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Comparison of Mineral Trioxide Aggregate and Biodentine for Open Apex Management in Children with Nonvital Immature Permanent Teeth: A Systematic Review

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Abstract

Tricalcium silicate cements have long been used in dentistry for management of open apex. Biodentine was introduced to overcome the disadvantages of mineral trioxide aggregate (MTA). The aim of this systematic review was to compare the success rates of biodentine and MTA as a material of choice for the management of open apex in children with nonvital immature permanent teeth. PubMed/Medline, Scopus, EMBASE, Cochrane, and Google Scholar were searched until November 30, 2021, with the search terms young permanent teeth, immature permanent teeth, open apex, MTA, and biodentine. Based on the inclusion criteria, the articles were selected following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and assessed for quality using a risk-of-bias assessment tool. The outcomes of the studies were qualitatively synthesized. A total of 379 studies were identified and after refinement only two studies met the eligibility criteria. Both the studies were performed in children with nonvital pulp status. One of the studies showed a clinical success of 91.66% for MTA and 100% for biodentine in revascularization cases while the other study showed 100% for both the materials in apexification cases. Radiographic success was 100% for both the materials at the end of the follow-up period in both the studies. Treatment modality can create heterogeneity that does not allow making a

Keywords
- immature permanent teeth
- mineral trioxide aggregate
- biodentine
- open apex

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pooled conclusion for the two materials collectively, which is the case in this review where one study used revascularization, while the other used apexification. An overall high risk of bias was noticed for the selected studies. With high risk of bias and low quality of evidence, a strong definitive conclusion cannot be arrived at. Further studies with proper randomization and minimal risk of bias are required to provide a conclusive result. However, as per the included studies, biodentine can be a material of choice for revascularization while both MTA and biodentine can be used for apexification procedures.

Introduction

Tooth development involves formation of the crown followed by the root structure.[1] At the time of tooth eruption, the root structure is still incomplete. It takes up to 3 years for completion of root structure, that is, the formation of minor constriction of the apical foramen. If the normal growth and development of root structure is disrupted, it leads to incomplete rhizogenesis, also known as open apices.[2] This refers to the absence of sufficient root development to provide a conical taper to the root canal's anatomy. It could be one of the two types: (1) blunderbuss canal, which is funnel shaped, that is, flaring and divergent in dimension; and (2) non-blunderbuss canal, which is cylindrical shaped, that is, broad and parallel in dimension.[3]

The most common etiology for incomplete root formation would be pulp necrosis due to trauma or dental caries.[4] The challenges faced by the practitioner in open apex situations are difficulty in root canal debridement, lack of apical stop that threatens quality obturation, and thin root canals that have a high risk of fracture.[5] The herculean task during management of such case scenarios is forming an apical barrier which can provide a strong hermetic seal that can aid in a good obturation of the root canal.[6] Literature searches have suggested management approaches by surgical,[7,8] non-surgical,[9–14] or sometimes no treatment.[15,16] In the 1960s, introduction of apexification as a possible solution to treat nonvital teeth with open apex conditions gained popularity within a decade due to its successful results.[17] A barrier would be created using calcium hydroxide that will be backed later with gutta-percha to obtain optimal obturation. The technique suggested took 4 to 6 months for getting an apical seal. Latter single-visit apexification came into practice with introduction of fast setting cements.[18] Although apexification provided promising prognosis, the thickness of the root dentin and the root length remained the same, which may lead to root fractures.[19–21] Also, the vitality of the tooth was not regained. Revascularization was introduced later which provided hopes on root morphology which was not given by apexification. Revascularization procedure involved sterilization of the canal space, followed by intentionally inducing bleeding at the periapical region up to cementoenamel junction or placing a scaffold in the pulp chamber and sealing using cement barrier that can promote healing like calcium silicate cements.[22,23] The root dentin thickened, the root length increased, and the vitality (sensitivity) was restored.[24–26]

