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Success of pulpotomy with MTA in primary and permanent teeth: A Systematic review

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***Abstract*---**MTA has long been used as a Pulpotomy agent to preserve the pulp vitality, but there is a need to have an evidence-based approach when selecting the most appropriate pulpotomy agent which will be suitable for both dentitions, as the pulp of primary and permanent teeth have many histological and morphological differences. This systematic review aimed to evaluate the success of pulpotomy with MTA in primary and permanent teeth. A computerized literature search was performed through five databases: PubMed, Google Scholar, Microsoft Academics, EBSCO, and Science.gov to

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identify articles up to December 2020. Randomized controlled trial studies were selected in accordance with the inclusion and exclusion criteria. Out of the 5070 publications initially identified, only 18 studies that fulfilled the inclusion criteria were included in the review. Out of those 18 studies, 9 were studies performed on primary teeth, and the other 9 were performed on permanent teeth. After thorough review and evaluation, it was found that overall treatment success in primary teeth was 88.89-100% and it was 85-100% in permanent teeth. Overall clinical and radiographic success rates after follow-up showed that MTA pulpotomy showed slightly better results in primary teeth as compared to permanent teeth.

***Keywords*---**dentition, MTA, pulpotomy, systematic review.

Introduction

Deep caries, traumatic injuries from extensive restorative procedures with minute exposure or near-exposure of the dental pulp invariably result in an irreversible pulpal inflammation.[1] Early management of such teeth should be done to avoid progressive destruction of dental hard tissue and subsequent loss of pulp vitality thus, vital pulp therapy has been proposed which aims to preserve and maintain pulp tissue affected by caries, traumatic injury, or other causes. Also, it is the treatment of choice for treating reversible pulpitis in both primary and permanent teeth. Vital pulp therapies include treatment procedures like a) Direct and indirect pulp capping, b) Pulpotomy in the initial stages.[2]

Pulpotomy is a dental procedure in which the coronal portion of the pulp is removed, and the remaining radicular pulp is preserved, followed by placement of suitable medicament over the remaining radicular pulp tissue, which has the potential to initiate healing, promote repair protect the pulp from further insult.[3] Various pulpotomy medicaments like ferric sulfate, glutaraldehyde, formocresol, calcium hydroxide, sodium hypochlorite, osteogenic protein, bone morphogenetic protein, laser have been introduced in recent years. They have been tested and advocated for use in pulpotomy procedures based on their properties such as biocompatibility and antimicrobial efficacy when placed in contact with the inflamed pulp.[4]

The Portland cement-based material known as mineral trioxide aggregate (MTA) was developed at Loma Linda University in 1993. It is a water-based material and composed of tricalcium silicate, dicalcium silicate, tricalcium aluminate, tetra-calcium aluminoferrite, calcium sulfate, and bismuth oxide. Since mid-1990s, MTA has been recognized as the reference material for the conservative vital dental pulp treatments and also indicated for various restorative, endodontic, and regenerative dental procedures like a) Vital pulp therapy b) Apexification c) Perforation repair d) Root-end filling e) Resorption repair. MTA has shown to stimulate the formation of dentin-bridge protecting the pulp markedly more than that observed with calcium hydroxide. Many studies have shown that it possesses many properties such as good biocompatibility, a high sealing capacity, an alkaline pH, and the fact that it sets in the presence of humidity. MTA can also

induce the formation of bone, cementum and dentin. It sets through a hydration reaction when mixed with distilled water (using a ratio of 3:1) results in the formation of a highly alkaline cement matrix comprising of by-products, such as calcium hydroxide and calcium silicate hydrate gel. The hydration of the MTA powder produces a colloidal gel, which solidifies and results in a solid structure. MTA presents a longer setting time of 2 h and 45 min. The initial pH of the MTA is approximately 10.2, but it increases to 12.5 after 3 hours immersed in solution. Several studies proved that MTA is successful in maintaining the pulp vitality in primary and permanent teeth. However, there are certain inherent drawbacks of MTA like tooth discoloration, long setting time, complex handling characteristics, and high cost.[5]

