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Evaluation of efficacy and sustainability of different platelet concentrates in regenerative endodontics: A systematic review

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Abstract

Background: Regenerative endodontics has emerged as a transformative field in modern dentistry, offering new hope for the treatment of dental pulp and periapical tissues damaged by trauma, infection, or developmental anomalies. This systematic review offers an in-depth exploration of an innovative approach that combines regenerative endodontics with platelet concentrates, a biologically active substance, to enhance the potential for dental tissue regeneration. Regenerative endodontics is focused on reinstating the vitality and functionality of dental tissues, particularly dentin, pulp, and periapical structures, by harnessing the body's natural regenerative capabilities. The process involves thorough sterilization of the root canal system, coupled with the utilization of bioactive agents such as stem cells and growth factors, aimed at stimulating the regeneration of damaged tissues. Platelet concentrates, including platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), obtained from the patient's own blood, contain a significant quantity of growth factors crucial for tissue revitalization. The primary objective of this study was to conduct a comprehensive literature review to identify research that adheres to the principles of evidence-based dentistry. The goal was to determine which autologous platelet concentrates are most effective in releasing growth factors for regenerative endodontics, including the recent platelet concentrate known as albumin PRF or alb PRF.

Conclusion: Progress in technological innovations within this field has yielded promising results with respect to the application of platelet concentrates in regenerative endodontic therapy. This systematically reviewed literature concludes that procedures with platelet concentrates play a successful role in treating necrotic or immature teeth. Hence the platelet concentrates can save a tooth by the development of root.

Keywords: Regenerative endodontic therapy, platelet concentrates, platelet-rich fibrin, ALBUMIN PRF, L-PRP, I-PRF, Revitalisation, revascularisation

Introduction

The rationale of endodontics declares that any endodontically affected tooth can be protected if the root canal structure can be sealed either surgically or non-surgically if the periodontal condition is healthy. Regeneration is the natural process through which animals or humans replace or restore damaged or missing organs to restore normal body parts. Regenerative growth is often initiated by pathways associated with cell death resulting from damage [1]. Traumatic injury, physical abuse, chemical irritation, periodontal disease, or microbial infection plays as a primary etiology in causing pulpal and periapical disease (irreversible pulpitis and apical periodontitis). The ideal goal of treating such established disease is to achieve wound healing [2, 3]. Wound healing is an essential process that aids in the restoration of the original structure and biological function of damaged tissue by combining repair and regeneration [4]. In the realm of endodontics, the concept of regeneration encompasses a range of treatment strategies. These encompass vital pulp therapy techniques, including direct pulp capping, indirect pulp capping, pulpotomy, and apexogenesis, all of which focus on maintaining the dental pulp's vitality. Additionally, there are non-vital pulp therapy procedures like pulpectomy, apexification, and revascularization, which are used when the dental pulp is non-vital or infected. These treatments aim to address various conditions and promote the restoration and healing of dental tissues [5].