A vast diversity of materials have been used to induce apical barrier formation for the past two decades like calcium hydroxide, resorbable ceramic, freeze-dried cortical bone, freeze-dried dentin, dentinal shavings, mineral trioxide aggregate (MTA), bone morphogenetic protein, and biodentine.[4,27] Calcium hydroxide was first introduced by Kaiser for apical closure which was later popularized by Frank. But it had disadvantages of prolonged treatment duration, likelihood for reinfections, and susceptibility to tooth fracture.[17,28,29] There was a paradigm shift in the treatment protocols due the works done by Parirokh and Torabinejad on MTA.[30] This Portland-cement based cement revolutionized apexification due to good hard tissue formation, better sealing ability, and higher biocompatibility with good antimicrobial properties.[31–34] But it has longer setting time, difficult handling properties, discoloration ability, and minimal washout resistance which led to a change in trend toward, a tricalcium-based silicate cement, biodentine in 2009.[35] Biodentine was able to produce thicker mineralized tissue bridge, enhanced compressive strength, least microleakage with good color stability, bio-interactivity, and mineralization capacity.[36–40] Since then, the battle between both the materials have revolutionized regenerative endodontics and vital pulp therapies with higher success rates. Both MTA and biodentine showed promising results in randomized controlled trials when used as direct pulp capping agent, pulpotomy agent in primary teeth,[41–43] immature first permanent molars,[44–46] and mature permanent molars[47] with carious pulp exposure and traumatized immature anterior permanent teeth.[48]

Although observational studies provide moderate levels of evidence and precisely performed randomized controlled trials provide high levels of evidence, a concise systematic review would provide the highest level of evidence to arrive at a conclusion. Earlier systematic reviews compared the efficacy of MTA and biodentine as a material of use in pulpotomy[49] and direct pulp capping,[50] and other vital pulp therapies in primary teeth and permanent teeth, but there are no systematic reviews done with regards to the management of open apex in immature nonvital permanent teeth. The aim of this systematic review was to compare the success rates of biodentine and MTA as a material of choice for the management of open apex in children with nonvital

immature permanent teeth. Accordingly, this systematic review will provide an overview on the evidence-based decision-making process for the dental practitioners to select the required material for the management of open apex in immature permanent teeth.

Methods

The protocol of this systematic review was registered at PROSPERO database under the registration number CRD42021294000.

Strategy of Literature Search

Online databases like PubMed/Medline (www.ncbi.nlm.nih.gov), Scopus (www.scopus.com), EMBASE (www.embase.com), Cochrane (www.cochrane.org), and Google Scholar (www.scholar.google.com) were used to search articles regarding the investigations of reported clinical cases relevant to the current systematic review. Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed.[51] Two independent reviewers performed this online search which included articles from the start date of the online source till November 30, 2021. The search strategy was based on the PICO analysis: Population: children between 6 and 16 years of age with nonvital immature permanent teeth due to trauma or carious exposure; Intervention: biodentine; Comparator: MTA; Outcome: clinical and radiographic success rate as mentioned in the outcome measures below. The search was aided by using a combination of other Medical Subject Headings terms and keywords like young permanent teeth, immature permanent teeth, open apex, MTA, mineral trioxide aggregate, and biodentine. The reference lists were hand-searched from the collected articles to obtain additional studies. Duplicates were removed and revision of title and abstracts were done and full-texts were checked to verify the content was relevant to the review. A third reviewer was involved in the search when there is uncertainty regarding eligibility of the studies. Once consensus was arrived, a decision was made to include or exclude from this review.

Study Selection Criteria

The inclusion criteria were: (1) randomized controlled trials, prospective and retrospective trials; (2) patients between 6 and 16 years of age with nonvital immature permanent teeth due to trauma or caries; (3) compared MTA versus biodentine; (4) minimum follow-up period of 6 months; and (5) reported clinical and/or radiographic success of the treated cases. The exclusion criteria were: (1) Letter to Editor, conference proceedings, literature reviews, and personal communications; (2) in vitro and animal studies; (3) case reports and case series, (4) in vivo studies which did not report clinical success; and (5) studies that compared the materials for reasons other than open apex management.

