REVIEW ARTICLE

Evaluation of the Treatment Protocols in the Management of Pulpally Involved Young Permanent Teeth in Children: A Systematic Review and Meta-analysis

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Abstract

Background: In children with young permanent teeth, dental caries and traumatic injuries are the most common problems leading to pulp necrosis. Since, root development is completed in two to three years after eruption of the tooth into the oral cavity, loss of pulp vitality in young permanent tooth creates distinctive problems. In spite of exceeding availability of treatment procedures there is a need to search for a substantial procedure to treat young permanent teeth effectively.

Aim: The aim of this systematic review was to evaluate the treatment protocols in the management of pulpally involved young permanent teeth in children.

Method: Systematic search was conducted on databases PubMed, Cochrane, and Google Scholar among studies published from 1st January 2010 till 31st May 2020. Studies meeting the inclusion criteria were included in the review and were then assessed for quality with the help of predetermined criteria which categorized studies into high, medium, and low.

Results: Search strategy yielded 4,846 articles . After screening through titles and abstracts, 33 articles remained which were further screened for full text. At the end, 14 articles were included in systematic review. Furthermore, the included articles were statistically evaluated by meta-analysis.

Conclusion: In apexogenesis and apexification procedures, newer biomimetic materials like mineral trioxide aggregate and biodentine have more success rate than conventionally used calcium hydroxide. Among regenerative endodontic procedures platelet-rich plasma and platelet-rich fibrin showed better results.

Clinical significance: To amend clinician perceptions towards acceptance of the newer regenerative procedures and their effectiveness in management of young permanent tooth.

Keywords: Apexification, Apexogenesis, Regenerative endodontic procedures, young permanent teeth.

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Introduction

Imperatively permanent first molar serves to be a veritable cornerstone of the oral cavity.[1] Being the first permanent tooth to erupt, it is the one which is most commonly affected with dental caries. Moreover, it plays a key role in balanced occlusion.[2]

A young permanent tooth is defined as, newly erupted permanent tooth with incomplete root apex formation.They require maintenance of the maximum amount of the noninflamed portions of the pulp tissue to enhance apexogenesis and root dentin formation.[3] Moreover, pulp tissue in immature teeth has potential for regeneration because of wide open apices, rich blood supply and potentially viable apical tissues.[4]

In children with immature permanent teeth, dental caries and traumatic injuries are the most common problems, leading to pulp necrosis.[5] Since, root development is completed in 2–3 years after tooth eruption into the oral cavity, loss of pulp vitality in the young permanent tooth creates distinctive problems.[6]

The primary aim, while treating young permanent tooth, should be to potentiate the regenerative capacity of the affected pulp.[7] Considerably the ability of the apical pulp tissue to survive under unfavorable necrotic conditions and proliferate under favorable conditions is the key principle behind revascularization.[8] Consequently, pre-eminent purpose of treating cariously or traumatically exposed dental pulps in these teeth is to maintain pulp vitality and allowing continuous root development and apical closure, the approach being known as apexogenesis.[9]

Meanwhile, for pulpally involved necrotic young permanent teeth, the finest treatment modality resides in the formation of an apical calcific barrier. Apexification, induction of a calcific barrier at open root apex of nonvital teeth for obtaining apical barrier preventing passage of bacterial toxins into periradicular tissue.[10]

Calcium hydroxide has been used widely as the gold standard material for Apexogenesis/Apexification for treatment of

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traumatized teeth, but recently with the invent of other biomimetic materials namely Mineral Trioxide Aggregate (MTA), Biodentin, Bioaggregate, etc.; it has been replaced for such usage.[11]

Notably, periapical tissues in immature teeth have rich blood supply, containing stem cells having potential for tissue regeneration. Hence, the concept of regeneration of immature nonvital teeth was advocated.[12] Regenerative endodontic procedures (REPs) have emerged as valuable alternatives, designed to restore damaged, insufficient and missing structures by healthy newly produced tissues, preserving the shape and function of the pulp-dentin complex.[13]

Newer methods based on the principles of revascularization have been tried and found better than conventional methods of apexification since it helps in physiological root maturation, unlike traditional methods which resulted in artificial calcific barrier formation without root lengthening.[14] The key target of the latest regenerative clinical guidelines by the American Academy of Endodontics (AAE) includes, preservation of vitality of the apical papilla and its stem cells.[15]

Thus, an archetypal outcome for teeth with an immature root and necrotic pulp would be the regeneration of pulp tissue into the canal capable of bolstering the continuation of normal root development.[16] Inspite of exceeding availability of the treatment procedures there is a need to search for a substantial procedure to treat effectively, an immature permanent teeth.

Hence, the aim of this systematic review is to determine clinical and radiographic success of varying materials using different treatment protocols along with exploration of the newer approaches that can be effectively used in pediatric dentistry for the treatment of young permanent teeth through critical evaluation of dental literature.

Focused Question

What are the clinical and radiographic outcomes while evaluating the efficacy of newer biomimetic materials with conventional materials on the regenerative potential of cells in the physiological root apex formation (apexogenesis), apical barrier formation (apexification), and REPs in pulpally involved young permanent teeth in children between 6 and 14 years of age?

PICO Format

P (Population)—Children in between 6 and 14 years of age with young permanent teeth **.** **I** (Intervention)—Clinical and radiographic evaluation of physiological root apex formation, apical barrier formation and REP in pulpally involved young permanent teeth in children. **C** (Comparison)—Comparative evaluation of newer biomimetic materials like mineral trioxide aggregate (MTA), Biodentine with conventional materials like calcium hydroxide on the regenerative potential of cells in the physiological root apex formation (apexogenesis), apical barrier formation (apexification) and REPs in pulpally involved young permanent teeth in children. **O** (Outcome)—(1) To evaluate clinical success rate on the basis of absence of pain, tenderness to percussion, swelling, absence of tooth discoloration, and restoration of pulp vitality. (2) To evaluate radiographically, the efficiency of apical end closure, root wall thickening, no loss of lamina dura, PDL widening, pathologic root resorption, and resolution of periapical radiolucency.