To stimulate the regeneration of pulp tissue, regenerative endodontics utilizes a combination of three essential components within the root canal space: stem cells, biomimetic scaffolding, and bioactive growth factors [6]. Regenerative endodontic procedures (REPs) have the capacity to promote root development, enhance canal wall thickness, and stimulate apical closure [7, 8]. Conventional root canal therapy typically entails disinfection through a combination of antibiotics and calcium hydroxide. In regenerative procedures, it is recommended to utilize biological disinfection techniques. These materials should be employed in diluted concentrations to encourage cell growth while avoiding harm. Subsequently, the root is filled with a blood clot that forms as a result of bleeding from the apical tissue. This blood clot functions as a scaffold and contains growth factors that attract stem cells, likely originating from the periapical papilla [9, 10]. Nonetheless, a persistent challenge has been the inability to generate an ideal blood clot and limited tissue regeneration.⁽¹¹⁾ As per certain reports, incomplete bleeding hinders the formation of an appropriate clot [12, 13]. Scaffolding materials serve the purpose of aiding in the repair, proliferation, migration, and organization of cells necessary for the structural and functional replacement of the target tissue [14]. Hence, it is important to note that even the most ideal procedure or scaffold may not possess the ability to induce pluripotent stem cells, potentially resulting in unpredictable outcomes in the regeneration of pulp-dentin tissue [15, 16]. The American Association of Endodontists has established a regenerative endodontic protocol that entails the flooding of root canals with blood via over-instrumentation. This approach is specifically designed for the management of teeth exhibiting necrotic pulp and an immature apex. Furthermore, the utilization of platelet-rich plasma (PRP), platelet-rich fibrin (PRF), or other autologous platelet concentrates as an alternative for inducing a blood clot is also acknowledged as a viable alternative (APCs) [17]. Platelets are cellular components that circulate in the bloodstream. Their primary and essential roles include responding to vessel injuries, regulating angiogenesis (the formation of new blood vessels), and contributing to the innate immune response [18]. Platelets serve important functions in hemostasis, inflammation, and regeneration. They are produced from megakaryocytes and are swiftly recruited to the site of vascular injury to facilitate hemostasis [19]. Autologous platelet concentrates (APCs) are derived from the patient's own blood, comprising activated platelets encased within a fibrin matrix scaffold. These APCs release crucial growth factors and cytokines that hold a central role in tissue regeneration. Their functions encompass the stimulation of cell proliferation, differentiation, extracellular matrix synthesis, facilitation of chemotaxis, and support for angiogenesis, the formation of new blood vessels. Due to their capacity to expedite the healing process in both soft and hard tissues, APCs have been successfully applied in both the medical and dental fields for an extended period.⁽²⁰⁾ The POSEIDO (Periodontology, Oral Surgery, Esthetic, and Implant Dentistry Organization) has put forth a classification system for autologous platelet concentrates (APCs). This system encompasses a range of categories, including Pure Platelet-Rich Plasma (P-PRP), Leukocyte- and Platelet-Rich Plasma (L-PRP), Pure Platelet-Rich Fibrin (P-PRF), Leukocyte-Poor Platelet-Rich Fibrin, and Leukocyte- and Platelet-Rich Fibrin (L-PRF) [21]. products, including fibrin glue, PRP, PRF, A-PRF, t-PRF, i-PRF, PRF lysates, and CGF Platelet concentrates have evolved significantly since their introduction as a source of blood proteins enriched with

growth factors aimed at promoting wound healing. These advancements have brought about the introduction of various innovations and products [22]. The concept of platelet concentrates originated in the field of haematology [23]. The scientific evidence concerning the potential advantages of employing autologous platelet concentrates (APCs) in regenerative therapies remains inconclusive. According to certain studies, both PRP and PRF appear to have a positive impact primarily on the early stages of healing in both hard and soft tissues, but the evidence suggests that their effect on final therapeutic outcomes may not always be significant [24]. Additionally, it has been documented that the utilization of platelet concentrates may have a positive impact on postoperative inflammation and provide relief from pain [25, 26].”

Aim

The objective of this current study was to conduct a systematic review of the existing literature while adhering to the standards of evidence-based dentistry. The primary goal was to ascertain which autologous platelet concentrates demonstrate superior effectiveness in releasing growth factors for regenerative endodontics.

Materials and Methods

The literature review was conducted systematically, following Goodman's methodology [15], this methodology consists of several key steps, which include defining the research question, developing a strategy for conducting a literature search, executing the literature search and obtaining relevant articles, extracting data from the selected articles, and finally, interpreting and evaluating the evidence gathered from the literature.

Research Question

Platelet concentrates are known for their enhanced healing properties, which is why a diverse range of platelet concentrates has been employed in the field of regenerative endodontics. The research question to be addressed in this systematic review was which platelet concentrates have a greater capacity to produce faster periapical healing, Apex closure, Root lengthening, and Dentine wall thickening

PICOS (Population, Intervention, Comparison, Outcome)

- **Population** - regenerative endodontic therapy
- **Intervention**- platelet concentrates
- **Comparison**- various other platelet concentrates
- **Outcome**- Periapical healing, Apex closure, Root lengthening and Dentine wall thickening

Inclusion Criteria

Prior to examining the retrieved titles, abstracts, and articles, the following inclusion criteria were agreed upon:

- Randomized control trials
- *In vivo* studies
- Full text articles in the english language
- Comparative studies

