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The Role Of Barriers In Regenerative Endodontics Procedures For Necrotic Permanent Teeth: A Systematic Review And Meta-Analysis

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Running Title - Platelet Barrier in Endodontic Regeneration

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Abstract

Aim:
The aim is to assess impact of Plasma Rich Platelet (PRP), and Plasma Rich Fibrin (PRF) on overall clinical success rate, periapical healing, and pulp sensibility outcomes in necrotic immature and mature permanent tooth with regenerative endodontic procedures (REPs).

Methodology:
This study protocol was registered in PROSPERO and a systematically conduct across multiple data bases, including PubMed, Cochrane, Web of Science, Open grey and Embase, covering articles from January 2014 to December 2024 using PICO -based queries.The quality of the included studies was appraised by the revised Cochrane RoB2. This meta-analysis evaluated 15 randomized controlled trials on REPs in necrotic mature and immature permanent teeth using Blood Clot (BC) and PRP, PRF barrier.

Result:
Meta-analysis revealed both PRP and PRF showed significantly higher success rates compared to blood clot, with PRP yielding the most favourable outcomes.PRP also significantly enhanced periapical healing, while PRF showed a non-significant trend. No significant differences were observed in pulp sensitivity recovery.

Conclusion:
This meta-analysis found that PRP and PRF significantly improved success rates in regenerative endodontics compared to BC with PRP showing the best outcomes.PRP also enhanced periapical healing, while pulp sensitivity recovery showed no significant differences. PRP appears to be the most effective scaffold overall

Keywords: Blood Clot, Biodentine, Endodontic Regeneration, MTA, Pulp Regeneration, Pulp Revascularization

Introduction

Previously, traditional methods of treating immature permanent teeth with open apices classified as necrotic were those which had been treated with a calcium hydroxide over a long period of time or the mineral trioxide aggregate (MTA) as apical plug in the apical barrier procedures. In these technique MTA and gutta-percha are unable to encourage root development or give necrotic teeth their vitality back. Regenerative Endodontic Procedure (REPs), a treatment that encourages the remaining undifferentiated mesenchymal cells to enter the canal space via a scaffold conduit in order to replace the pulp-dentin complex which can lead to thickening of the root canal walls, elimination of symptoms, periapical tissue repair with apical closure and give vitality back.[1]The tissue formed ,that was a mixture

of bone-like material and fibrous connective tissue with certain features that resemble arteries.[2]

Arslan et al. (2019) demonstrated that a growth of a crucial tissue in the root canal system of a mature tooth is a possible outcome after REPs.This discovery was novel because it can generate an element and with successive structures which resembles those found in the root canals of the immature teeth.[3]

Previously REPs typically use Blood Clot (BC) to accomplish biological obturation and promote healing instead of mechanical obturation, like with gutta-percha, which results in the development of immune response-systems to fend off-reinfection.[1]

Nowadays, the use of platelet concentrate scaffolds in revascularization techniques has been the subject of numerous recent investigations as it has the capacity to stabilize BC, sustain growth factor levels, and encourage tissue regeneration.[4]Two concentrated platelet sources that are frequently utilized in REPs are PRP and PRF.[5]

A number of study is done by taking consideration of immature tooth in their participation pool. However mature group of pool remain unexplored. Hence this review evaluates the effects of intracanal scaffolds in both immature and mature permanent teeth in participation pool to broaden clinical applicability.

Material and methods

Protocol and registration

This current systematic review and meta-analysis took place in compliance with the Preferred Reporting Items (PRISMA) 2020 guidelines of reporting systematic review and meta-analysis.[1] Also, the research plan was prospectively enrolled in the PROSPERO database under the. ID CRD420251002724.

Search strategy

An extensive electronic search was carried out using PubMed, Cochrane Library, Web of Science and Embase databases. The search included only articles published from January 2014 to December 31, 2024. The search terms Pulp regeneration, Endodontic regeneration, Pulp revascularization, PRF, PRP, Blood Clot, MTA and Biodentine. The search term was used alone or combined using Boolean operators “AND” and “OR.”. (Figure1)