Objectives

The objective are to evaluate and compare the clinical and radiographic success rates of newer biomimetic materials with conventional materials on the regenerative potential of cells in the physiological root apex formation (apexogenesis), apical barrier formation (apexification), and REPs in pulpally involved young permanent teeth in children between 6 and 14 years of age.

Methods

Protocol and Registration

The review has been registered in PROSPERO; International prospective register of systematic reviews funded by National Institute of Health Research and produced by CRD (Centre for Reviews and Dissemination) an academic department of the University of York. The registration number of this review is **CRD 420,201 85,920** and can be accessed on the website http://www.crd.york.ac.uk/prospero/index.php.

Eligibility Criteria

Inclusion Criteria

- Study setting should be clinical.
- Study design should be randomized control trials, quasi-randomized, control clinical trial, retrospective or a cohort study, case series and case reports.
- Study population should be children between 6 and 14 years of age with young permanent teeth.
- Study assessing the efficiency of Apexogenesis, Apexification and Regenerative endodontic procedures of young permanent teeth in children.
- Study published between 1st January 2010 and 31st May 2020.
- Studies written in English language and studies written in any other language but are possible to get translated into English.

Exclusion Criteria

- Studies conducted on animal.
- Article reported as a review and systematic review.
- Participants aged below 6 years of age.
- Studies not reporting the clinical and radiographical outcomes of Apexogenesis, Apexification and Regenerative endodontic procedures of young permanent teeth in children.
- Clinical or radiographic outcomes mentioned through letter to editor and short communication.
- Studies recording clinical and radiographic outcomes as a secondary objective

Literature Search and Search Strategy

Search Strategies

Literature search strategy was developed using keywords related Apexogenesis/Apexification/Regenerative endodontics, young permanent teeth, and children. Data were searched through the databases, PubMed, Google Scholar, Cochrane from 1st January 2010 till 31st May 2020. Detailed items including search strategies used, no of articles searched and selected are illustrated. Cross-references were checked, grey literature and hand searching of articles was done when full texts of the relevant studies were unavailable through electronic database.

Study Selection

One review author (NS) independently screened the titles and abstracts obtained by search strategy and included them if they met the inclusion criteria. Later full texts of all the included studies were obtained and screened by reading them entirely and segregated based on the inclusion criteria. Whenever there was uncertainty regarding any study regarding inclusion, problem was resolved by discussing it with the second review author (SMH). For inclusion of articles for meta-analysis the quality assessment of each article was done by the reviewer independently (NS) and later it was crosschecked by other reviewers (SMH, NS). Finally, the search yielded 14 studies to be included in systematic review. All the excluded studies were recorded with reason for exclusion of each study (Fig. 1).

Data Extraction (Study Characteristics)

Data extraction was performed using a standardized outline. General information such as author name, year of publication was collected from each study. Study characteristics like (1) Study setting (2) Age-group (3) Sample Size (4) Material used (5) Follow-up (6) Clinical success rate (7) Radiographic success rate (8) Success rate (Clinical + radiographic) (9) Results were tabulated for the studies selected (Table 1).

Risk of Bias

Risk of bias within each study is mentioned in figure and the studies are categorized into high (Red), medium (Yellow), and low (Green) risk bias studies according to Cochrane handbook for systematic review using RevMan 5.4.[36] Most trials were at low risk of bias in seven domains, i.e, random sequence generation, allocation concealment, blinding of participants and personnel, incomplete outcome data, selective reporting, and other bias that we assessed. Summary of the risk of bias for individual study as well as the judgments of the risk of bias for each domain is mentioned. Risk of bias for non-randomized studies has been done using Modified Newcastle Ottawa Quality assessment scale (Fig. 2 and Table 2).

Result

The result of our search strategy identified 145 and 4,701 articles through database searching in Cochrane, PubMed, Google Scholar, respectively. Total 4,846 articles were retrieved. Second step was screening through titles after which 4,687 articles were excluded because they did not meet the objectives of the systematic review. A total of 159 articles which remained were screened for duplicates through Endnote Software VersionX7. Out of 159, 86 articles were found to be duplicates and thus, remaining 73 articles were screened through abstracts subsequently. Through abstract screening 40 articles were excluded as they did not meet the eligibility criteria. Finally, 33 articles were screened for full text out of which, 19 were excluded reason of which have been mentioned.

Finally, 14 articles were selected out of which four were randomized controlled trials, seven were controlled clinical trials and three were case reports. All the studies were then qualitatively analyzed after which they were included in the systematic review.

Meta-analysis

For meta-analysis 14 articles were reviewed and were statistically evaluated using statistics and data software (STATA). The results obtained from the analysis showed high precision values considering 95% confidence interval. Moreover, less heterogeneity