Exclusion criteria

- *In vitro* studies
- Human studies evaluating platelet concentrates in a case report or case series if controls were not present

Information sources and search strategy and study selection: An electronic search was conducted on the four main databases of PubMed, EMBASE, Cochrane, and Google scholar. The keywords and phrases that were used included "platelet", "platelet concentrate", "platelet rich plasma", "platelet rich fibrin", "plasma rich in growth factor",

"injectable platelet rich fibrin", "PRF", "PRP", "I-PRF", "PRGF", "regeneration", "endodontic", "dentine pulp complex", "revitalization" in this electronic research alone or in combination by means of Boolean operators include "AND", "OR" and "NOT".

Table 1: Keywords and search data base summary

Keywords	Database				No of Articles
	PubMed	Cochrane	LILACS	Science Direct	
(Platelet rich plasma) and (Regeneration) and (Endodontic) and (Platelet concentrate)	30	2	5	505	542
Platelet concentrates in endodontic therapy	49	11	15	224	299
Various platelet concentrates in regenerative endodontic therapy)	24	1	2	156	183
Total	103	14	22	885	1024

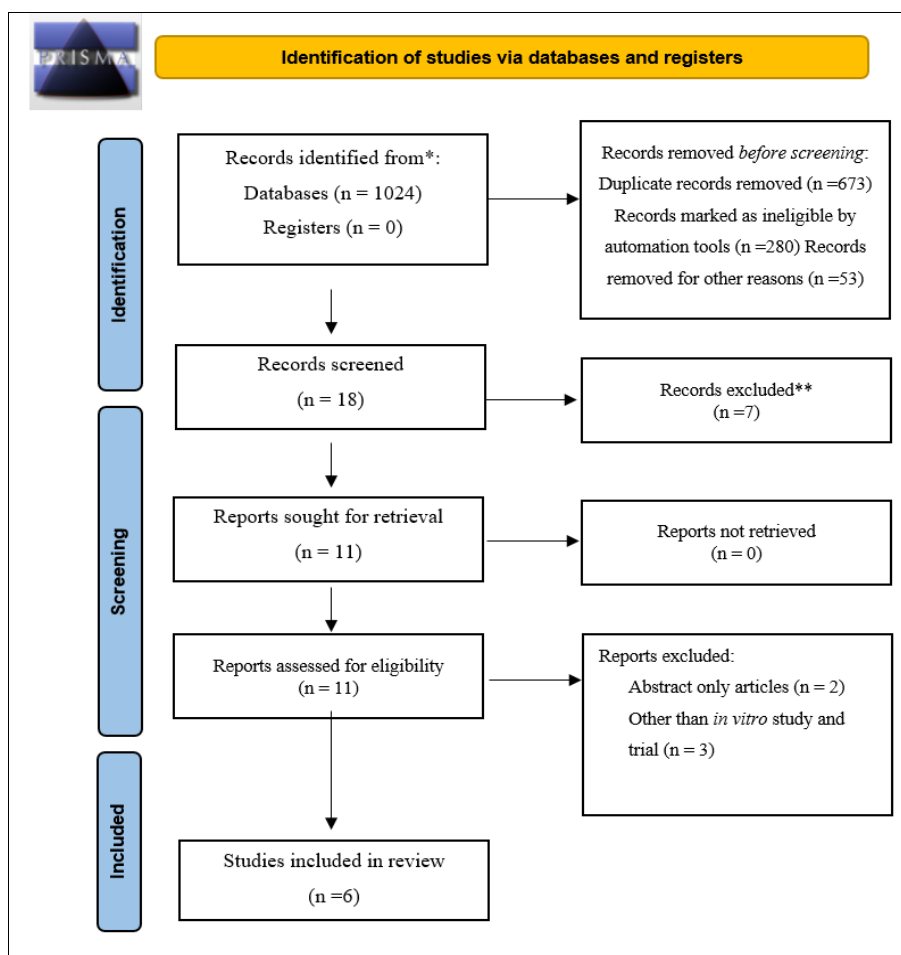


Fig 1: Prisma flow diagram

Data collection and analysis

Data Extraction: Data extraction encompassed the collection of general characteristics of the studies and variables related to the outcomes. This process involved the creation of an Excel spreadsheet using Microsoft Office (Microsoft, Redmond, WA), which organized and recorded information for each individual study (Tables 2 & 3)