In permanent dental pulp the cell rich zone is thicker than in primary teeth, which may indicate a higher regenerative potential for new dentin formation in permanent teeth. Also, the presence of odontoblastic layer of permanent teeth contains more odontoblasts than that of primary teeth, where it is much thinner, resulting in the reduced regenerative capacity of the pulp of primary teeth [6] which eventually may alter the response of primary dental pulp to MTA pulpotomy. Bardellini E, Amadori F, Santoro A, Conti G, Orsini G, Majorana A. (2016) characterized pulps from primary teeth by reduction of odontoblastic layer and greater occurrence of apoptotic odontoblast. Their findings suggested that odontoblasts have a predominant pro-apoptotic phenotype in primary teeth, which led them to a conclusion that odontoblasts of primary teeth can be assumed to have a lower reparative activity when compared to odontoblasts of permanent teeth [7]. Keeping the above facts in mind we have conducted a systematic review with the aim of evaluation of success of pulpotomy with MTA in primary and permanent teeth which may eventually help in selection of proper material for pulpotomy in primary and permanent teeth.

Material and Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist, which is an evidence-based minimum set of items for reporting in systematic review and meta-analysis.[8] The study protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) under the protocol number CRD42021235492. The focused question was structured according to the PICO format (population, intervention, comparison, and outcome): Do the clinical and radiographic success rates of MTA Pulpotomy reported in randomized controlled trials on human primary teeth differ from human permanent teeth?

- Population: Children, adolescents and adults with extensive caries or dental trauma with pulp exposure involving vital dental pulp in primary and/or permanent teeth.
- Interventions: MTA pulpotomy
- Comparison: Efficacy of MTA Pulpotomy in primary teeth as compared to permanent teeth.
- Outcome: success of treatment after at least 1 year of follow-up. Clinical success was defined as an absence of clinical features like spontaneous pain, mobility, tenderness to percussion or palpation, swelling, and sinus

tract. Radiographic success was determined by the absence of any evidence of external and internal resorption and periradicular/interradicular (furcation) radiolucency. Overall success was defined as the achievement of both clinical and radiographic success.

Inclusion criteria

- Human in vivo studies
- Randomized controlled trial studies.
- Studies reporting clinical, radiographic or overall success rate with a follow up of at least 1 year, were selected.
- Studies reporting only in the English language were selected.

Exclusion criteria

- In vitro studies on human and animals.
- Non-randomized controlled trials, case reports, survey studies, literature reviews and systematic reviews.
- Studies with follow up period of less than 1 year.
- Studies reported in other than English language.

Search strategy

We defined a search strategy based on the controlled vocabulary (MeSH terms) of the PubMed database along with the free keyword. using the following search terms and key words alone or in combination with the Boolean operator “AND” & “OR”: MTA, pulpotomy, primary teeth, permanent teeth, deciduous teeth. Studies conducted from year 2005 to 2020 were included in this review. Moreover, references of the eligible studies and relevant systematic reviews on the topic were manually checked and screened. Other electronic databases used to identify the trials to be included were Google Scholar, Microsoft Academics, EBSCO and Science.gov. References were managed by reference management software Zotero 5.0.96.0. and duplicated results were removed. The search data from all databases were included in Figure 1. Full-text versions of the papers that appeared to meet the inclusion criteria were retrieved for further assessment and data extraction (Table 1).

Study selection

First, the titles and abstracts were independently reviewed by the authors and selected if they met the predetermined inclusion criteria. Duplicated publications were removed using Zotero 5.0.96.0. Literature reviews, case reports, and studies on other aspects (such as not investigating the efficacy of MTA) were excluded. The full texts of the remaining studies were retrieved. In-vivo randomized controlled trial studies investigating the efficacy of mineral trioxide aggregate (MTA) as pulpotomy agent in primary and permanent teeth with or without control groups were selected for analysis in this systematic review.