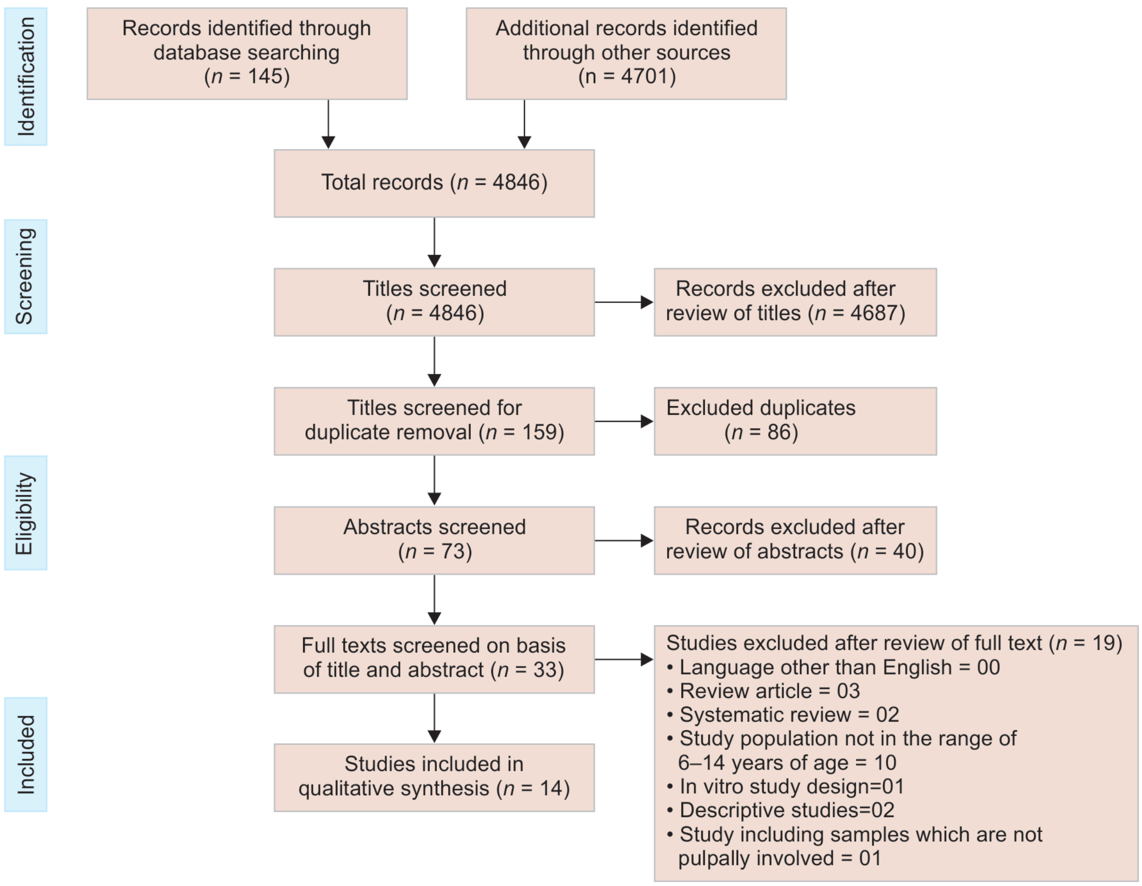


Fig. 1: Flow diagram depicting the process of selection and exclusion of articles at each step

Table 1: Table showing qualitative analysis of the studies selected for the systematic review

Sl. No	*Author name*	*Year of publication*	*Study setting*	*Age*	*Sample size*	*Material used*	*Follow-up*	*Clinical success rate*	*Radiographic success rate*	*Success rate (clinical + radiological)*	*Result*
1	Santha kumar M et al.	2018	In vivo	7–12 years	40	PRF gel, PRF membrane	6,12, and 18 months	PRF gel = 94.73% PRF membrane = 94.73%	PRF gel = 94.73% PRF membrane = 89.47%	PRF gel = 94.73% PRF membrane = 89.47%	PRF gel-94.73%
2	Torabi nejad M et al.	2011	In vivo	11 years	1	Triple antibiotic paste + PRP	6, 12 months	PRP = 100%	PRP = 100%	100%	PRP–100%
3	Bezgin T et al.	2015	In vivo	7–13 years	22	Blood clot, PRP	3, 6, 9, 12, and 18 months	PRP = 100%, Blood clot = 100%	PRP = 100%, Blood clot = 90.09%	PRP = 100%, Blood clot = 95.45%	PRP–100%
4	Narang I et al.	2015	In vivo	< 20 years	20	Blood clot, PRP, PRF	6, 18 months	Blood clot = 100%, PRP = 100%, PRF = 100%	Blood clot = 57%, PRP = 74.50%, PRF = 50%	Blood clot = 78.5%, PRP = 87.25%, PRF = 75%	PRF = 87.25%
5	Nagy MM et al.	2014	In vivo	9–13 years	36	MTA + (blood clot scaffold) + (blood clot scaffold + fGF)	3, 6, 12, and 18 months	MTA = 100%, REG = 90% FGF = 80%	MTA = 100%, REG = 90% FGF = 90%	MTA = 100%, REG = 90% FGF = 80%	MTA-100%,
6	Li Wan Lee et al.	2010	In vivo	7–10 years	32	Calcium hydoxide	1 and 3 months	Calcium hydoxide = 100%	Calcium hydoxide = 96.4 %	Calcium hydoxide = 98.2%	Calcium hydoxide -98.2%
7	Vidal K et al.	2016	In vivo	9 years	1	Absorbable collagen matrix + Biodentine	3, 6, and 18 months	Biodentine = 100%	Biodentine = 100%	Biodentine = 100%	Biodentine -100%
8	Tolugu N et al.	2016	In vivo	7–11 years	26	MTA, BioAggregate	3, 6, 9, 12, 15, 18, 21, and 24 months	MTA = 84.61% BioAggregate = 100%	MTA = 100% BioAggregate = 100%	MTA = 92.30% BioAggregate = 100%	BioAggregate-100%
9	Chaudary S et al.	2016	In vivo	11 years	1	Er,Cr:YSGG Laser + Biodentine	3, 6, 18 months	Er,Cr:YSGG Laser + Biodentine = 100%	Er,Cr:YSGG Laser + Biodentine = 100%	Er,Cr:YSGG Laser + Biodentine = 100%	Biodentine-100%
10	Moore A et al.	2011	In vivo	10 years	22	ProRoot MTA, Angelus (White MTA)	3, 6, 12, 18, 24 months	ProRootMTA = 81.8%, White MTA (Angelus) =100%	ProRoot MTA = 72.72%, White MTA (Angelus) = 100%	ProRoot + White MTA-95.5%	White MTA (Angelus) -95.5%
11	Damle SG et al.	2012	In vivo	8–10 years	30	MTA, Calcium hydroxide	3, 6, 9, and 12 months	MTA = 100%, Calcium hydroxide = 93.30%	MTA = 100%, Calcium hydroxide = 93.30%	MTA = 100%, Calcium hydroxide = 93.30%	MTA = 100%
12	Norsat A et al.	2012	In vivo	6–10 years	51	CEM, MTA	6, 12 months	CEM = 95.83%, MTA = 96%	CEM = 86%, MTA = 79%	CEM = 90.61%, MTA = 87.5%	Calcium-enriched mixture CEM-90.61%,