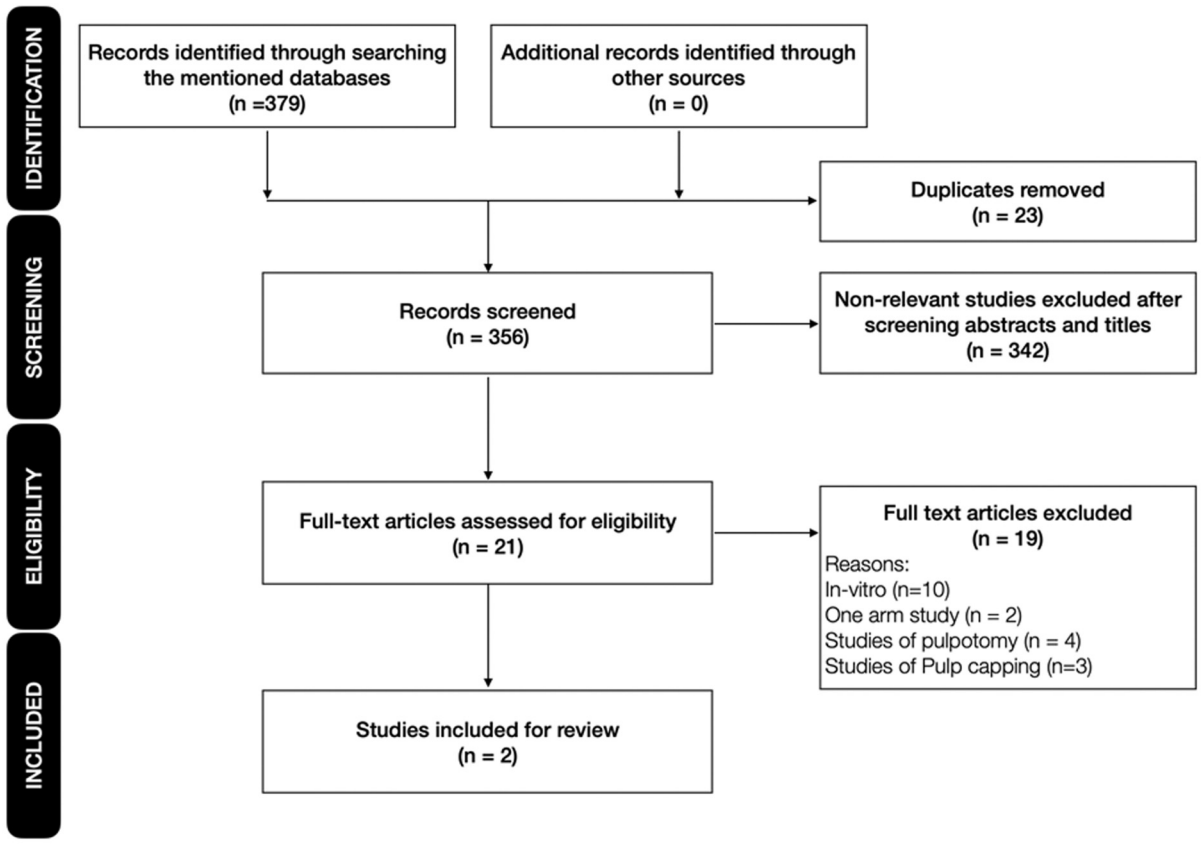

Fig. 1 Flowchart of article selection performed in the systematic review.

