.40±0.009 16 weeks: 0.90±0.12 Bone density: 8 weeks: 0.27±0.08 16 weeks: 0.63±0.09 Trabecular pattern 8 weeks: 0.30±0.09 16 weeks: 0.50±0.09	Lamina dura - 8 and 16 weeks:YES (p<0.001) Bone density - 8 and 16 weeks:YES (p<0.001) Trabecular pattern -8 and 16 weeks:YES (p<0.001)	Postoperative pain (VAS) was high on the first day and decreased on subsequent days for both groups; however, it was lower in the group with PRF (p<0.05). The percentage of facial edema was higher for those without PRF on the third day and gradually reduced in the following days (p<0.05). Regarding bone healing (lamina dura, bone density and trabecular pattern) (p<0.001) it was greater in week 16 in relation to week 8 in sockets with PRF
Nilima Kumar, et al.[30]	Extraction of impacted mandibular third molar	Edema, probing depth, bone density	Clinical and radiographic evaluation	Lamina dura50% absent50% considerably thinned Total densityPRF: 68.7% mild to moderate.31.3% severe increase Trabecular patternPRF: 68.7% moderate25% severe1% mild	Hard lamina: 60% absent40% considerably thinned Total density: 93.3% mild to moderate.6.7% severe increase. Trabecular pattern: 93.3% moderate6.7% mild	The difference was not statistically significant	Application of PRF reduces the severity of immediate postoperative sequelae, reduces preoperative pocket depth, and accelerates bone formation.

Table 2 Continued.....

Author	Dental piece - reason for extraction	Variables	Evaluation method	PRF result in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue.	Result of physiological healing and/or biomaterials in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue	Statistical significance YES/NO	Effect of platelet concentrate reported in the study
Amrendra Kumar, et al.[31]	Third molar extraction	Pain, edema, bone density	Clinical and radiographic evaluation	Postoperative: 107.40Month 1: 114.01Month 2: 124.13Month 6: 135.15	Postoperative: 107.55Month 1: 108.45Month 2: 115.59Month 6: 124.26	revealed a statistically significant difference (P=0.01) for pockets with a dense homogeneous trabecular pattern, a borderline statistically significant difference in trabecular pattern for bone volume (P=0.06) favoring platelet-rich concentrate use, and there were no significant differences for trabecular separation (P =0.66), trabecular length (P = 0.16), trabecular width P = 0.16), and trabecular number (P = 0.38).	PRF proved to be an autologous biomaterial with useful characteristics that enabled effective filling of post-extraction bone defects and faster bone regeneration.
Aayush Malhotra, et al.[32]	Mandibular third molar extraction	Swelling, periodontal pocket depth, alveolar bone height, bone density	Clinical and radiographic evaluation	Postoperative alveolar bone heightImmediately: 4.34±0.31 mm1 month: 2.84±0.18 mm2 month: 2.15±0.15 mm4 month: 1.30±0.11 mm	Postoperative alveolar bone height Immediately: 4.58±0.29 mm1 month: 3.79±0.19 mm2 month: 2.72±0.16 mm4 month: 1.89±0.12 mm	It was statistically significant 1, 2 and 4 months after the operation P < 0.001	PRF proved to be an autologous biomaterial with useful characteristics that enabled effective filling of the post-extraction bone defect and faster bone regeneration.
Manzoor Mohammad, et al.[33]	Extraction of impacted mandibular third molars	Soft tissue and bone healing	Clinical evaluation. Radiographic evaluation	PRF: week 12, 100.0%	week 12, 90.0%	Yes: 12 weeks (p=0.237)	PRF gel has a beneficial effect on socket healing

Table 2 Continued.....