(*Continued*)

Table 1: (*Continued*)

Sl. No	*Author name*	*Year of publication*	*Study setting*	*Age*	*Sample size*	*Material used*	*Follow-up*	*Clinical success rate*	*Radiographic success rate*	*Success rate (clinical + radiological)*	*Result*
13	Ghoddusi J. et al.	2012	In vivo	< 14 years	28	MTA, Zinc Oxide Eugenol (ZOE)	6, 12 months	MTA = 91.7% ZOE = 100%	MTA = 100% ZOE = 83.3%	MTA = 95.85% ZOE = 91.5%	MTA-95.85%
14	Omar Meligy El AS et al.	2011	In vivo	6–12 years	30	Calcium Hydroxide, MTA	3, 6, 12 months	Calcium hydroxide = 86.66%, MTA = 100%	Calcium hydroxide = 86.66%, MTA = 100%	Calcium hydroxide = 86.7%, MTA = 100%	MTA-100%

CEM: calcium-enriched mixture; MTA: mineral trioxide aggregate

Table 2: Quality assessment of studies using a Newcastle-Ottawa scale

Case reports	*Selection*			*Comparability*	*Outcome*		*Total*
	Representativeness of exposed cohort (⋆)	Selection of non-exposed cohort (⋆)	Ascertainment of exposure (⋆)	(⋆⋆)	Assessment of outcome(⋆)	Adequacy of follow-up(⋆)	
Vidal K. et al (2016)	–	⋆	⋆	⋆	⋆	⋆	5
Chaudhary S. et al (2016)	–	⋆	⋆	⋆	⋆	⋆	5
Torabinejad M. et al (2011)	–	⋆	⋆	⋆	⋆	⋆	5

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

and high precision has been seen among the articles evaluated for the systematic review owing to the lesser selection bias and more standardization. The articles selected were found to be in accordance with the objectives laid down for the subsequent evaluation. The results obtained are shown with the help of Forest plot and funnel plot in Figures 3A and B , Figures 4A and B , Figures 5A and B, respectively.

Discussion

Summary of Evidence

This systematic review commenced with the aim to evaluate and compare different biomimetic materials on the regenerative potential of cells in the physiological root apex formation (apexogenesis), apical barrier formation (apexification), and REPs in pulpally involved young permanent teeth in children. The criteria used for the evaluation and the clinical and radiographic success rates have been described.

Calcium Hydroxide: Hermann in 1920, first described a material named as calcium hydroxide in dentistry. It can be regarded as a multipurpose agent as it is used widely as direct and indirect pulp capping, apexogenesis, apexification, treating root resorption, iatrogenic radicular perforations, root fractures, and as an intracanal medicament. Moreover, its use in the treatment of immature permanent teeth through apexogenesis (vital tooth) and apexification[18] (nonvital tooth) has been greatly seen and acknowledged.

The low solubility and higher pH makes it a good material for efficiently using in the clinics as it is not soluble when it comes in contact with the tissue fluids in case of direct contact with the vital tissues. Moreover, being a strong base it dissociates calcium and hydroxyl ions which on coming in contact with the vital tissues aid in induction and formation of calcific tissue deposition. It also has additional antibacterial properties. Calcium ions also help in the remineralization process. Hydroxyl ions being alkaline in nature increases the pH aids in initiation of the healing process.[27]

A total of 93.32 and 100% clinical success rates were seen when Apexogenesis in vital immature permanent teeth were carried out. Clinically most of the teeth were asymptomatic. The reasons cited for this was the superior antimicrobial effect of calcium hydroxide. Hydroxyl ions released cause damage to bacterial DNA and denaturation of proteins. They added that the high pH of calcium plays a key role in periapical repair and calcific tissue formation.[9,10] However, at the end of 12 months follow-up period, clinical success rate was 86.60% when a few teeth showed pathologic signs. The reason cited was, failure resulted from bacterial contamination through microleakage and through the porous bridge formation.[28]

A total of 96 and 100% of radiographic success rate was seen.[10,28] However, at the end of 18 months, few teeth showed up with pathologic signs and symptoms and internal resorption. Radiographic success rate of 86.66% with periapical radiolucency and widening of lamina dura is seen. The reason for this has been, the prolonged contact with calcium hydroxide which induces significant decrease in the intrinsic properties of exposed dentin resulting in increased root fracture and internal resorption before the completion of treatment.[9]

Mineral Trioxide Aggregate

Mohmoud Taorabinejad at Loma Linda University, California, USA in 1993 first introduced a biomimetic material Mineral Trioxide Aggregate in the field of dentistry. On the basis of color MTA is available in two types known as gray and white MTA.