- Author name
- Year
- Type of study
- Sample selected for the study
- Medication and time
- Preparations used
- Restoration method
- Measuring time

Quality assessment

"Individual risk of bias assessment was conducted using the Cochrane risk assessment tool. The quality of all studies included in the analysis underwent independent evaluation for risk of bias. This assessment focused on five key parameters: random sequence generation, allocation concealment, selective reporting, and the presence of other potential sources of bias. For each of these parameters, two reviewers assessed and provided their judgment using one of three options: low risk of bias, high risk of bias, or unclear risk of bias. This assessment adhered to predefined criteria as outlined in the study protocol. The evaluation of bias risk in individual studies was then used to generate an overall risk-of-bias assessment for the entire body of evidence

Table 2: Data extraction table

S. No	Author name	Year	Type of study	Sample selected for the study	Medication and time	Preparations used	Restoration method	Measuring time
1	Hongbing Lv <i>et al.</i> ^[27]	2018	A retrospective controlled cohort study	“Patients having nonvital, immature incisors or premolars with radiographic evidence of periapical lesions were included.”	2% lidocaine without adrenaline, antibiotic paste flushed with sterile normal saline, irrigation with 10ml of 17% EDTA solution	“5 ml of whole blood was drawn into 10-ml test tubes without anticoagulant reagent and was centrifuged at 400 g for 10 min. The PRF layer was separated using sterile scissors, and PRF clots were pressed into a membranous film with sterile dry gauze. The PRF membrane was then cut into approximately 3 × 3-mm ² pieces.”	Group 1: Regenerative endodontic Therapy with a Blood clot Group 2: Regenerative endodontic therapy with a PRF	1 year follow up study
2	Hazim Mohamed Rizk ^[28]	2019	A split mouth double- blinded Randomized Controlled Trial	15 patients with bilateral maxillary immature permanent central incisors with necrotic pulp.	2% lidocaine with 1:100,000 adrenaline, 10% povidone iodine (BETADINE antiseptic solution), Irrigation with 2% NaOCL followed by irrigation with EDTA 17%, Filled with triple antibiotic paste containing ciprofloxacin tablets—250 mg; Metronidazole tablets—250 mg and minocycline capsules 100 mg	PRP preparation by Dohan and Choukroun method. Blood was centrifuged immediately using a soft spin at 2,400 rpm for 10 mins, again centrifuged at a higher speed at 3,600 rpm for 15 mins. PRP is removed separately and mixed with 0.5 ml 10% calcium chloride and soaked on a 2x2 ml of sterile collagen sponge	Group 1: Regenerative endodontic Therapy with a Blood clot Group 2: Regenerative endodontic therapy with a PRP	3,6,9,12
3	Ayca Tuba Ulusoy ^[29]	2019	A Prospective Randomized Trial	“Sixty-seven healthy children (aged 8-11 years) with 88 immature necrotic incisors”	2 step revascularization Step 1: 2% lidocaine with 1: 100000 adrenaline; 20 mL 1.25% sodium hypochlorite and a triple antibiotic paste containing 20 mg of clindamycin, 20mg of ciprofloxacin and 20 mg of metronidazole, temporary sealing with 4mm thick conventional GIC Step 2: 2% mepivacaine, 2% chlorhexidine irrigation, antibiotic paste removal by gentle irrigation with 10ml sterile saline, 1ml of 17% EDTA irrigation	“20 mL blood was placed in the test tube containing 15 mL citrate solution for PRP preparation. Citrated blood was centrifuged for 15 minutes at 1250 revolutions per minute (rpm) to obtain PRP without erythrocytes and leukocytes. The PRP sample was placed into the canal space to a level 3 mm below the cementoenamel junction (CEJ) using sterile 27-G needle tips” “10 mL blood was collected as with group 1 in a sterile tube without anticoagulant and centrifugated immediately for 10 minutes at a speed of 3000 rpm. The PRF was removed from the test tube with sterile pliers, and the excess red blood cells were removed with sterile gauze pad. The prepared PRF sample was then cut into fragments, and the fragments were placed incrementally in the canal space to a level of 3 mm below the CEJ using sterile hand pluggers” “PRP group, and then a second centrifugation was performed for 10 minutes at 4000 rpm. The PP concentrated at the bottom was taken, leaving platelet-poor plasma.” “The PP sample was placed into the canal space to	Group 1- PRP group Group 2 - PRF group Group 3 -PP group	Every 3 months for first year