Author	Dental piece - reason for extraction	Variables	Evaluation method	PRF result in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue.	Result of physiological healing and/or biomaterials in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue	Statistical significance YES/NO	Effect of platelet concentrate reported in the study
Iwona Niedzielska, et al.[34]	Exodontia of 2 homonymous maxillary or mandibular pieces: endodontic failure, crown fracture.	Alveolar bone height and width Bone density	Clinical evaluation, radiographic evaluation (CBCT)	PRF:Width: 9.43±1.74mm Height: 1.49±0.84mm Bone quality: A: 308.16±128.15	Blood clot:Width: 9.15±1.51 Height: 1.85±0.86 Bone quality: A: 279.40±136.23	NO immediate post-exodontia: width and height of alveolar process. YES 6 months post-exodontia: width and height of alveolar process (p=0.0085)	Changes in the alveolar process. Changes in the height of the alveolar process.
Warisara Ouyyamwongs, et al.[35]	Extraction of mandibular premolars prior to orthodontic treatment	Soft tissue and bone healing	Clinical and radiographic evaluation	Week 0: 23.39±7.62 mmWeek 2: 23.02±6.74 mmWeek 4: 31.32±14.50 mmWeek 6: 31.28±13.42 mmWeek 8: 35.85±15.15 mm	aDTM-PRFWeek 0: 37.17±7.21 mmWeek 2: 38.91±6.00 mmWeek 4: 45.22±13.27 mmWeek 6: 48.03±8.95 mmWeek 8: 44.84±9.12 mm	The results were only statistically significant during the first 6 weeks (P= 0.05)	Application of aDTM with PRF membrane is useful for ridge preservation by reducing horizontal ridge collapse and promoting bone healing as shown clinically and radiographically.
Rahul Sharma, et al.[36]	Extraction of impacted mandibular third molars	Soft tissue and bone healing	Clinical and radiographic evaluation	Bone maturation1 day: 0.50±0.51mmWeek 1: 1.35±0.59 mmWeek 4: 2.05±0.55 mmWeek 8: 2.55±0.51 mm	Bone maturation 1 day: 0.35±0.49 mmWeek 1: 0.95±0.60 mmWeek 4: 1.75±0.44 mmWeek 8: 2.35±0.49 mm	At no time was a statistically significant difference observed between the two groups. P< 0.05	The use of PRF to improve soft and hard tissue healing. Although bone regeneration could be differentiated in both groups only at the second month interval, pain scores were better with PRF in most cases.
Ankit Sharmaa, Snehal Ingoleb, et al.[37]	Extraction of mandibular teeth from both sides	Wound healing and bone regeneration	Clinical and radiographic evaluation	Bone regeneration. Gray scale16 weeks:PRF: 4,214±5.1 mm	Bone regeneration. Gray scale 16 weeks: Clot: 3.298±4.09 mm	There was no statistically significant difference in the gray scale value (p value > 0.05)	PRF is significantly better at promoting soft tissue healing and also accelerates bone formation in the extraction socket

Table 2 Continued.....

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BS Shilpa, Prasad V. Dhadse, et al.[38]	Extraction of teeth due to root fractures, endodontic failures, non-restorable carious lesions, prior implant placement	Alveolar bone level	Clinical and radiographic evaluation (periapical)	PRF: 14.1±1.0mmmes 3: 12.7±0.8	N/E	N/E	Ridge preservation using PRF as space filler after atraumatic extraction was found to be an effective procedure for implant placement.
Baratam Srinivas, et al.[39]	Upper or lower teeth with/without chronic periodontal condition	Alveolar bone height and bone density	Histological and radiographic evaluation	PRF:24 hours and 3 months Bone height: 24 hours: 13.93±3.56mm 3 months: 12.28±3.84mm Bone density (socket): 24 hours: 319.79±95.472 3 months: 564.76±94.856 Periapical region: 24 hours: 530.39±203.289 3 months: 748.02±202.878	Blood clot:24 hours and 3 months Bone height: 24 hours: 14.68±4.32mm 3 months: 12.78±3.82mm Bone density (socket): 24 hours: 194.82±78.986 3 months: 295.87±87.217 Periapical region: 24 hours: 518.84±266.518 3 months: 613.15±237.926	YES: 24h - 3months - WITHOUT PRF Alveolar height: p<0.001 Bone density: 0.003 Periapical region: 0.043 YES: 24h - 3months - WITH PRF Alveolar height: p<0.001 Bone density: p<0.001 Periapical region: 0.05	Appreciable healing of wounds and bone. Regeneration was observed in the experimental group compared to control sites where PRF was not used, corroborating the use of PRF as a cost-effective autologous material for socket preservation and future rehabilitation.
Tipu Sultan, et al.[40]	Extraction of upper premolars	Soft tissue and bone healing	Clinical and radiographic evaluation	PRF-CSMean horizontal contraction of: 1.27±0.82 mmVertical resorption for mesial bone height: MBH = 0.56±0.25 mmBuccal bone height: BBH = 1.62±0.91 mmBone height palatal: PBH = 1.39±0.87 mm.	PRF-XDistal bone height: D BH = 0.44±0.45 mmPalatal bone height: P BH = 0.39±0.34 mmMean horizontal contraction of: 1.40±0.85 mmVertical resorption for bone height medial: MBH = 0.28±0.14 mm Buccal bone height: B BH = 0.63±0.39 mm Palatine bone height: P BH = 0.39±0.34 mm	The difference was insignificant between the groups (all p>0.05)	PRF-CS grafted sites showed no significant differences with PRF-X grafted sites in linear and volumetric dimensional changes and may show clinical benefits for socket augmentation.