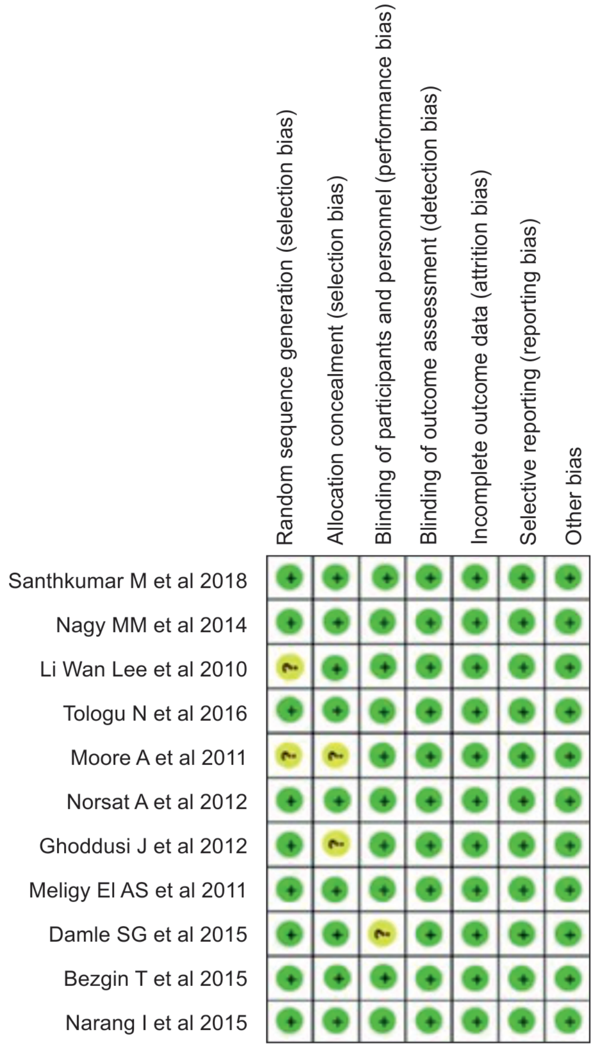


Fig. 2: Graph showing summery of risk of bias: Review authors' judgements about each risk of bias item for each included study

The differences being, concentrations of aluminum, magnesium and ferrous oxide. MTA shows no signs of solubility and when exposed to water it releases calcium hydroxide ($CaOH_2$). $CaOH_2$ is responsible for its cementogenesis inducing property. During setting reaction if mix is exposed to acidic environment it does not interfere in the setting. It is also regarded as superior to the other traditional root-end filling materials due to excellent sealing ability which may occur because MTA expands during setting reaction. In presence of moist environment sealing ability of MTA is enhanced due to the setting expansion.[29]

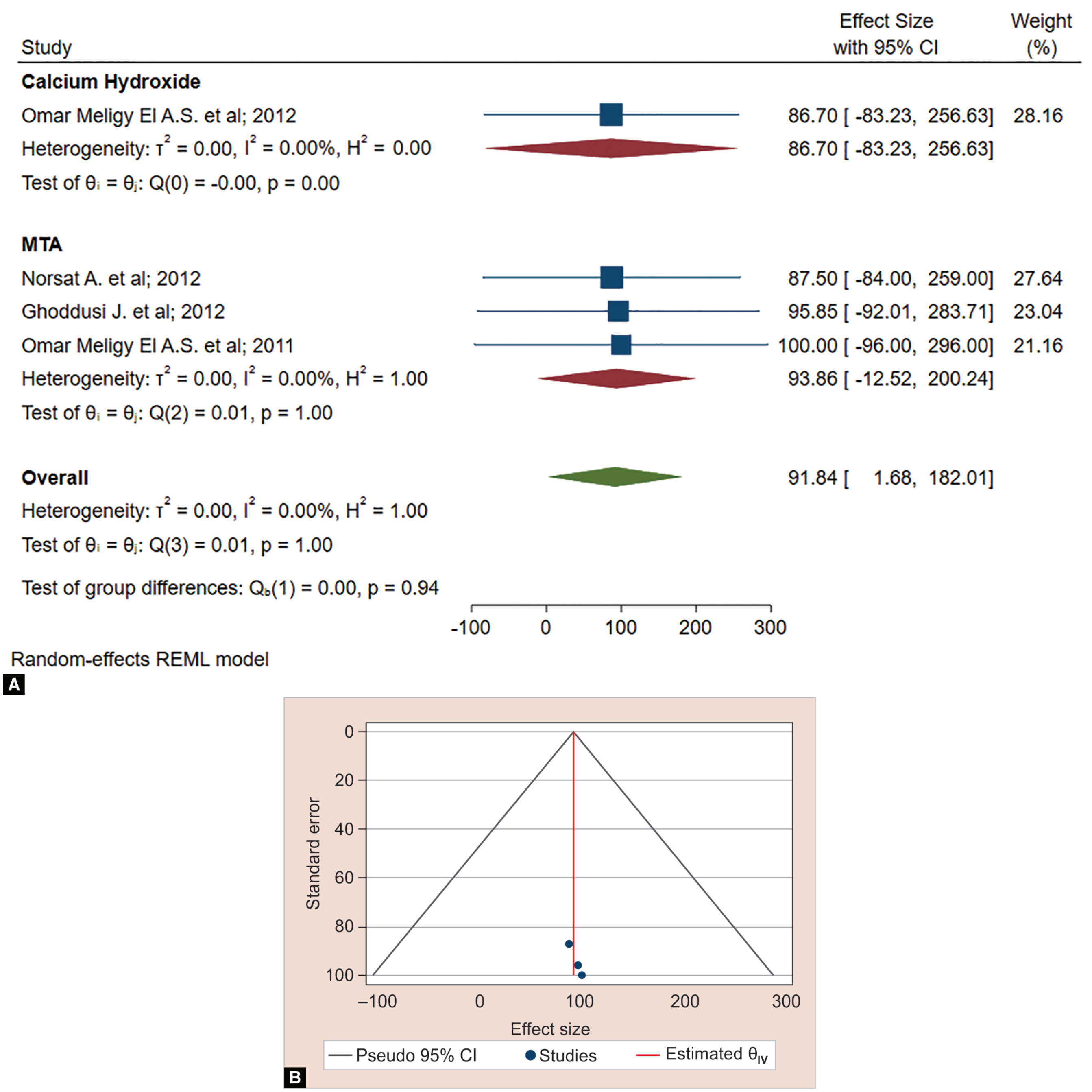
A total of 94.63–100% clinical success rates were seen. All teeth were asymptomatic.[9,28,30,31] However, at the end of 18 months, authors observed a success rates of 86.66 and 96% as coronal discoloration has been observed in some cases. The reason given by the author for this is use of chlorhexidene as an irrigating solution. It is substantive and does not possess tissue dissolving properties which may lead to the discoloration. Furthermore, leaching of MTA components through the dentin may also lead to the cervical staining. Also, the presence of metal oxides contained in the material is considered one of the chief reason.[16,32]