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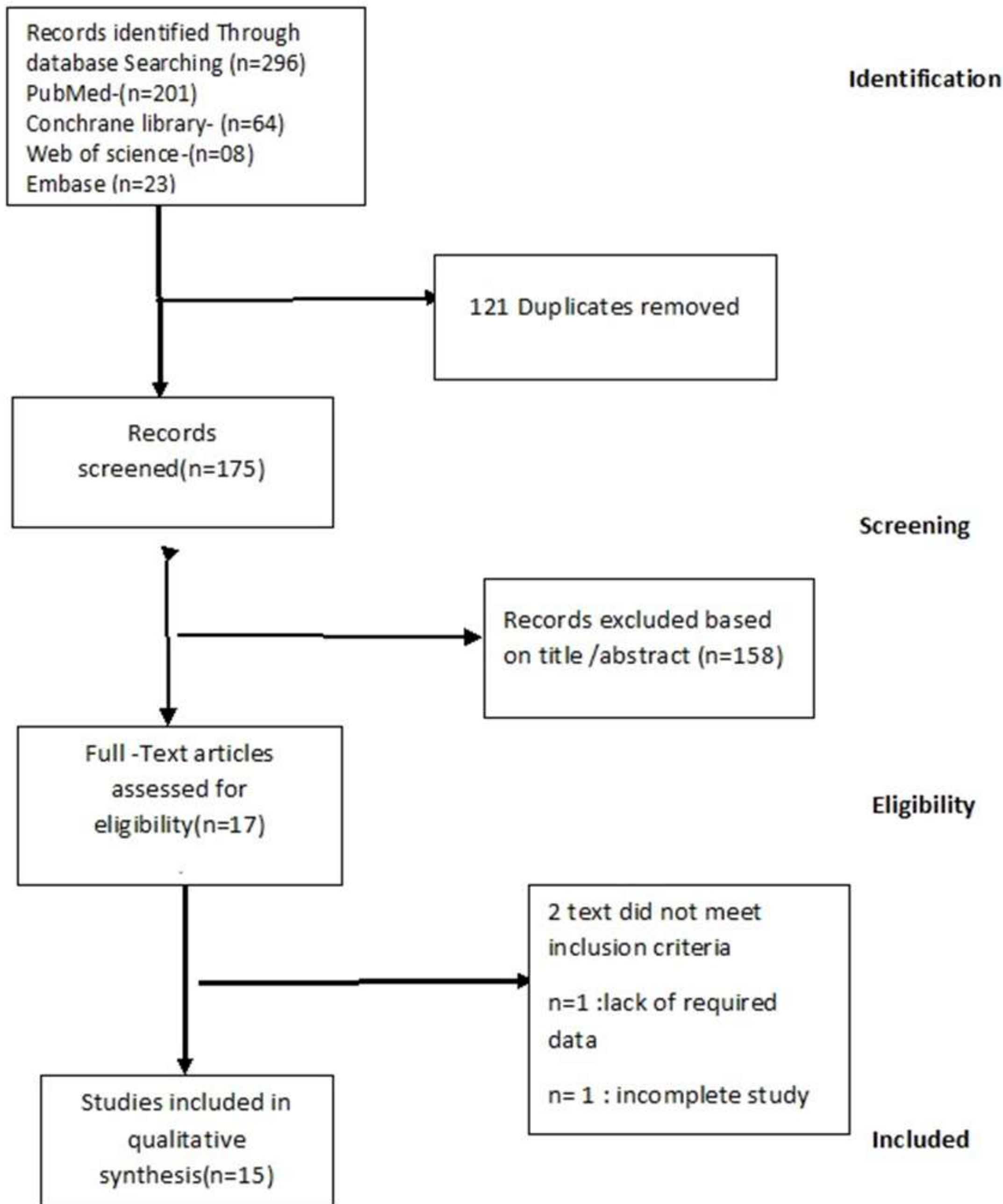
Figure 1: Preferred Reporting Items for Systematic Reviews and Meta analyses flowchart.



PICO question and eligibility criteria

The structured question used to determine the research questions in this review was grounded on the use of PICO framework as follows -Whether use of regenerative endodontics procedures using various barriers on mature and immature necrotic permanent teeth increases. the effectiveness in periapical healing, pulp sensitivity rate and success rate?

Population(P) -Patients with necrotic teeth, including both immature and mature permanent teeth.

Intervention(I) –The primary intervention involved REPs targeting necrotic teeth.

Comparison (C)-The comparison was made between different approaches to pulp revascularization, specifically examining the use of various scaffolds such as BC, PRP and PRF.

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Outcome(O) -The outcomes were evaluated in terms of overall treatment success rate, the return of pulp sensitivity, and the extent of periapical healing.

Study selection

Inclusion criteria - This review included Randomized control trial (RCTs) that investigated REPs in both mature and immature permanent teeth. The outcomes were evaluated based on clinical and radiographic indicators, specifically focusing on treatment success rate, periapical healing, and recovery of pulp sensitivity.

Exclusion criteria- The exclusion criteria encompassed studies lacking comparison groups, in vitro studies, those involving primary teeth, animal or histological investigations, cross-sectional designs, case reports or case series, opinion articles, review papers, abstracts, and studies published in languages other than English.

Data extraction

Two authors extracted relevant data of the included studies in duo. The data that was extracted consisted of first author(s), year of publication, age of patient, sample size, type of teeth, cause of necrosis, intracanal disinfection medication, capping material, use of matrix, type of scaffold, follow-up, duration. (Table 1)

Quality assessment

The Cochrane Risk of Bias tool helped to determine the Risk of Bias (RoB) in the studies that have been reviewed and makes consideration of five areas reporting bias, performance bias, detection bias, incomplete outcome data bias, and random sequence generation bias. This review has been evaluated by two reviewer and if any discrepancy is found third reviewer has been consulted.