Search Results

Details of the study selection process are outlined in Figure 1. From the database searches, we found 5070 articles; after that, we removed the duplicate articles and 4931 remained. We evaluated the eligibility of studies after a thorough screening phase from where the articles were distributed among the reviewers for independent title and abstract reading. This showed 4861 ineligible studies, which therefore were excluded, as they were not directly associated with the objectives and the purpose of the research. Two of us (YJK and SNY) then searched the studies with randomized control trial and excluded 34 non-randomized control trial study articles. Further, we excluded 13 articles as they were animal studies and 5 more articles because the outcome measure was different from the outcome measure in our study criteria. Finally, remaining 18 studies (Table 1) that met our inclusion criteria were selected for the systematic review and processed for quality analysis.

Assessment of risk of bias

Risk of bias of included studies was evaluated by two independent reviewers (YJK and SNY) using a specific study design-related risk of bias developed by Cochrane Collaboration (Cochrane Handbook for Systematic Reviews of Interventions 5.1.0). The criteria include six domains related to randomization, blinding outcome data, and characteristics of the sample at baseline. We assessed the of risk of bias by rating each of the study criteria as low risk of bias, high risk of bias, or 'unclear' (not possible to find information or uncertainty over the potential for bias). Any disagreement between the reviewers was resolved by discussion and mutual agreement. The results of the risk of bias evaluation can be found in Table 2.

Quality analysis

The quality of the included studies was assessed using the Cochrane risk of bias assessment tool. Table – 2 shows a summary of the risk of bias in the included studies. The selection bias risks for 14 studies seems to be low due to proper implementation of random sequence generation, 4 studies [4,9–11] showed unclear risk of bias because the investigators stated only that they randomly allocated participants to each group and did not describe the exact way that they conducted the random allocation. In the assessment of the allocation bias in the included studies, 8 studies [4,9,10,12–16] had an unclear risk of bias because the investigators did not mention the method they used for allocation concealment. However, 10 studies had low risk of bias for using sealed opaque envelopes for allocation concealment. The dentist performing the pulpotomy could not be blinded because of the different natures of the medicaments. 8 studies [4,9,10,14,15,17–19] had an unclear risk of performance bias and 5 studies [13,16,20–22] showed high risk. We could not determine detection bias for 4 studies [9,10,15,16] and considered detection bias for these studies to be unclear. Investigators in 15 of the included studies defined the blinding method for the assessment of results, so these studies had a low risk of bias. All of the included studies except 3 [9–11] had a low risk of attrition bias because they had no missing data. 15 studies had a low risk of reporting bias because their protocol was available and the investigators reported all of the pre-specified outcomes. For 2 studies,[4,14] the protocol was not

available, so we labelled the risk as unclear. In the assessment of other bias, we assigned a low risk of bias to 14 studies that had comprehensive and strong inclusion and exclusion criteria, and we assigned an unclear risk of bias to all of the other studies that did not have strong exclusion criteria.

Discussion

Systematic review is a "review of clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies included in the review". It is considered to be the highest-ranked evidence. Dental practitioners and oral health care providers should be aware of the best existing evidence to support their clinical practice.[8] This systematic review is the first one with the goal to systematically review the available information on MTA as pulpotomy dressing agent for treating primary and permanent teeth, which would help paediatric dentists to make treatment choices based on the best scientific evidence available. The evaluation of the included studies suggested that MTA can be considered the material of choice for pulpotomies.

Although it showed successful clinical performances over time, the majority of the authors agreed on its drawbacks, such as high costs, difficult storage and long setting time. Therefore, in some cases, alternative materials may be used. MTA has been indicated as a valid option in the pulpotomy procedures of primary as well as permanent teeth; however, the efficacy of MTA in both cases has rarely been discussed or assessed together. Thus, to supply a systematic review on the topic, studies that evaluated and assessed the efficacy of MTA as pulpotomy agent on either primary or permanent teeth are included. Eighteen randomized clinical trial studies that fit our inclusion criteria considered for this systematic review with comprehended clinical study design, results, analysis and interpretation, aiding readers to understand easily. Out of these 18 studies, 9 were performed on primary teeth, and 9 were performed on permanent teeth. In all of the included studies, the efficacy of MTA as pulpotomy agent was assessed and compared with other medicaments too, with a minimum follow up period of 1 year.