						a level 3 mm below the CEJ using sterile 27-G needle tips.”		
						“Bleeding from the periapical region was induced with a #15 K-file 1-2 mm beyond the apex. The tooth was allowed 10 minutes to form a BC after the bleeding reached to at least 3mm below the level of the CEJ.”	Group 4- BC group	
4	A.S Elsheshtawy <i>et al.</i> ^[30]	2020	a randomized controlled trial	Twenty-six healthy patients with immature permanent anterior teeth with necrotic pulps	“Local analgesia was delivered using Articaine 4% and 1: 200 000 Epinephrine, irrigation with 20 mL of 5.25% sodium hypochlorite, Triple antibiotic paste, using Minocycline 100mg, ciprofloxacin 250 mg and Metronidazole 500mg”	In the experimental group, Platelet-Rich Plasma (PRP) was prepared following the protocol outlined in Dohan <i>et al.</i> (2006)	Experimental group: revitalization endodontic procedure using autologous platelet-rich plasma (RET-PRP)	Baseline and 12 months
						In the control group, a pre-curved size 20 K-file was inserted to a depth of 2 mm beyond the apical foramen to induce bleeding, which was confirmed under magnification. Subsequently, a slightly moistened, sterile cotton pellet was positioned within the canal, approximately 3-4 mm apical to the Cementoenamel Junction (CEJ), and left in place for 7-10 minutes to facilitate the formation of a blood clot.	Control group interventions: regenerative endodontic procedures using blood clot	
5	Veera Jayadevan ^[31]	2021	A Prospective clinical study	30 traumatized immature non-vital maxillary incisors in 28 patients aged between 8-27 years.	“Local anesthesia containing 2% lignocaine hydrochloride and 1:80,000 adrenaline was administered irrigation with 1.5% sodium hypochlorite (NaOCl) using a 30-G side venting needle about 2 mm short of the root end. The canal was then irrigated with saline and 17% ethylenediaminetetraacetic acid (EDTA). Minimal canal debridement was done using K-files, modified triple antibiotic paste was placed containing an equal proportion (1:1:1) of sugar-free tablets of ciprofloxacin, metronidazole and cefaclor was powdered and mixed with 1 ml of propylene glycol (vehicle) to obtain a stock solution of 100mg/ml, which was diluted to obtain a final concentration of 1mg/mL.”	“A-PRF, 10 ml of intravenous blood was drawn into a tube without anticoagulant and centrifuged at 1500 rpm for 14 min”	Advanced PRF	6months and 12 months
						“For PRF, 10 ml of intravenous blood was drawn into a tube without anticoagulant and centrifuged at 2700 rpm for 12 min.”	PRF	
6	Asha Nara <i>et al.</i> ^[32]	2021	A clinical study	10 patients with non-vital immature permanent single rooted teeth	A 20ml solution of 1% sodium hypochlorite was used, and the Triantibiotic paste was prepared and inserted into the canals below the Cementoenamel Junction (CEJ)	“For Group I, using no # 20 k-file apical bleeding was induced and allowed for blood clot to form till cementoamel junction. After this, white MTA was placed to a thickness of 3mm followed by GIC and Composite restoration	Group I: blood clot	18 months
						For Group II, the I-PRF was prepared using Choukroun’s method, where 6 ml of venous blood was centrifuged at 60 G at 700 RPM for 3 min. Freshly prepared i-PRF (0.5ml) was placed in the coronal third of the canal MTA placed in coronal third of the root, restored with GIC, Composite”	Group II: i-PRF	