Table 1 Reasons for excluding the initially selected studies

No.	Author and year	Manuscript title	Reason for exclusion
1	Claudia Brizuela et al 2017	Direct pulp capping with calcium hydroxide, mineral trioxide aggregate, and biodentine in permanent young teeth with caries: a randomized clinical trial	Study on pulp capping
2	Burcu Nihan Çelik et al 2019	The evaluation of MTA and biodentine as a pulpotomy materials for carious exposures in primary teeth	Study on pulpotomy in primary teeth
3	Akhila Abbas et al 2020	Efficacy of mineral trioxide aggregate and biodentine as apical barriers in immature permanent teeth: a microbiological study	In vitro study
4	Gihan Mohamed Abuelniel et al 2020	A comparison of MTA and biodentine as medicaments for pulpotomy in traumatized anterior immature permanent teeth: a randomized clinical trial	Study on pulpotomy
5	G. M. Abuelniel et al 2021	Evaluation of mineral trioxide aggregate and biodentine as pulpotomy agents in immature first permanent molars with carious pulp exposure: a randomized clinical trial	Study on pulpotomy
6	R. Yasin et al 2021	Effect of mineral trioxide aggregate and Biodentine™ on fracture resistance of immature teeth dentine over time: in vitro study	In vitro study
7	Lama Awawdeh et al 2018	Outcomes of vital pulp therapy using mineral trioxide aggregate or biodentine: a prospective randomized clinical trial	Study on pulp capping
8	Shilpa Ahuja et al 2020	Comparative evaluation of success of biodentine and mineral trioxide aggregate with formocresol as pulpotomy medicaments in primary molars: an in vivo study	Study on pulpotomy in primary teeth
9	Swaroop Hegde et al 2017	Clinical evaluation of mineral trioxide aggregate and biodentine as direct pulp capping agents in carious teeth	Study on pulp capping
10	Nessrin A. Taha et al 2018	Full pulpotomy with biodentine in symptomatic young permanent teeth with carious exposure	One arm study
11	Léa Haikal et al 2020	Biodentine pulpotomies on permanent traumatized teeth with complicated crown fractures	One arm study
12	A. Sogukpinar et al 2020	Comparative evaluation of four endodontic biomaterials and calcium hydroxide regarding their effect on fracture resistance of simulated immature teeth	In vitro study
13	Parinaz Esteki et al 2021	In vitro antimicrobial activity of mineral trioxide aggregate, biodentine, and calcium-enriched mixture cement against Enterococcus faecalis, Streptococcus mutans, and Candida albicans using the agar diffusion technique	In vitro study
14	Pooja Nitin Mapara et al 2020	Comparative evaluation of calcium release of the apical plugs formed by mineral trioxide aggregate, biodentine, and EndoSequence root repair material with and without 2% triple antibiotic powder: an in vitro study	In vitro study
15	Zahrasadat Madani et al 2019	Evaluation of tooth discoloration after treatment with mineral trioxide aggregate, calcium-enriched mixture, and Biodentine ® in the presence and absence of blood	In vitro study
16			In vitro study

(*Continued*)

Table 1 (*Continued*)

No.	Author and year	Manuscript title	Reason for exclusion
	Pandi Prasanthi et al 2019	Effect of 17% ethylenediaminetetraacetic acid and 0.2% chitosan on push out bond strength of biodentine and ProRoot mineral trioxide aggregate: an in vitro study	
17	Priyanka Jain et al 2019	Effect of acidic environment and intracanal medicament on push-out bond strength of biodentine and mineral trioxide aggregate plus: an in vitro study	In vitro study
18	Amr M. Elnaghy et al 2016	Fracture resistance of simulated immature teeth filled with biodentine and white mineral trioxide aggregate - an in vitro study	In vitro study
19	M. Juez et al 2019	In vitro comparison of apical microleakage by spectrophotometry in simulated apexification using White Mineral Trioxide Aggregate, TotalFill Bioceramic Root Repair material, and BioDentine	In vitro study

Data Extraction

From the studies that were included, the following data were extracted: name of the first author, year of publication, country, study design, sample size in each group, participants' age and gender, teeth evaluated, management protocol, intervention, control, follow-up period, and clinical and radiographic outcomes. Any disagreements about the data extraction were resolved in consultation with a third reviewer or by group discussion. Fields for which information could not be found in a publication or online abstract were entered as "unknown."

Quality Assessment

Risk-of-bias assessment tool provided in the Cochrane Handbook for Systematic Reviews of Interventions[52] was used to assess the methodological quality of the selected studies individually. Domains that were evaluated specifically were random sequence generation, allocation concealment, blinding of patients and treating or evaluating personnel, blinding of outcome assessment, incomplete data outcome, and selective reporting risk.

We categorized risk of bias of each individual study according to the following criteria:

1. Low risk of bias: studies for which we identified all items as being "low risk."
2. Moderate risk of bias: studies for which we identified one or more items as being "unclear."
3. High risk of bias: studies for which we identified one or more items as being "high risk."