In four studies [4,9–11] out of 9 conducted on primary teeth, authors have evaluated the efficacy of MTA and compared it with Biodentine only, and MTA showed 100% clinical and radiographic success in three of them whereas in the study conducted by Cuadros-Fernández C, Lorente Rodríguez AI, Sáez-Martínez S, García-Binimelis J, Mercadé M.[9] MTA showed 95.34% clinical success and 100% radiographic success at the end of 1 year follow up period. In remaining five studies conducted on primary teeth, MTA was compared with different medicaments like Tempophore, antioxidant mix and Formocresol including Biodentine. In all of those studies, MTA showed 80-100% clinical and radiographic success at the end of 1 year follow up period.

Of the nine studies conducted on permanent teeth, four compared MTA with calcium hydroxide(CH) two compared calcium-enriched mixture (CEM) with MTA,[21,23] one compared platelet-rich fibrin (PRF) with MTA [22] and one compared MTA, triple antibiotic paste (TAP) and abscess remedy.[16] After thorough review and evaluation, it was found that, overall treatment success in primary teeth was

88.89-100% and it was 85-100% in permanent teeth. Looking at the thickness of odontoblastic layer and cell rich zone in the pulp, permanent teeth should show better outcomes in MTA pulpotomy treatment but primary teeth pulpotomy showed better results. There are few probable reasons for lower success rate in permanent teeth which should be taken into consideration. It has been suggested that more fibrous and less resistant nature of dental pulp in permanent teeth may limit the pulp's ability to overcome an injury, potentially affecting the success of a pulpotomy.[24,25] The size of pulp exposure may have an impact on the treatment outcome. It has been showed that pulp exposures greater than $5mm^2$ might result in more unfavorable treatment outcomes.[26] It is also important to control bacterial leakage at the tooth-restoration interface.[27] Post endodontic restoration in the included studies on primary teeth was done using glass ionomer cement followed by stainless steel crown. Glass ionomer cement restoration shows minimal microleakage when compared to amalgam and composite restoration.[28,29] Final restoration after MTA pulpotomy in permanent teeth was composite resin or amalgam in the majority of studies included in this review, which again compromised the success of treatment.

Study criteria and case selection play a vital role in deciding the fair prognosis of the tooth. The sample sizes in the included studies varied from 30 to 413 teeth. The age of patients was described and ranged from 3 to 65 years old. Follow-up periods also varied in these studies, ranging from 12 to 24 months. The colour of bleeding after pulp exposure was not mentioned. More specificity regarding inclusion criteria of caries involvement or remaining tooth structure or restorable tooth would have been authenticated if carious involvement of marginal ridge were included. Also, history from children regarding pain, swelling and fistula in the past is not reliable. Teeth selected for the study were not identical. Few studies did not mention about quadrant and which molars were used specifically.

Limitations of study

Criteria for radiographic success were also different among the included studies, which hindered the data synthesis. After evaluating all the included studies, there remains a conflict in whether the complete apical closure should be a factor to be considered. According to the guideline of the American Academy of Pediatric Dentistry, the objective of pulpotomy is to prevent the clinical symptoms, avoid root resorption and breakdown of periodontal tissue as well as radiographically observe continued root growth. Neither of the authors of included studies mentioned that complete apical closure must be achieved.[30] Therefore, it is vital to unify the criteria of success for pulpotomy treatment.

Reporting of pulpotomy data concerning the exfoliations, dropouts, and success/failures should be standardized. The success of pulpotomy depends on the material used in the treatment along with careful diagnosis and technique of performance such as caries removal prior to opening the pulp chamber, complete isolation of the surgical field, avoiding contamination of pulp tissue while using the cutting instruments to remove caries. Interpretation of the clinical and radiographic results also have an essential role, which in primary teeth, are complicated due to the presence of the permanent successor and the follicle

around. The interval between pulpotomy and tooth restoration should also be considered for a good performance by pulpotomy medicament.