Results

Table 3: Outcome of the data included in the studies

S. No	Author	Year	Outcome	Result
1	Hongbing Lv <i>et al.</i> ^[27]	2018	At 1year follow up, periapical healing, apical closure, root lengthening, dentinal wall thickening, clinical sign and symptom resolution was similar in both the groups	There was no statistically significant difference between the groups in terms of root development, periapical healing and clinical sign resolution ($P>0.05$)
2	Hazim Mohamed Rizk ^[28]	2019	All the 26 treated teeth survived during 3,6,9 and 12 month followup period with 100% success rate	“PRP-treated teeth showed a statistically significant increase in radiographic root length and width, periapical bone density, and a decrease in apical diameter when compared with blood clot. At the end of 12 months, all treated teeth did not respond to the sensibility test. Blood clot displayed a significantly higher amount of crown discoloration compared to the PRP group.”
3	Ayca Tuba Ulusoy ^[29]	2019	With the exception of 2 teeth in both the Platelet-Rich Fibrin (PRF) group and the Blood Clot (BC) group, all other teeth demonstrated similar and high success scores in terms of periapical healing, radiographic root development, and a positive response to sensitivity tests. This assessment was made after an average follow-up period of 28.25 ± 1.2 months	“The linear measurements indicated a similar increase in root length and width among all groups ($P>0.05$), the RRA of the BC group was significantly greater than those of the PRF and PP groups, and the RCA of the BC group was significantly greater than PRP, PRF, and PP (all $P<0.05$) when the follow-up time was not used as a factor.”
4	A.S. Elsheshtawy <i>et al.</i> ^[30]	2020	Overall success rate was 90% i.e., 28 out of 31 teeth	Changes in RL, RDT, AFW, RRA and PAD, over time, were found to be significant for both groups.
5	Veera Jayadevan ^[31]	2021	The survival rate for teeth treated with A-PRF was 78.5% and the survival rate for teeth with PRF was 77%.	There was a statistically significant difference found between the groups in root thickness and root length.
6	Asha Nara <i>et al.</i> ^[32]	2021	Increases rate of root lengthening and periapical healing was seen in injectable PRF	Significant difference in both the groups from baseline to postoperative clinical findings.

RRA- Radiographic root area, PRP - Platelet rich plasma, PP- Platelet pellets, PRF- Platelet rich fibrin, BC- Blood clot

Table 4: Level of evidence

S. No	Author	Study design	Level of evidence
1	Hongbing Lv <i>et al.</i> ^[27]	a retrospective controlled cohort study	2
2	Hazim Mohamed Rizk ^[28]	A Split Mouth Double-blinded Randomized Controlled Trial	1
3	Ayca Tuba Ulusoy ^[29]	A Prospective Randomized Trial	1
4	A.S. Elsheshtawy <i>et al.</i> ^[30]	a randomized controlled trial	1
5	Veera Jayadevan ^[31]	A Prospective clinical study	1
6	Asha Nara <i>et al.</i> ^[32]	A clinical study	1

Quality Assessment - Risk of Bias: In the study's risk-of-bias evaluation, it was categorized as having a "High risk" of bias if it did not receive a "LOW" rating in three or more of the four main categories. It was classified as being of "Moderate Risk" if two out of the four categories did not

receive a "LOW" rating. In contrast, it was designated as "Low Risk" if all four categories, namely randomization, assessor blinding, and completeness of follow-up, received an "Adequate" rating

S. No	Author	Random sequence generation	Allocation concealment	Selective reporting	Incomplete outcome data	Blinding of outcome assessment	Blinding participants and personals
1	Hongbing Lv <i>et al.</i> ^[27]						
2	Hazim Mohamed Rizk ^[28]						
3	Ayca Tuba Ulusoy ^[29]						
4	A.S. Elsheshtawy <i>et al.</i> ^[30]						
5	Veera Jayadevan ^[31]						
6	Asha Nara <i>et al.</i> ^[32]						

Low risk of bias  High risk of bias  Unclear risk of bias 

Discussion

In this systematic literature review, a comprehensive selection of clinical trials was considered to assess the effectiveness of

various platelet concentrates in regenerative endodontic therapy. One of the studies included in this review was the retrospective controlled clinical study conducted by Hongbing