Certainty of Evidence

The certainty of the evidence of each primary outcome was determined by GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) framework. This method considers six important domains which are study design, risk of bias, inconsistency, indirectness, imprecision, and publication bias. RCTs were initially rated as high-certainty evidence. However, the certainty could be downgraded based on concerns related to five factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias. According to the following criteria, the confidence of each outcome was rated as one of four levels, high, moderate, low, or very low. (Table 2)

Results

Literature search:

The PRISMA flowchart depicting the study selection process. An initial search yielded 296 records through database screening, of which 121 were identified as duplicates and subsequently removed. After title and abstract screening, 158 articles were excluded based on the inclusion criteria. 17 text articles were reassessed for eligibility, among which one lacked essential data and another was an incomplete study. Finally, 15 studies were included for qualitative synthesis. (Figure 1)

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Table 1: Data Extraction

AUTHOR	SAMPLE	AGE	TOOTH	CAUSE OF NECROSIS	FOLLOW UP	IRRIGATION PROTOCOL	INTRACANAL MEDICAMENT	CELL/SCAFFOLD	USE OF MATRIX	CAPPING MATERIAL
MM aly *et al* 2019 [6]	26	8-15yr	Immature	carious	12 mnth	1.5% Naocl,17% EDTA	DOUBLE ANTIBIOTIC	BC	NR	MTA and Biodentine
AYD Hady *et al* 2022 [7]	20	8-12yr	Immature trauma or carious	trauma	12 mnth	1.5% Naocl,17% EDTA	CAOH	A-PRF,BC	Collagen	MTA
HM rizk *et al* 2019 [8]	13	8-14 yr	Immature	NR	12 mnth	2% Naocl,17% EDTA	TAP	BC, PRP	NR	MTA
M Kavitha *et al* 2022 [9]	16	15-35yr	Immature	NR	18 mnth	1.5% Naocl,17% EDTA,2% CHX	TAP	PRF,CGF	NR	BIODENTINE
N Meschi *et al* 2021 [10]	29	6-25 yr	Immature	NR	36 mnth	1.5% naocl,17 EDTA,Saline	$CA(OH)_2$	BC, PRF	Membrane	MTA
N mittal *et al* 2021 [11]	36	16-34 yrs	Mature	NR	12 mnth	1.5% Naocl,17% EDTA	DAP	PRF,COLLAGEN,HYDROXYAPATITE	NA	BIODENTINE
Vasundara *et al* 2017 [12]	60	6-28yrs	Immature	trauma or carious	12 mnth	5.25%Naocl, Saline	TAP	PRP, PRF ,BC	NA	NA
Y ahmed *et al* 2022 [13]	28	9-30yrs	Necrotic	NA	12 mnth	1.5%Naocl,17%Edta	DAP	PRP	ColaCote membrane	MTA
Y zhang *et al* 2024 [14]	56	7-16 yrs	Immature	NA	12 mnths	2.5%Naocl	TAP	BC, CGF	NA	NA
Ah youssef *et al* 2022 [15]	20	18-40 yrs	Mature	NA	12 mnths	5.25% Naocl,17%EDTA	TAP	BC,NCS,CHITOSAN	NA	MTA
A.S. elsheshtawy *et al* 2020 [16]	26	12-13 yrs	Immature	NA	12 mnths	5.25 Naocl,EDTA, saline	TAP	PRP,BC	Collagen	MTA
M nagy *et al* 2014 [17]	36	9-13 yrs	Immature	NA	18 mnths	2.6%Naocl, saline	TAP	BC/FGF	NA	MTA
AT Ulusoy *et al* 2019 [18]	88	8-11 yrs	Immature	trauma	11 mnths	1.25%naocl,2%chx,17%EDTA	TAP	PRP,PRF ,BC	NA	MTA
Al rawhani t al 2024 [19]	36	10-35 yrs	Mature	NA	12 mnths	1.5%Naocl,17%Edta	$CA(OH)_2$	BC	NA	MTA
Tatiana *et al* 2019 [20]	15	6-25 yrs	Immature	trauma	12 mnths	2.5%Naocl,17% edta	$CA(OH)_2$	BC	NA	MTA

Table 1-Caoh: calcium hydroxide apexification; MTA: mineral trioxide aggregate apexification; BC: blood clot revascularisation; TAP: triple antibiotic paste; EDTA: ethylenediaminetetraacetic acid; PRF- Plasma rich fibrin. PRP -Plasma rich Platelet,CGF: Concentrated Growth Factors, FGF- Fibroblast Growth Factor, Naocl -Sodium Hypochlorite.