Conclusion

In the light of available evidence, we can conclude that MTA showed slightly better outcomes of pulpotomy in primary teeth as compared to permanent teeth. Further, well-designed, long-term trials are required to provide more convincing evidence. The outcomes of the present systematic review should be taken with caution due to the presence of uncontrolled confounding factors and a variable risk of bias in the included clinical trials.

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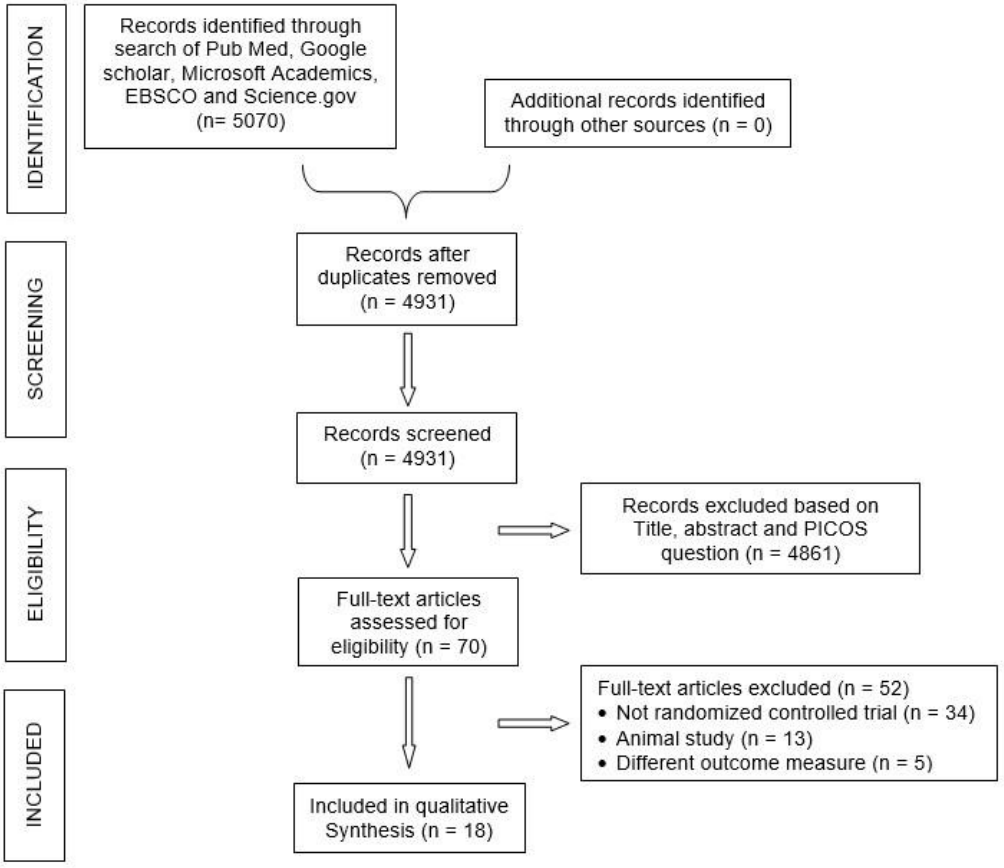