LV *et al.* in 2018 (reference #27). In this study, platelet concentrates were employed as a structural framework in regenerative endodontic treatment, with the objective of evaluating and contrasting the efficacy of platelet-rich fibrin (PRF) against that of a blood clot in terms of stimulating root development and facilitating the recovery of periapical lesions. Two groups were involved in the study: Group 1 received regenerative endodontic therapy with a blood clot, while Group 2 received regenerative endodontic therapy with PRF. Clinical signs and symptoms were assessed over a one-year follow-up period. The results of this study revealed that approximately 80% of cases in both groups exhibited favorable outcomes, which included phenomena like root elongation, thickening of dentinal walls, and closure of the apex. From a scientific standpoint, this suggests that no statistically significant difference was detected between the two groups concerning the resolution of clinical symptoms, the advancement of root development, and the facilitation of periapical lesion recovery. The reason might be that they have not induced periapical bleeding before PRF placement, so it served only as a bio scaffold rather inducing root development, periapical lesion healing. This emphasize that PRF placement along with induced periapical bleeding can bring out better clinical outcomes.”

“The split-mouth double-blinded randomized controlled trial, carried out by Hazim Mohamed Rizk *et al.* in 2019 (reference #28), investigated the clinical and radiographic results in the context of bilateral immature permanent maxillary central incisors with necrotic pulp. The study focused on the application of both blood clot and platelet-rich plasma (PRP) scaffolds in these cases. Regenerative endodontic therapy with blood clot was assigned as Group 1 and RET with PRP as Group 2. The study evaluated both the primary and secondary clinical and radiographic outcomes. The primary clinical outcomes comprised assessments related to pain, swelling, tooth mobility, and the presence of sinus/fistula. Meanwhile, the secondary clinical outcomes involved evaluating tooth discoloration and conducting sensibility tests. Regarding radiographic outcomes, the main emphasis was on quantifying enhancements in root length and root thickness. Secondary radiographic criteria encompassed the evaluation of alterations in bone density and a decrease in apical diameter. Notably, over the entire follow-up duration, all cases included in the study exhibited a 100% clinical success rate in both groups. This outcome indicated that there was no statistically significant difference between the two groups in terms of their clinical success rates. This suggests that both blood clot and PRP treatments were superior to conventional root canal treatment. Throughout the entire follow-up period, it was observed that the PRP group exhibited increased root length and greater root dentin thickness compared to the blood clot (BC) group. The suggested explanation for this phenomenon was the potential presence of residual vital pulp within the root canal system. It was hypothesized that this remaining vital pulp may have transformed into odontoblasts, guided by the intact epithelial root sheath of Hertwig. However, it's important to note that this reason conflicted with the findings of your review because the study in question had only collected samples from teeth with necrotic pulp. The study proposed an alternative hypothesis, suggesting that PRP elevates the concentration of growth factors, subsequently attracting stem cells situated within the apical tissues, thereby contributing to improved regenerative results. Notably, throughout the follow-up period, all revascularized teeth did not exhibit a response to the pulp sensibility test. Several

factors could account for the observed findings, with one potential explanation being the coronally positioned layer of Mineral Trioxide Aggregate (MTA), which acts as an insulating agent and may play a role in enhancing regenerative processes. Another possibility is that a longer duration, exceeding the 12-month follow-up period, might be necessary for the complete development of blood vessels and nerve fibers within the root canal. Nonetheless, the study's overall conclusion was that PRP represents a highly desirable and effective alternative treatment to blood clot in regenerative endodontic procedures.

The efficacy of blood clot, PRP, PRF and platelet pellet in regenerative endodontic treatment was evaluated by the author Ayca Tuba Ulusoy ^[29] *et al.* in the year 2019. The author asserted that all four groups exhibited comparable rates of complete apical closure. The PRF, PRP and PP group has rapid initial response time to sensitivity tests than the Blood clot group. This study has an advantage when compared to other study because an additional parameter of root canal area was evaluated. The blood clot group exhibited a greater root canal area when compared to the PRP, PRF, and PP groups. However, the radiographic root area of the blood clot group and PRP group appeared similar. In conclusion, the study found that the PRP, PRF, and PP groups displayed similar clinical and radiographic outcomes when compared to the blood clot group. Importantly, these outcomes were achieved without the need for prior apical bleeding, indicating the effectiveness of these platelet concentrates in regenerative endodontic procedures. Importantly, these findings indicated a reduced tendency for root canal obliteration in the regenerative endodontic treatments that used PRP, PRF, and PP as scaffolds.”