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Table 2- Certainty of the evidence (GRADE)

Outcome	Number of Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Certainty
Success Rate (BC, PRP)	4	RCT	No serious inconsistency	Serious[b]	No serious inconsistency	Serious[c]	No serious inconsistency	⊕⊕⊕⊖/ B
Success Rate (BC, PRF)	4	RCT	No serious inconsistency	Serious[b]	No serious inconsistency	No serious inconsistency	No serious inconsistency	⊕⊕⊕⊖/ B
Sensitivity Rate (BC, PRF)	4	RCT	Serious[a]	No serious inconsistency	No serious inconsistency	No serious inconsistency	Serious[d]	⊕⊕⊕⊖/ B
Sensitivity Rate (BC, PRP)	3	RCT	No serious inconsistency	No serious inconsistency	No serious inconsistency	Serious[c]	Serious[d]	⊕⊕⊕⊖/ B
Periapical Healing (BC, PRF)	3	RCT	Serious[a]	No serious inconsistency	No serious inconsistency	No serious inconsistency	Serious[d]	⊕⊕⊕⊖/ B
Periapical Healing (BC, PRP)	3	RCT	No serious inconsistency	No serious inconsistency	Not serious	Serious[c]	No serious inconsistency	⊕⊕⊕⊖/ B

A: Refers to a high certainty of evidence; B: Refers to a moderate certainty of evidence. GRADE: Grading of Recommendations, Assessment, Development and Evaluation, PRF: Platelet-rich fibrin, PRP: Plasma-rich platelet, BC: Blood clot, RCT: Randomized controlled trial. ; a-Failure to follow intention to treat principle in analysis, b-As it shows heterogenicity of 95 %, c-high heterogenicity, and small sample size, d-selective outcome reporting and lack of registered protocol.

Characteristics of the Included Studies

The predominant characteristics of the 15 studies included that had undergone regenerative endodontic treatment with scaffold had mature or immature teeth and their diagnosis in the studies was different. The studies involved 11 immature,3 mature,1 necrotic tooth in the work so far as to give results of seamless success rate between BC and PRF and PRP, Pulp sensibility rate and Periapical healing. **Pulp sensitivity** is positive response to any **cold, heat, or electric pulp tests** . **Periapical** healing shown after increase in bone density and PAI score.

Risk of Bias of Included Studies

The bias was assessed in each of the domains. All the studies were rated to have a low risk of bias due to incomplete outcome data.For reporting bias, nine

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studies. were deemed low risk and the remaining six were marked as unclear. Performance bias results varied, with six studies showing a low risk and nine rated as unclear. Tatiana et al study was classified as high risk. Detection bias was considered low in ten studies with five studies labelled unclear (Figure 2) In terms of randomized sequence bias, ten studies were low risk and five were unclear because of insufficient information about allocation.

Figure 2: Risk of bias table, D1: Reporting Bias D2: Performance Bias D3: Detection Bias D4: Incomplete outcome Data Bias D5: Randomization Sequence Bias.

Study	Risk of bias domains					
	D1	D2	D3	D4	D5	Overal
Mariam Mohsen Aly (2019)	+	+	+	+	+	+
Amr Yosry Abd El-Hady (2022)	-	-	-	+	+	-
H.M. Rizk (2019)	+	+	+	+	+	+
Nastaran Meschi (2021)	-	-	-	+	-	-
Neelam Mittal (2021)	-	-	-	+	-	-
Vasundara Y. Shivashankar (2017)	+	+	+	+	+	+
Yassmin Elsayed (2023)	+	-	+	+	+	+
Y. Ziang (2024)	+	+	+	+	+	+
Ahmed Ali Youssef (2022)	-	-	-	+	-	-
A.S. elsheshtawy(2020)	+	-	+	+	+	+
M.M. Nagy (2014)	-	-	-	+	-	-
A.T. Ulusoy (2019)	+	+	+	+	+	+
Al-Rawhani (2024)	+	-	+	+	+	+
Tatiana M. Botero (2017)	+	X	-	+	+	X

Judgement: High; Some; Low

Grade Assessment

The overall certainty of evidence across all outcomes was rated as moderate, primarily due to issues of inconsistency, imprecision, and potential bias. Variations in clinical protocols, case selection, and outcome assessment methods led to heterogeneity among studies, reducing confidence in the pooled results. Several trials also had small sample sizes and wide confidence intervals, contributing to imprecision. In some studies, lack of adequate blinding, unclear randomization, and possible selective publication introduced risk of bias and publication bias. Despite these limitations, other domains remained acceptable, "supporting a moderate level of confidence in the comparative effectiveness of BC, PRP, and PRF for success rate, sensitivity recovery, and periapical healing outcomes.

Meta-Analysis

RevMan 5.0 was used to provide the meta-analysis. The information used in the studies that were used in the quantitative analysis includes the following: event of success rate, sensitivity and periapical healing

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between BC (control) vs PRF (experimental) and PRP (experimental).