Figure 1. Preferred Reporting Items for Systematic Review study flow diagram

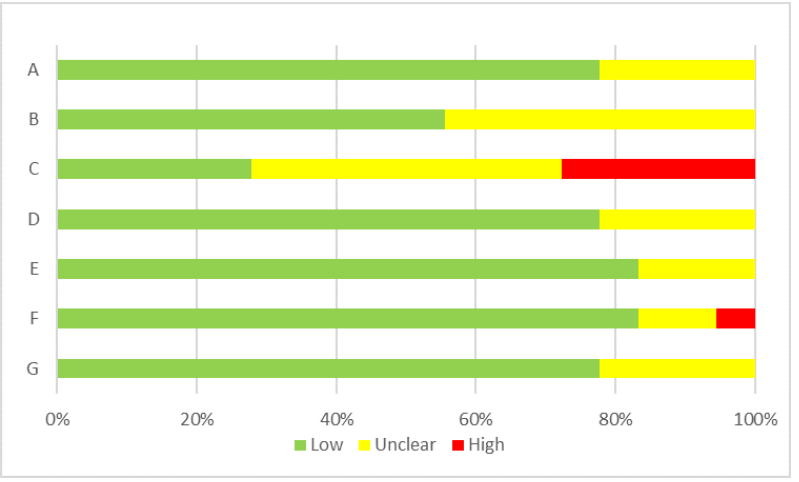

Figure 2. Risk of bias of included studies

Table 1
Summary of the studies included in the review

Study ID	Age	Sample Size	Group distribution	Restoration	Follow up period	Outcomes
Daya Shrinivasan (2011)[9]	4–6 years	100 mandibular primary molar teeth	MTA (n = 50) Formocresol (n = 50)	GIC followed by Stainless Steel crown	3, 6, 9, 12 months	Clinical success MTA- 100% at the end of 12 months Radiographic success MTA - 100% at the end of 12 months
C. Cuadros-Fernández (2016)[10]	4-9 years	68 patients 84 primary molars	MTA (n = 43) Biodentine (n = 41)	Stainless steel crowns cemented with glass ionomer cement	6 and 12 months	Clinical success MTA- 92% at the end of 12 months. Radiographic success MTA- 97% at the end of 12 months.
Harshini Togaru (2016)[11]	4–9 years	90 patients 90 primary molars	MTA (n = 45) Biodentine (n = 45)	GIC followed by Stainless Steel crown	1,3, 6, 9 and 12 months	Clinical success MTA- 100% at the end of 12 months. Radiographic success MTA- 95.5% at the end of 12 months.
O Carti (2016)[4]	5–9 years	25 patients 50 primary carious molars	MTA (n = 25) Biodentine (n = 25)	Resin modified glass ionomer cement (RMGIC) followed by	1, 3, 6 and 12 months	Clinical success MTA- 96% at the end of 12 months. Radiographic success MTA- 80 % at the end of 12 months.

				Stainless Steel crowns		
Rajasekharan et al. (2017)[12]	3-8 years	58 patients 82 primary molars	MTA (n = 29) Biodentine (n = 25) Tempophore (n = 25)	GIC followed by Stainless Steel crown	6, 12 and 18 months	Clinical success MTA- 12 months and 18 months. Radiographic success MTA- 92% at the end of 12 months and 91% at the end of 18 months.
Kathal Sommyta (2017)[13]	6–9 years	40 primary molars	MTA (n = 20) Antioxidant mix (n = 20)	GIC followed by Stainless Steel crown	6 and 12 months	Clinical success MTA- 88.89% at the end of 12 months Radiographic success MTA- 88.89% at the end of 12 months
Juneja et al. (2017)[14]	5–9 years	38 patients 51 primary molars	MTA (n = 17) Biodentine (n = 17) Formocresol (n = 17)	RMGIC followed by Stainless Steel crown	3, 6, 12 and 18 months	Clinical success MTA- 100% at the end of 12 months and 18 months. Radiographic success MTA- 100% at the end of 12 months and 18 months.
Çelik, B.N. et al. (2019)[15]	5–9 years	38 patients 38 teeth	MTA (n = 24) Biodentine (n = 20)	Stainless Steel crown restoration	3, 6, 12, 18, and 24 months	Clinical success MTA- 100% at the end of 12, 18, and 24 months. Radiographic success MTA- 100% at the end of 12, 18, and 24 months.
Silva L.L.C. et al. (2019)[16]	5–8 years	39 patients 45 teeth	MTA (n = 15) CH+ saline (n = 15) C CH+PEG (n = 15)	RMGIC	3,6, and 12 months	Clinical success MTA- 100% at the end of 12 months. Radiographic success MTA- 100% at the end of 12 months.
Omar A.S. El Meligy (2006)[17]	6-12 years	15 patients 30 permanent teeth	MTA (n = 15) H (n = 15)	Bonded composite for anterior teeth and amalgam for posterior teeth	3, 6, and 12 months	Overall success MTA- 100% at the end of 12 months.
M.A. Qudeimat (2007)[18	6.8-13.3 years	34 patients 64 permanen	MTA (n = 32) CH (n = 32)	Amalgam or pre-formed metal crowns	3, 6, 12 months	Overall success MTA- 93 % at the end of 12 months.