A total of 91–100% radiographic success rates at the end of 18 months were seen while evaluating the vital pulp therapy in immature permanent teeth using MTA. The reasons being biocompatibility, nonresorbable property, lower solubility, higher compressive strength, and induction of tissue regeneration when placed in contact with dental pulp and periradicular tissues. Moreover, complete formation of lamina dura was also observed. The reason cited by the author is the presence of several mineral oxides in its composition that have good reparative and regenerative potential.[9,16,28,30,31,32]

Biodentine

Biodentin (Septodont Ltd., Saint Maur des Fausse´s, France) is a new tricalcium silicate (Ca_3SiO_5)-based inorganic restorative commercial cement which is also called as 'bioactive dentine substitute'. The material possesses better physical and biological properties compared to other tricalcium silicate cements such as MTA and bioaggregate. Physical properties like (increased compressive strength, push-out bond strength, density, and porosity), biologic (immediate formation of calcium hydroxide, higher release and depth of incorporation of calcium ions) and handling properties makes it an ideal biomimetic material for the induction of calcific barrier formation in immature permanent teeth.[33]

A total of 100% clinical and radiographic success rate of biodentin was seen when used for apical calcific barrier formation in non-vital immature permanent tooth. The follow up at 18 months period showed the patient with no reportable clinical symptoms. The reason cited by the author for remarkable success was, the



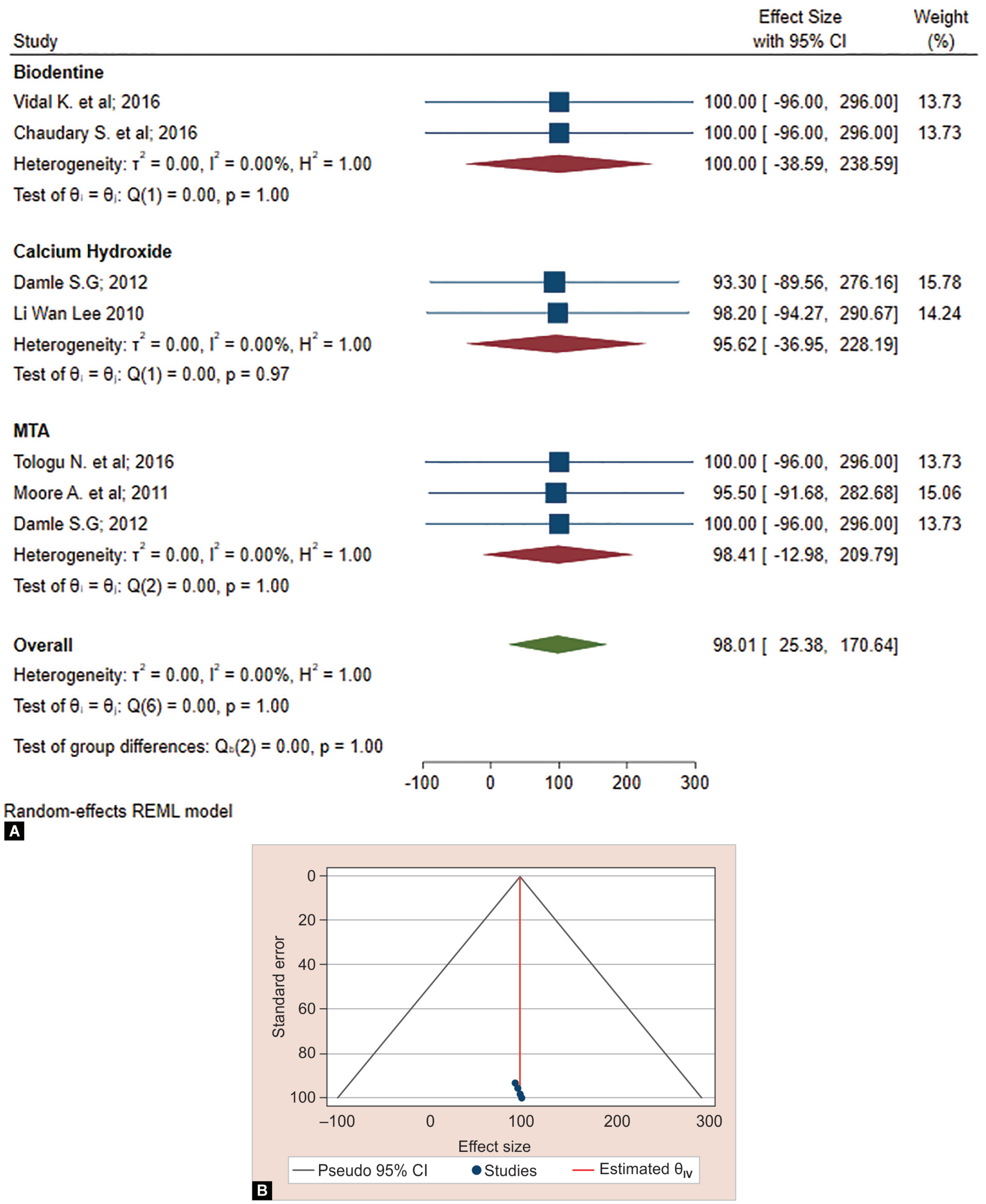
Figs 3A and B: (A) Forest plot showing pooled data obtained from meta-analysis of Apexogenesis group. (B) Funnel plot showing pooled data obtained from meta-analysis of Apexogenesis group