1.Success rate

In the **BC vs PRP** analysis, a significant overall mean difference of **0.64 [95% CI: 0.43 to 0.85]** was observed, favouring the PRP group (**P < 0.00001**). However, **heterogeneity was high (I^2 = 92%)**, indicating notable inconsistency across the studied. Individual study results vary, with AS Elshtamy (2020) showing the largest effect **(1.25 [0.94, 1.56])**. For **BC vs PRF**, the pooled mean difference was **0.45 [95% CI: 0.38 to 0.52]**, also statistically significant (**P < 0.00001**), again favouring PRF. **Heterogeneity remained high (I^2 = 90%)**, suggesting results should be interpreted cautiously. Among the studies, Amr Hady (2022) contributes the highest weight **(93.80%)** with a mean difference of **0.50 [0.43, 0.57],** strongly influencing the overall effect. Both PRP and PRF groups demonstrated improved success rates compared to controls. (Figure3:A and B)

2. Pulp Sensitivity Rate

In the **PRP vs BC** group, two of three studies had zero events in both groups, making them **not estimable**. Only one study (Vasundara et al, 2017) contributed usable data, with an **odds ratio of 1.00**, indicating **no difference** between groups (**P = 1.00**). Since only one study contributes data, heterogeneity is **not applicable**, and the results should be interpreted with caution due to the limited number of events. The wide confidence interval reflects the uncertainty in the estimate, and the **P-value of 1.00** suggests no statistical significance.

In the **PRF vs BC** group, the pooled odds ratio was **1.81 [95% CI: 0.62 to 5.31]**, suggesting a higher likelihood of the event occurring in the PRF group compared to the control group, but the result is not statistically significant (**Z = 1.08, P = 0.28**).. However, the result was **not statistically significant (P = 0.28)**, and the wide confidence interval reflects considerable uncertainty. **Heterogeneity was low (I^2 = 0%)**. There is no conclusive evidence that either PRF or PRP significantly reduces pulp sensitivity when compared to controls (Figure.3:C and D)

3. Periapical Healing

The **PRP vs BC** comparison showed a statistically significant improvement in the PRP group with more events and a **significant overall effect (P = 0.02)**. **Heterogeneity was low (I^2 = 25%)**, supporting the reliability of this result. PRP significantly enhanced periapical healing compared to control, with consistent findings. In the **PRF vs BC**, a total of 26 events occurred in the PRF group and 22 in the control. Although PRF showed a higher success rate, the difference was **not statistically significant** (**P = 0.26**). Importantly, **heterogeneity was low (I^2 = 0%)**, suggesting consistent results. (Figure 3: E and F)

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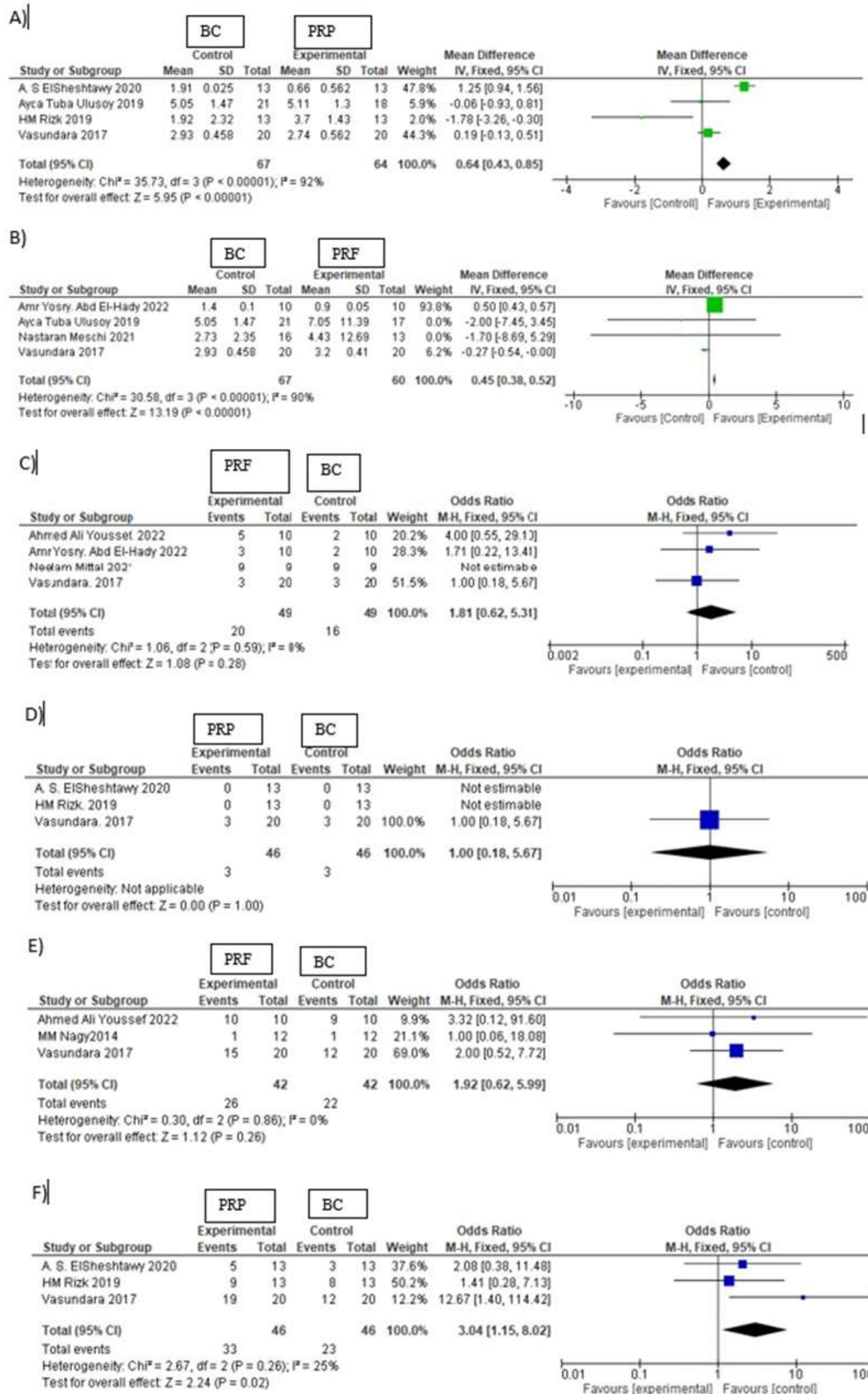
Figure 3 :Forest plots of Success Rate -A)BC vs PRP B) BC vs PRF;.Pulp Sensitivity Rate -C) BC vs PRP D) BC vs PRF; Periapical Healing E) BC vs PRP F) BC vs PRF