Overall risk of bias was assessed based on the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) system which assesses the quality of evidence as well as helps clinicians decide the strength of the recommendation provided for an intervention.

Outcome Measures

The primary outcome was the clinical success rate. For apexification, the clinical success was assessed based on the presence or absence of pain, tenderness on percussion, swelling, abscess, and tooth mobility. For revascularization, the clinical success was assessed based on the requirements provided for apexification also including crown discoloration. Secondary outcomes were radiographic success rate. For apexification, the radiographic success was assessed based on the presence or absence of periapical radiolucency, widening of periodontal ligament, and extent of material at the apex. For revascularization, length of the root was assessed for radiographic success.

Results

Study Selection

►**Fig. 1** depicts the process of search protocol and article selection for the systematic review. A total of 379 studies were identified by searching through the abovementioned databases. About 23 duplicates were removed. Around 342 articles were nonrelevant to the search strategy and finally 21 full-text articles were examined for eligibility. Only two studies were included in the final review after excluding 19 articles for reasons mentioned in ►**Fig. 1** and ►**Table 1**.

Study Characteristics

►**Table 2** summarizes the characteristics of the studies included in this review. One study was conducted in 2019 from Egypt and the other was in 2020 from India. Both were randomized controlled trials where they treated maxillary incisors. The control group for both the studies was children receiving MTA while the intervention group was children receiving biodentine.

The study performed by Aly et al compared the materials in revascularization procedure which they reviewed periodically every 3 months till 12 months. Their clinical success rate was 91.66% for the MTA group and 100% for the biodentine group. Biodentine group showed 100% resolution of tenderness on percussion, swelling, sinus, or fistula and mobility while tenderness was resolved by 91.66% in the

Table 2 Data of selected studies

First author, year, and country	Study design	Sample size (teeth)	Study subjects (age and gender)	Teeth evaluated	Management protocol	Control	Intervention	Follow-up period (with intervals)	Clinical outcome	Radiographic outcome
Aly et al, 2019 (Egypt)[53]	RCT	25	8–15 years, both genders	Incisors	Revascularization	MTA	Biodentine	12 months	MTA - 91.66% Biodentine - 100%	MTA - 5.02% increase in working length Biodentine - 5.64% increase in working length
Yadav et al, 2020 (India)[54]	RCT	60	6–15 years, both genders	Incisors	Apexification	MTA	Biodentine CPC	9 months	MTA - 100% Biodentine - 100% CPC - 100%	At 3 months, biodentine showed better results than MTA and CPC but at 9 months of the follow-up period, CPC showed greater periapical healing than MTA and biodentine

Abbreviations: CPC, calcium phosphate cement; MTA, mineral trioxide aggregate; RCT, randomized controlled trial.

MTA group. The radiographic outcome showed 5.02% increase in working length of the tooth in the MTA group while 5.64% increase in working length in the biodentine group, which were not statistically significant. Both clinical and radiographic outcomes were not statistically significant. The lesser the time lapse between date of injury and referral, there is higher increase in root length.[53]

The study done by Yadav et al compared the materials in apexification procedure which they reviewed periodically every 3 months till 9 months. They had a second intervention group with children receiving calcium phosphate cement. Their clinical success rate was 100% for all the groups. There was 100% resolution of tenderness on percussion, swelling, sinus, or fistula and mobility for both MTA and biodentine. There were no significant differences based on clinical outcomes at baseline and 3-month follow-up. On examining the radiographic success, biodentine performed better than MTA during the 9-month follow-up period.[53,54] Comparison on periapical radiolucency was statistically significant at 3-, 6-, and 9-month follow-up with better results using biodentine compared with MTA.

Risk of Bias within Studies

Both the studies had low risk of bias in relevance to random sequence generation, allocation concealment, and blinding of outcome assessment. Unclear risk in performance and reporting bias and high risk in attrition bias was noticed for one study. Common limitations noticed were nonreporting of data lost to follow-up, absence of explanation for reduction in follow-up period, and inadequate mentioning about blinding of the patient and personnel (►**Table 3**, ►**Fig. 2**).