bioactive property which induces differentiation of odontoblast like cells that increase pulpal cell proliferation and biomineralization. Also, the response of dental pulp after direct capping with Biodentine revealed a complete dentinal bridge formation and a layer of odontoblast like cells under the osteodentin. It had also shown the lack of cytotoxicity, and its ability to stimulate collagen fiber and fibroblast formation.[34,35]

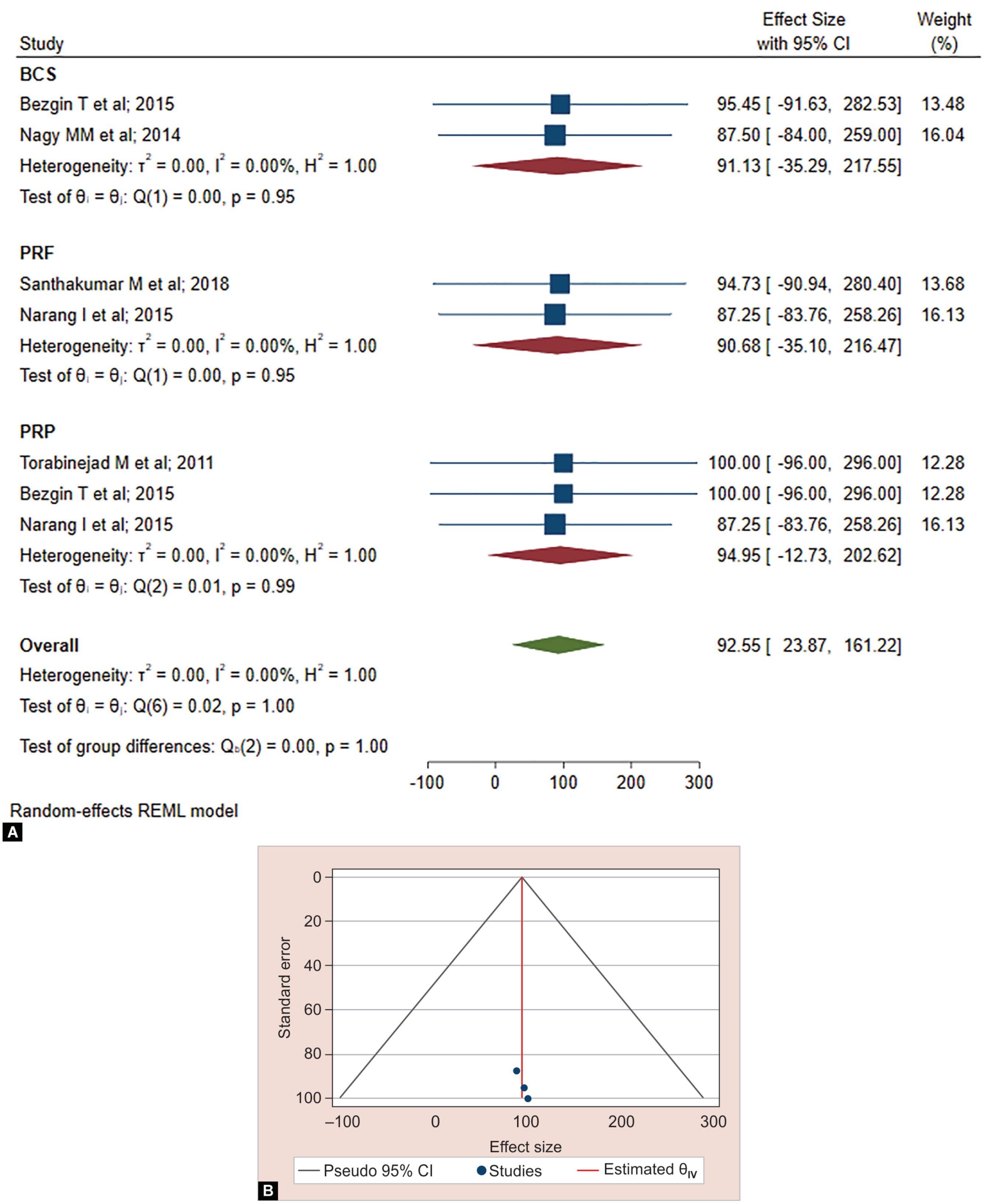
Various materials having the potential of regeneration and revascularization obtained through critical evaluation of dental literature have been discussed as follows,

Platelet-rich Fibrin

Dr Joseph Choukroun of France was the first to describe Platelet-rich Fibrin (PRF) which has been referred to as the second-generation platelet concentrate. Platelet-rich Fibrin, can be defined as a platelet gel that aids in wound healing, growth of bone and maturation rendering graft stabilization, sealing of wound and hemostasis.[17] It can be utilized as Platelet-rich Fibrin membrane that has several advantages such as, ease of preparation. It does not includes biochemical handling of the blood, hence leading to an autologous preparation.[19]