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Discussion

Barrier selection is a key factor in regenerative endodontic procedures (REPs), as scaffolds—along with stem cells and signaling molecules—are critical for success.[5]This systematic review and meta-analysis of 15 RCTs compares blood clot (BC), platelet-rich plasma (PRP), and platelet-rich fibrin (PRF) scaffolds in necrotic permanent teeth. Inclusion of both mature and immature teeth and standardized outcomes like clinical success, periapical healing, and pulp sensitivity enhance the clinical relevance and credibility of the findings.

The assessment indicates that, overall, the included studies were of **moderate to high methodological quality**, with most domains showing low risk of bias. This suggests that the findings of the review is having moderate validity. Tatiana et al study was classified as high risk in performance bias because the outcome would be influenced by the lack of blinding.. For reporting bias, nine studies were deemed low risk as study protocol is available and all the prespecified outcome are of interest in the review, while the remaining six were marked as unclear as there is insufficient information A **low risk of bias** indicates that a study was well-designed and conducted, with proper randomization, blinding, and complete outcome reporting, reducing the chances of systematic errors. In contrast, a **high risk of bias** suggests methodological flaws—such as inadequate blinding or selective reporting—that may distort the results and limit the reliability of the findings. Detection bias was considered low in eight studies as blinding of outcome assessed is done, with seven studies labelled unclear as no information is there. (Figure 2) In terms of randomized sequence bias, ten studies were low risk as conceal allocation is present and five were unclear because of insufficient information about allocation.

In grade assessment, the included studies provide a reasonably reliable body of evidence, as most outcomes showed no serious inconsistency. Overall, The moderate certainity of evidence indicating that every clinical case is different and sample size has to increase. However, the high heterogeneity and small sample sizes in the success rate outcome reduce the precision and certainty of this specific estimate, suggesting that the true effect may vary across populations. This heterogeneity should be considered when interpreting the results, as differences in methodology, sample characteristics, or other factors may influence the observed effects. The GRADE framework assigned high certainty to the evidence regarding the success rate of PRP and PRF, given the consistency of results across well-conducted trials. However, the certainty was downgraded to moderate for periapical healing and sensitivity outcomes due to heterogenicity and imprecision. These findings emphasize that while scaffold materials play a pivotal role in REP outcomes, further robust data are necessary, particularly in outcomes involving pulp regeneration and long-term pulp vitality.

This review showed that both PRP and PRF scaffolds produced noticeably higher success rates when compared to the conventional blood clot scaffold, which is in line with results from Jadhav g et al and Neelam Mittal et al[11,21]**.** In this context, the success rate is defined by the absence of symptoms as well as the reduction or elimination of periapical lesions, with PRP and PRF being favoured according to the aggregated estimates. Despite the noteworthy outcomes, the considerable heterogeneity seen in both analyses ($I2 > 90\%$) means that these results should be regarded cautiously. This discrepancy could be explained by variations in treatment regimens, ethology, follow-up periods, and tooth maturity among the studies. In a comparative analysis, PRP outperformed PRF and traditional blood clot scaffolds in promoting periapical lesion resolution.[22]

As per result, PRP significantly enhances periapical healing over BC, while PRF shows improvement without statistical significance. Neelam Mittal *et al* concluded that PRP and PRF both include concentrated growth factors and cytokines that are known to support angiogenesis and tissue regeneration [11].This finding are in line with the molecular mechanisms that have been hypothesized for them. Nonetheless, PRP's improved periapical healing results might be explained by the more rapid and plentiful release of bioactive molecules [5]. PRP has been shown in both in vitro and in vivo studies to **increase the migration and proliferation of stem cells,** which are essential for pulp-like tissue regeneration and periapical healing [16].

One of the more difficult parts of regenerative endodontics is still pulp sensitivity recovery. When compared to BC, neither PRP nor PRF showed statistically significant improvements in pulp

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sensitivity restoration in this review. The odds ratio for the PRF comparison was 1.81, although the PRP analysis was constrained by the lack of estimable data. This implies that although periapical healing and structural repair are possible, full neurovascular reinnervation of the pulp is still unknown [4].