Table 2 Continued.....

Author	Dental piece - reason for extraction	Variables	Evaluation method	PRF result in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue.	Result of physiological healing and/or biomaterials in preservation of the alveolar ridge (width, length, depth) and/or quality of bone tissue	Statistical significance YES/NO	Effect of platelet concentrate reported in the study
Deborah Sybil, et al.[41]	Mandibular third molar extraction	Soft tissue and bone healing	Clinical and radiographic evaluation	Bone heightPreoperativePRF: 2.88±0.78 mm Month 3:PRF: 1.92±0.86 mm Month 6PRF: 1.44±0.77 mm	Bone heightPreoperative 2.84±0.85 mm Month 3: 2.24±0.83 mm Month 6: 1.76±0.83 mm	Yeah. A greater improvement was observed on the control than on the test side (P < 0.001)	PRF is a very viable and useful biomaterial for soft tissue healing and relief of patient symptoms; however, it does not help in the healing of hard tissues with respect to cortical bone.
Mathew P. et al.[42]	Extraction of impacted lower third molar	Soft tissue and bone healing	Clinical and radiographic evaluation	Percent bone fillPRF: 57.90 (SD±26.789) %	Bone filling percentage Clot: 46.74 (SD±17.713) %	The mean value of the percentage of bone fill was significantly higher for patients in the PRF category. (P< 0.05)	There was evidence of improved bone regeneration and soft tissue healing occurring in response to PRF.

Discussion

The purpose of this research is to analyze the use of platelet-rich fibrin in the bone regeneration of post-exodontic tooth sockets; PRF has been used in dentistry in an attempt to reduce postoperative complications and improve bone regeneration from these platelet concentrates. However, there is no evidence of significant values in comparison with physiological regeneration.

Alzahrani & cols,[20] in their study conducted in 2017, in which the study variables were alveolar ridge width and post-exodontic bone regeneration evidenced that the loss of ridge width was lower in the test group (PRF) 8.58% compared to the control group which was 13.54% at the fourth week of control; bone filler in the test group was 74.03±1.22%, in the control group 82.54±3.33%.[20] Agrees with Doiphode & cols,[21] in the study they indicated that PRF demonstrates good results when used as an adjunct for bone regeneration, although there was no significant difference in mean bone values. At the second month of control in the test group bone density showed 120.60±8.42 mm, while in the control group it was 75.87±8.38 mm.[21] Varghese & cols,[22] in their study conducted in 2017, about postextraction bone healing, reported that the percentage of bone fill was significantly higher for the test group (p<0.05), evidenced better bone regeneration with the use of PRF.[22]

Andwanter & cols, for their part,[23] in 2016 did not observe significant differences for bone filling radiographically (-0.06±3.84mm p> 0.07).[23] Which coincides with Kanokporn & cols, who, in their study carried out in 2019, indicated that there was no significant improvement in new bone formation after extraction in the test group as in the control group (p> 0.05). They further mention that, the use of PRF does not improve bone regeneration after tooth extraction in relation to physiological healing.[24]

Baslarli & cols,[25] in their 2015 study, reported that there was no significant difference in methylene diphosphonate uptake as an indicator of improved bone healing at 1 month control, PRF 4.71% and control group 4.6%.[25]