Overall Quality Assessment

Based on the GRADE system of assessment, there is an overall low quality of evidence as there is high risk of bias in one of the included studies and heterogeneity of treatment done in the included studies (►**Table 4**). Based on this lack of strong evidence, it is not ideal to arrive at a conclusion or provide a recommendation whether to use MTA or biodentine for apexification or revascularization. Only further randomized controlled clinical trials which are properly done with minimum bias would help us provide a definitive conclusion.

Discussion

The sole objective of this systematic review was to determine whether MTA or biodentine would provide higher success percentage for open apex management in immature permanent teeth. The necessity for such a research question was due to the fact that an agreement was not arrived with respect to use of these materials owing to their eccentric pros and cons. The obtained data showed that there is insufficient evidence to support or contradict the use of both materials included in this review.

The primary objective of apexification is to ensure the formation of a hard calcific barrier that can assist in obturation. Other objectives include thickening of root dentin and

Table 3 Risk of bias table

Yadav et al 2020		
Bias	**Authors' judgment**	**Support for judgment**
Random sequence generation (selection bias)	Low risk	Selected were randomized in the group by using envelop draw method. A total of 60 envelopes were used, divided into three groups of 20 envelopes each for group I, group II, and group III, respectively. The patients were instructed to pick up any envelope randomly
Allocation concealment (selection bias)	Low risk	The envelopes contained information in the form of coded alphabets, regarding the type of material chosen for apexification procedure
Blinding of participants and personnel (performance bias)	Unclear risk	The patients were instructed to pick up any envelope randomly. The envelopes contained information in the form of coded alphabets, regarding the type of material chosen for apexification procedure
Blinding of outcome assessment (detection bias)	Low risk	All the clinical and radiographical observations were performed by two independent observers, blind to the intervention used
Incomplete outcome data (attrition bias)	High risk	Not mentioned
Selective reporting (reporting bias)	Unclear risk	The patient was recalled at 1, 3, 6, 12, and 15 months postoperatively for clinical and radiographical evaluation. The postintervention (1, 3, 6, and 9 months) presence of clinical signs and symptoms are summarized
Aly et al. 2019		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Simple randomization was used to divide patients using the sealed envelope method with 1:1 allocation ratio into two groups. Sequence generation was done for the patient number (1–26) using computer sequence generation
Allocation concealment (selection bias)	Low risk	Each of the 26 papers numbered from 1 to 26 was individually packed in opaque envelopes after folding each paper 8-folds. Each patient picked an envelope after their enrolment in the study and before the start of treatment
Blinding of participants and personnel (performance bias)	Low risk	Parallel, double-blinded (patients and assessor), randomized clinical trial
Blinding of outcome assessment (detection bias)	Low risk	Parallel, double-blinded (patients and assessor), randomized clinical trial
Incomplete outcome data (attrition bias)	Low risk	Exclude from analysis ($n = 1$) in group II in ►**Fig. 2**
Selective reporting (reporting bias)	Low risk	All the outcome variables are reported

also increasing the root length. The material of choice should fulfill the above requirements and also maintain an antibacterial environment for faster healing. Setting reactions of MTA and biodentine is based on hydration of the silicate powder components. This helps in the formation of silicate gel which later polymerizes and hardens forming the calcific barrier which consistently releases calcium ions and maintains a high pH. Higher pH helps in antibacterial activity and the release of calcium ions helps in remineralization of demineralized dentin and to form three-dimensionally stable nonporous calcific barrier.[55,56]

Calcium hydroxide was considered as the gold standard material for managing open apex cases affected by carious exposures or trauma. MTA from the Loma Linda University made its entry to revolutionize multivisit apexification to a single-visit apexification due to its setting duration of 3 to 4 hours and allowing a proper hermetic seal at the apex.[57,58] MTA also helps in consistent formation of