The current results align with earlier meta-analyses and systematic reviews, such as those conducted by Alrashidi et al. and Rahul et al., which indicated positive results with platelet concentrates [24,25]. Significantly, a prior review indicated that there was no difference in apical radiolucency healing between BC and PRP, a finding that is somewhat reflected in this review concerning PRF. Nevertheless, the root development parameters were not consistently evaluated across the studies included here, which hinders a straightforward comparison. Differences in reported outcomes across studies might also arise from variability in follow-up durations, patient demographics, and scaffold preparation protocols.

The effective use of REPs in mature permanent teeth is linked to the regenerative capabilities of platelet-based scaffolds like PRP and PRF, which are abundant in growth factors and cytokines that encourage angiogenesis and tissue repair. The meta-analysis indicates that PRP yielded significantly better results compared to blood clot in terms of clinical success and periapical healing, even in mature teeth, as evidenced by studies including Mittal et al. (2021) and Youssef et al. (2022). These scaffolds support the recruitment and growth of stem cells, which is a crucial aspect of regeneration. [11,15]

Clinical Significance

This Review provides strong evidence supporting the use of platelet concentrates especially PRP, PRF in regenerative endodontics for both mature and immature necrotic teeth. By including diverse cases and applying standardized outcomes, it guides clinicians toward more effective, biologically based scaffold choices, promoting better healing and treatment success. The findings highlight the potential of PRP to enhance periapical healing and clinical outcomes consistently.

Future Implication

To enhance the evidence base, upcoming clinical trials must implement standardized REP protocols, which encompass scaffold preparation, methods for intracanal disinfection, and criteria for measuring outcomes. Specifically, employing sophisticated imaging techniques like cone-beam computed tomography (CBCT) and biological indicators of recovery may improve diagnostic precision. Moreover, prolonged follow-up periods and collaborations across multiple centres would enhance the statistical strength and generalizability of forthcoming results.

Limitations-

Initially, significant variability in main outcome evaluations, especially success rates, diminishes the accuracy of combined estimates. Secondly, information on pulp sensitivity was restricted because of the few studies documenting this result and the low occurrence rates. Third, the definitions of outcomes and clinical protocols differed among studies, potentially introducing bias and impacting the reliability of comparisons

Conclusion

This meta-analysis concludes that both PRP and PRF scaffolds improve the success rates and periapical healing in regenerative endodontic procedures for necrotic permanent teeth, with PRP yielding the most positive results. However, neither scaffold demonstrated a significant enhancement in pulp sensitivity. These results endorse the clinical application of platelet concentrates, especially PRP, as viable alternatives to conventional blood clots.

Reference

1. Li J, Zheng L, Daraqel B, Liu J, Hu Y. Treatment Outcome of Regenerative Endodontic Procedures for Necrotic Immature and Mature Permanent Teeth: A Systematic Review and Meta-Analysis Based on Randomised Controlled Trials. Oral Health Prev Dent. 2023 17;21:141-152.
2. Minic S, Vital S, Chaussain C, Boukpessi T, Mangione F. Tissue Characteristics in Endodontic Regeneration: A Systematic Review. Int J Mol Sci. 2022 11;23(18):10534.
3. Arslan H, Ahmed HMA, Şahin Y, Doğanay Yıldız E, Gündoğdu EC, Güven Y, Khalilov R. Regenerative Endodontic Procedures in Necrotic Mature Teeth with Periapical Radiolucencies: A Preliminary Randomized Clinical Study. J Endod. 2019;45(7):863-872.