Valdoné & cols, in 2022 through their study showed that there was no significant difference in bone tissue dimensions after tooth extraction (p> 0.04)[24] Unlike the study carried out by El Zahra & cols, in 2015, who indicate that there was a difference in bone height between the test side (17.6 mm) compared to the control side (15.3 mm).[26] Fontes & cols,[28] reported in their study conducted in 2020 that tissue mineralization using PRF may have some potential to increase it, however, no significant differences were evidenced between the test and control group (P> 0.05).[27] Gasparro et al,[29] in 2020 reported that PRF shows better results in clinical insertion loss (CAL) gain and probing depth reduction, but there was no significant difference, PRF (0.47±0.41 mm) compared to the control group (0.60±0.46 mm).[28] Guzmán & cols,[30] in their 2017 study, showed that there was a difference in bone tissue healing at 60 days of control (p< 0.015).[29] Coinciding with Jeyaraj & cols[31] in 2018, they indicated that in the test group there was faster bone regeneration than in the control group (p< 0.001).[30] Kapse & cols,[32] in their 2018 study, by radiographic evaluation noted bone healing (trabecular pattern, lamina dura, bone density) was higher at week 16 in the test group (p<0.001).[31] Kumar & cols,[34] in 2015, by clinical and radiographic evaluation reported that the application of PRF accelerates bone formation in the control

group total bone density was 31.3% and in the control group 6.7%.[32] Agrees with Malhotra & cols,[33] in their study conducted in 2020, in which they evaluated bone density by radiographs, indicated that the use of PRF induces much faster bone regeneration. It was statistically significant 1, 2 and 4 months after extraction ($p<0.001$).[33] Kumar & cols,[35] in 2016, in their study conducted indicated that PRF is useful post extraction for faster bone regeneration, showed a statistically significant difference ($p<0.01$).[34] Manzoor & cols, in their study conducted in 2018, where they evaluated soft tissue and bone tissue healing, referred that PRF has a beneficial effect on both soft tissue and bone healing, there was a significant difference at week 12 control ($P< 0.02$).[35] Niedzielska & cols,[37] in the study performed in 2022, evaluated the height and width of the alveolar bone post-exodontia and reported that there were changes in the height of the alveolar process, presenting a significant difference ($p< 0.008$).[36]

Ouyyamwongs & cols,[38] in their study conducted in 2019 where the study variables were soft tissue and bone tissue healing, after radiographic evaluation, indicated that the results were significant during the first 6 weeks in the test group ($p<0.05$), further mentions that the use of PRF is useful for ridge preservation and promotes better bone healing.[37] However, Sharma & cols,[39] in 2019 in their study in which they evaluated bone tissue healing by radiographic analysis, indicated that no significant difference was observed between the two groups ($p>0.05$), because the differentiation in bone regeneration could only be differentiated in the second month interval.[38] Sharma & cols,[40] in their study conducted in 2020, in which they investigated about wound healing and bone regeneration, by clinical and radiographic evaluation found that it was higher in the PRF test group (4.21±5.1mm) compared to the control group (3.2±4.09 mm) ($p>0.05$), they also indicate that PRF accelerates bone formation in the alveolus post-extraction.[39] Shilpa & cols,[41] in 2017 in their study in which they evaluated the post-exodontic alveolar bone level of dental pieces, by periapical radiographic analysis said that the test group had better PRF bone regeneration (14.1±10.mm), indicating that ridge preservation using PRF is an effective procedure for implant placement.[40] Srinivas & cols,[42] in 2018 evaluated in their study alveolar bone height and postexodontic bone density by histological and radiographic evaluation, they reported that, if there were significant differences in the test group in relation to the control group, alveolar height ($p<0.001$), bone density ($p<0.001$). they observed better bone regeneration in the test group so they corroborate that the use of PRF helps in the preservation of the alveolus.[41] Sultan & cols,[43] 2020, conducted a study where bone healing was evaluated by clinical and radiographic analysis, they showed that the difference was insignificant between test and control group ($p>0.05$), they also said that PRF showed no difference in dimensional and volumetric changes, but could show clinical benefits for alveolar augmentation.[42] Sybil & cols,[44] , in their 2020 study investigated bone healing by radiographic analysis, and reported that they observed significant differences for patient symptom relief, but not for hard tissue healing with respect to cortical bone, PRF (1.44±0.77mm) at 6 months, compared to the control group (1.76±0.83mm).[43]

Conclusion

The use of PRF reinforces and induces post-exodontic bone regeneration, preserving the dimensions of the alveolar ridge both in width and high width of the alveolar ridge, it is also of great help in cell proliferation which decreases bone loss in a longer postoperative time, however, current evidence reports that in most cases there is no significant difference between the test and control groups after tooth extraction.

Acknowledgments

None

Conflicts of interest

The authors declare that there are no conflicts of interest.

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