Figs 4A and B: (A) Forest plot showing pooled data obtained from meta-analysis of Apexification group. (B) Funnel plot showing pooled data obtained from meta-analysis of Apexification group



Figs 5A and B: (A) Forest plot showing pooled data obtained from meta-analysis of regenerative endodontic group. (B) Funnel plot showing pooled data obtained from meta-analysis of Regenerative endodontic group

If comparison is done between PRF and Platelet-rich plasma (PRP), no requirement of an anticoagulant exists in PRF and neither there is a need to neutralize it. Moreover, in PRF, bovine dispossessed thrombin is not essential for bringing about the conversion of fibrinogen to fibrin. This conversion slowly occurs with small quantities of physiologically available thrombin directly from the blood.[20,21] The year of 1980s came up with an important physiological property of tissue oxygenation which became crucial for initiation of wound healing. This oxygenation enhanced the bactericidal capability of the immune system present in the host cells.[22]

A total of 100% clinical success rate was observed when PRF was used as a regenerative material while treating nonvital immature permanent teeth. Patients were asymptomatic clinically.[23] However, clinical success rate was 94.73% at the end of 18 months as few teeth observed pain and mobility. The reason cited by the author is that, the loss amount of some growth factors from PRF gel while making it into the membrane.[13]

A total of 94.73% radiographic success rate was observed. At the end of 12 months, PRF showed great success. Root lengthening and achievement of adequate crown to root ratio were achieved.[13] At the end of 18 months, 98% of the teeth showed periapical healing, 40% showed closure of root end, 99% showed root lengthening, and 60% showed dentinal wall thickening. The reason cited for this is the presence of reduced amount of the growth factors.[23]

Platelet-rich Plasma

Whitman et al. in 1997 was the first one to introduce Platelet-rich Plasma (PRP). It is composed of fibrinogen in a higher concentration which is one of its chief constituent. On addition of calcium chloride to PRP, alpha granules of platelets together with higher amount of factors are released. It constitutes of diverse group of polypeptides known as growth factors, which plays an important role in the regulation of growth and differentiation of many tissues. It facilitates the increase in collagen synthesis and thus in turn increases osteogenesis. Also it enhances the vascularity of the tissues by increasing angiogenesis. It leads to increasing epithelial cells and granulation tissue production and has an antimicrobial effect.[22]

A total of 100% clinical and radiographic success rate was observed when PRP was used as a regenerative material while treating non-vital immature permanent teeth. Clinically, it showed excellent results. The reason cited for the successful treatment with the use of PRP is the presence of growth factors stimulating collagen production. Also, there is loss of some growth factors from PRF gel while making it into the membrane. However, they stated that due to the ease of handling and the lesser time taking procedure they recommend the use of PRF membrane as reliable as PRF gel.[24,25] It aids in the recruitment of other cells at the site of injury which produces anti-inflammatory agents that initiates vascular in growth by inducing cellular differentiation and also aids in improving wound healing.[23,24,25]

However, at the end of 18 months, PRF showed periapical radiolucency where as root lengthening and achievement of adequate crown to root ratio were achieved. Also, root lengthening as well as dentinal wall thickening was seen among 40 and 20%, respectively. The reason cited for lesser success rate was lesser healing kinetics on osteoblasts that leads to leaching out of the growth factors.[23]

Blood Clot Scaffold

Blood clot scaffold can be defined as a physiological or biological three dimensional structure that provides micro environment aiding in tissue construction for effective cellular growth and differentiation. Inbuilt natural polymers like collagen and glycosaminoglycans offers great biocompatibility and activity.

A total of 100% clinical success rate is seen while using blood clot as a scaffold for the regeneration potential of necrotic immature teeth. All the teeth were clinically asymptomatic.[11,23] However, in some cases clinical success rate accounted to be 90% when periapical inflammation is observed. The reason being, blood clot scaffold alone did not prove to be more effective when used along with carrier proteins such as collagen.[24]

A total of 100% radiographic success rate is seen at the end of 18 months.[11,23] The reason can be stated as, the blood clot seems to be the reservoir of growth factors. The expression of these have a chief regenerative effect on immature permanent teeth.[11] However, 10% of the teeth exhibited enlargement of pre-existing periapical pathosis with success rate accounting to 90%. In accordance with the other studies the author stated that using blood clot scaffold alone did not prove to be more effective when used along with carrier proteins such as collagen.[24]

Limitations and Future Implication

During the literature search we encountered a few lacunae, one of which was found to be that very few studies were conducted in between the span of 2010–2020. The major drawbacks were that some articles did not have a proper follow up regime. Thus, more meticulous research is needed to be carried out in this direction with long term follow-up periods involving larger sample size with the use of biomimetic materials on apexogenesis, apexification, and regenerative procedures so that a better conclusion and a proper protocol can be laid down.

Clinical Significance

This systematic review aids in amending the clinician perceptions towards acceptance of the newer regenerative procedures and to gain knowledge regarding their effectiveness in management of young permanent tooth in children.

Conclusion

With the surge in research, there has been a paradigm shift regarding the widely available biomimetic materials in pediatric dentistry. A million dollar question still prevails on which is the best material for the effective treatment of an immature permanent teeth in children. Thus, systematic review and meta-analysis concludes:

- In the Apexogenesis and Apexification groups, though either of the biomimetic and conventional materials are found to be good but the newer biomimetic materials such as mineral trioxide aggregate, biodentine showed better results than conventionally used calcium hydroxide.
- In the regenerative endodontic group, though all the scaffolds are found to be good but the newer biomimetic materials such as PRP and platelet-rich fibrin showed better results.

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