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4. Liu H, Lu J, Jiang Q, Haapasalo M, Qian J, Tay FR, Shen Y. Biomaterial scaffolds for clinical procedures in endodontic regeneration. Bioact Mater. 2021 14;12:257-277.
5. Salah T, Hussein W, Abdelkafy H. Regenerative potential of concentrated growth factor compared to platelet-rich fibrin in treatment of necrotic mature teeth: a randomized clinical trial. BDJ Open. 2025 3;11(1):10.
6. Aly MM, Taha SEE, El Sayed MA, Youssef R, Omar HM. Clinical and radiographic evaluation of Biodentine and Mineral Trioxide Aggregate in revascularization of non-vital immature permanent anterior teeth (randomized clinical study). Int J Paediatr Dent. 2019 ;29(4):464-473.
7. El-Hady AYA, Badr AE. The Efficacy of Advanced Platelet-rich Fibrin in Revascularization of Immature Necrotic Teeth. J Contemp Dent Pract. 2022 1;23(7):725-732.
8. Rizk HM, Al-Deen MSS, Emam AA. Regenerative Endodontic Treatment of Bilateral Necrotic Immature Permanent Maxillary Central Incisors with Platelet-rich Plasma versus Blood Clot: A Split Mouth Double-blinded Randomized Controlled Trial. Int J Clin Pediatr Dent. 2019 ;12(4):332-339.
9. Kavitha M, Shakthipriya S, Arunaraj D, Hemamalini R, Velayudham S, Bakthavatchalam B. Comparative Evaluation of Platelet-rich Fibrin and Concentrated Growth Factor as Scaffolds in Regenerative Endodontic Procedure: A Randomized Controlled Clinical Trial. J Contemp Dent Pract. 2022 1;23(12):1211-1217.
10. Meschi N, EzEldeen M, Garcia AET, Lahoud P, Van Gorp G, Coucke et al. Regenerative Endodontic Procedure of Immature Permanent Teeth with Leukocyte and Platelet-rich Fibrin: A Multicenter Controlled Clinical Trial. J Endod. 2021;47(11):1729-1750.
11. Mittal N, Baranwal HC, Kumar P, Gupta S. Assessment of pulp sensibility in the mature necrotic teeth using regenerative endodontic therapy with various scaffolds - Randomised clinical trial. Indian J Dent Res. 2021 ;32(2):216-220.
12. Shivashankar VY, Johns DA, Maroli RK, Sekar M, Chandrasekaran R, Karthikeyan et al. Comparison of the Effect of PRP, PRF and Induced Bleeding in the Revascularization of Teeth with Necrotic Pulp and Open Apex: A Triple Blind Randomized Clinical Trial. J Clin Diagn Res. 2017 ;11(6):ZC34-ZC39.
13. Ahmed YE, Ahmed GM, Ghoneim AG. Evaluation of postoperative pain and healing following regenerative endodontics using platelet-rich plasma versus conventional endodontic treatment in necrotic mature mandibular molars with chronic periapical periodontitis. A randomized clinical trial. Int Endod J. 2023 ;56(4):404-418.
14. Zhang Y, Sheng M. Clinical and radiographic evaluation of regenerative endodontic procedures (REPs) with or without concentrated growth factor (CGF) as scaffolds for non-vital immature mandibular premolars. J Clin Pediatr Dent. 2024 ;48(4):168-175.
15. Youssef A, Ali M, ElBolok A, Hassan R. Regenerative endodontic procedures for the treatment of necrotic mature teeth: A preliminary randomized clinical trial. Int Endod J. 2022 ;55(4):334-346.
16. ElSheshtawy AS, Nazzal H, El Shahawy OI, El Baz AA, Ismail SM, Kang J, Ezzat KM. The effect of platelet-rich plasma as a scaffold in regeneration/revitalization endodontics of immature permanent teeth assessed using 2-dimensional radiographs and cone beam computed tomography: a randomized controlled trial. Int Endod J. 2020 ;53(7):905-921.
17. Nagy MM, Tawfik HE, Hashem AA, Abu-Seida AM. Regenerative potential of immature permanent teeth with necrotic pulps after different regenerative protocols. J Endod. 2014 ;40(2):192-8.
18. Ulusoy AT, Turedi I, Cimen M, Cehreli ZC. Evaluation of Blood Clot, Platelet-rich Plasma, Platelet-rich Fibrin, and Platelet Pellet as Scaffolds in Regenerative Endodontic Treatment: A Prospective Randomized Trial. J Endod. 2019 ;45(5):560-566.

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19. Al-Rawhani AH, Ibrahim SM, Abu Naeem FM. Regenerative Treatment of Mature Teeth with Pulp Necrosis and Apical Periodontitis Using Biodentine Compared with MTA: Randomized Controlled Clinical Trial. Eur Endod J. 2024 20;9(4):365-373.
20. Botero TM, Tang X, Gardner R, Hu JCC, Boynton JR, Holland GR. Clinical Evidence for Regenerative Endodontic Procedures: Immediate versus Delayed Induction? J Endod. 2017 ;43(9S):S75-S81.
21. Jadhav G, Shah N, Logani A. Revascularization with and without platelet-rich plasma in nonvital, immature, anterior teeth: a pilot clinical study. J Endod. 2012 Dec;38(12):1581-7.
22. Galler KM, D'Souza RN, Federlin M, Cavender AC, Hartgerink JD, Hecker S et al. Dentin conditioning codetermines cell fate in regenerative endodontics. J Endod. 2011 ;37(11):1536-41.
23. He L, Kim SG, Gong Q, Zhong J, Wang S, Zhou X et al. Regenerative Endodontics for Adult Patients. J Endod. 2017 ;43(9S):S57-S64.
24. Alrashidi AS, Sadaf D, Alabdulrazaq RS, Alrashidi AS, Alajlan MA, Aljuhani AA. Effectiveness of various scaffolds on the success of endodontic tissue regeneration: Asystematic review and meta-analysis of randomized controlled trials. Saudi Endodontic Journal. 2021; 1;11(2):129-41.
25. Rahul M, Lokade A, Tewari N, Mathur V, Agarwal D, Goel S et al. Effect of Intracanal Scaffolds on the Success Outcomes of Regenerative Endodontic Therapy - A Systematic Review and Network Meta-analysis. J Endod. 2023 ;49(2):110-128.

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