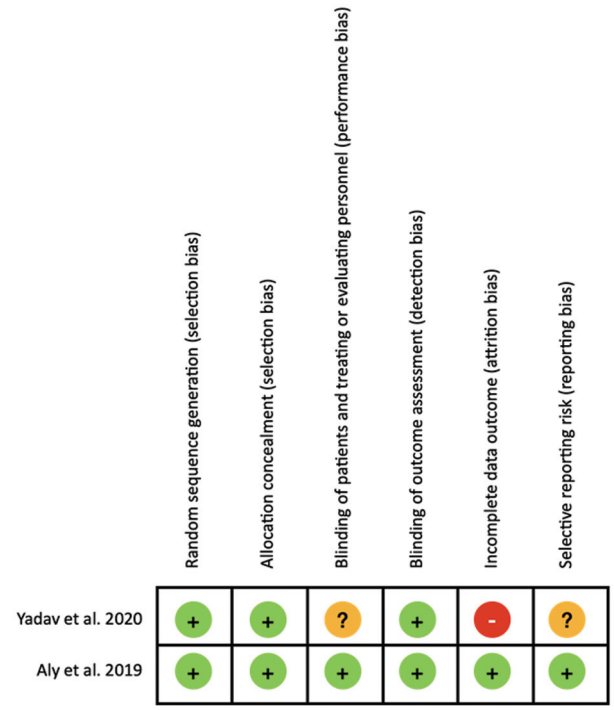

Fig. 2 Risk of bias of the included studies.

cementum and promotes periodontal tissue regeneration.[34] The research question then was whether MTA performed similar or better than calcium hydroxide in cases that contained necrotic pulp which required closure of apex. Previous systematic reviews on material of choice for apexification have compared calcium hydroxide and MTA which showed that both materials showed similar success rates and shorter treatment time of MTA would improve compliance from the patient.[59–62] A more recent systematic review supports the use of MTA and discontinue the use of calcium hydroxide for apexification procedure.[63] This tricalcium silicate cement earned its place as the material of choice for treating open apex cases. With advancements in the field of science and dentistry, newer tricalcium silicate cements were manufactured which can overcome the drawbacks of its predecessors.

Biodentine was introduced to overcome the drawbacks of MTA which are longer setting, discoloration, and difficult handling properties.[64–66] Silicate ingredients in the powder content sets faster with the liquid content containing calcium chloride thereby setting in 10 minutes. Change in opacifier, that is, zirconium oxide reduces discoloration and improves handling properties. After a decade, the research question has changed onto which of the two tricalcium silicate cements perform better. Previous systematic reviews with MTA and biodentine have been attempted as a choice for different endodontic treatment protocols and showed varied results. Biodentine performed better than MTA as root-end filling.[67] Biodentine performed similarly to MTA as a direct pulp capping agent[50,68] and pulpotomy agent.[49] MTA performed better as a pulpotomy agent for primary teeth.[69] The current systematic review assessed their efficacy for the management of open apex case scenarios which showed that biodentine performed better.

Only two studies made to the final assessment in this systematic review. Among the two, one of the studies had a low risk of bias which gives its results a stronger internal validity although the external validity is still questionable. The other study had a high risk of bias in terms of performance, attrition, and reporting of data. This reduces the validation of the study by pertaining the results only to the study environment. There is a dire need for conducting high-quality randomized controlled trials with lower risk of bias so as to validate the results with higher precision that can be used to improvise the evidence-based decision-making skills of the dental practitioners.

Few drawbacks were noticed during this systematic review. The number of studies included was small. Only one study was of high quality. Results of the protocols could vary based on the operator's clinical expertise. There were slight variations in the treatment outcomes as the protocol of treatment varied due to lack of studies over one specific treatment protocol. These limitations suggest that high-quality treatment-specific studies are needed in the future to compare the results more specifically based on the material's efficacy.

Conclusion

With high risk of bias and low quality of evidence, a strong definitive conclusion cannot be arrived at. Further studies with proper randomization and minimal risk of bias are required to provide a conclusive result. However, as per the included studies, Biodentine can be a material of choice for revascularization while either MTA or biodentine can be used for apexification procedures.

Table 4 GRADE assessment

Study	Risk of bias	Inconsistency	Indirectness of evidence	Imprecision	Publication bias	Quality of evidence
Yadav et al 2020	High	No	Yes	No	No	Low
Aly et al 2019	No	No	Yes	No	No	Moderate

Abbreviation: GRADE, Grading of Recommendations, Assessment, Development, and Evaluations.

Conflict of Interest
None declared.

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