“In 2020, A.S. Elsheshtawy *et al.* conducted a randomized controlled trial (reference #30) to evaluate the effectiveness of platelet-rich plasma (PRP) as a scaffold in regenerative endodontics, utilizing both Cone Beam Computed Tomography (CBCT) and two-dimensional radiographs. The study observed complete healing in all the samples at both the baseline and the 3-month review stage. Significantly, no statistically significant differences were identified between the blood clot and PRP groups in terms of the characteristics of the treated teeth. As a result, the trial concluded that the regenerative endodontic technique, employing PRP and blood clot as scaffolds, yielded successful clinical and radiographic outcomes when applied to immature traumatized permanent teeth with necrotic pulps over a 12-month period.”

“In 2021, Veena Jayadevan and her research team conducted a prospective clinical study (reference #31) with the aim of assessing the efficacy of advanced platelet-rich fibrin (A-PRF) and platelet-rich fibrin (PRF) in regenerative endodontic treatment for traumatized, immature, non-vital permanent anterior teeth. The study revealed that the survival rate for teeth treated with A-PRF was 78.5%, while the survival rate for teeth treated with PRF was 77%. Both groups demonstrated periapical healing during the follow-up period, as evidenced by radiological findings. Notably, there was no statistically significant distinction between the two groups in this aspect. However, the study did identify a notable contrast between the groups in terms of root thickness and root length. The A-PRF group exhibited increased root thickness, while the PRF group displayed enhanced root length during the follow-up. Given the similar outcomes in both groups, the author concluded that root thickness is a crucial consideration in the context of immature teeth. Consequently, A-PRF may be considered a preferred option over PRF for such cases.”

A comparative study on the effectiveness of blood clot and injectable Platelet-Rich Fibrin (PRF) in regenerative endodontic therapy for vital immature permanent teeth was conducted by Asha Nara and her team^[32]. In 2021. The study consisted of two groups, each comprising 5 patients. Group 1 received a blood clot treatment, while Group 2 received i-PRF treatment. Significant differences were observed in both groups when comparing baseline and postoperative clinical findings. These differences were characterized by a significant reduction in clinical symptoms and manifestations. However, the injectable PRF showed increased rate of root lengthening, soft and hard tissue healing than the blood clot group. Hence in the author conclusion injectable PRF was preferred over blood clot.

Ultimately, all six studies reviewed in this systematic review reached the conclusion that different platelet concentrates exhibited superior efficacy in regenerative endodontic therapy compared to conventional root canal treatment and the use of a blood clot. However, it's important to note that in five out of the six studies, the maximum duration of follow-up was 12 months. In contrast, the study by Asha Nara *et al.* extended the follow-up period to 18 months. This longer-term follow-up is essential to further assess and confirm the ongoing efficacy of these regenerative techniques.

In the field of regenerative dentistry, a range of growth factors have been employed to accelerate the generation of both hard and soft tissues. A recent innovation in this regard is the development of Albumin-rich Platelet-Rich Fibrin (Alb PRF), which offers several advantages. Notably, Alb PRF is a blood byproduct that doesn't contain any additives and is derived solely from autologous blood. Alb PRF has a capacity of releasing growth factors continued up to 10 days. Alb PRF has the capacity to release elevated levels of various growth factors, most notably PDGF-AA, PDGF-AB, PDGF-BB, TGF- β 1, VEGF, EGF, and IGF-1. These growth factors play a pivotal role in promoting tissue regeneration and healing processes^[33, 34]. But there are less clinical trials on this new innovation. Further future clinical trials are recommended for analysing its excellent results in regenerative endodontic therapy.

Conclusion

Platelet concentrates have been employed in various dental applications for many years. Technological advancements in this field have yielded promising results for the use of platelet concentrates in regenerative endodontic therapy, highlighting their potential in enhancing dental treatments. This systematically reviewed literature concludes that procedures with platelet concentrates play a successful role in treating the necrotic or immature teeth. Hence the platelet concentrates can save a tooth by the development of root.

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