]		t molars				
Asgary Saeed (2013)[19]	9-65 years	413 patients 413 permanen t molars	MTA (n = 208) CEM (n = 205)	Silver amalgam restoration	1 day, 1 week and 12 months	Clinical success MTA- 98% at the end of 12 months. Radiographic success MTA- 95% at the end of 12 months.
Ali Nosrat (2013)[20]	6-10 years	51 patients 51 immature permanen t molars	MTA (n = 25) CEM (n = 26)	Self-cure glass ionomer	6 and 12 months	Overall success MTA- 73.8 % at the end of 12 months.
Deepa Keswani (2014)[21]	6-12 years	62 patients 62 permanen t 1st and 2nd molars	MTA (n = 31) PRF (n = 31)	ZOE followed by amalgam	6, 12, and 24 months	Overall success MTA- 80.07% at the end of 12 months.
Chung-Min Kang et al. (2017)[22]	29.3 14.8 years	82 patients 104 permanen t teeth	ProRoot MTA (n=33), OrthoMTA (n=36), RetroMTA (n=35)	RMGIC or Composite resin	1, 3, 6 and 12-months	Overall success MTA - ProRoot MTA, 96.0%; OrthoMTA, 92.8%; and RetroMTA 96.0% at the end of 12 months.
Nessrin A. Taha (2017)[23]	20-52 years	50 patients 50 teeth	MTA (n = 27) Calcium Hydroxide (n = 23)	Either amalgam or resin composite	6, 12 and 24 months	Overall success MTA- 83% at the end of 12 months, and 85 % at the end of 24 months
Beste Özgür (2017)[24]	6-18 years	63 patients 80 permanen t teeth	NaOCl and MTA (n=20), Saline and MTA (n=20), NaOCl and CH (n=20); Saline and CH (n=20)	GIC and Composite resin	6, 12, 18, and 24 months	Clinical success MTA- 97.5% at the end of 12 months. Radiographic success MTA - 97.5% at the end of 12 months.
Hanmant h Reddy Eppa (2018)[25]	6–14 years	60 patients 60 permanen t teeth	MTA (n = 20) Triple antibiotic paste (n = 20) Abscess remedy (n = 20)	GIC followed by Stainless Steel crown	1, 6, 9, 12, 18, and 24 months	Overall success MTA - 93%, at the end of 12 months.

Table 2
Assessment of risk of bias of included studies evaluated with Cochrane Collaboration's tool

Author	A	B	C	D	E	F	G
Daya Shrinivasan (2011)	Low	Low	Low	Low	Low	Low	Low
C. Cuadros-Fernández (2016)	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Harshini Togaru (2016)	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Unclear
O Carti (2016)	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear
Rajasekharan et al. (2017)	Low	Unclear	Low	Low	Low	High	Low
Kathal Sommyta (2017)	Low	Unclear	High	Low	Low	Low	Low
Juneja et al. (2017)	Low	Unclear	Unclear	Low	Low	Unclear	Unclear
Çelik, B.N. et al. (2019)	Unclear	Low	Low	Low	Unclear	Low	Low
Silva L.L.C. et al. (2019)	Low	Low	Low	Low	Low	Low	Low
Omar A.S. El Meligy (2006)	Low	Low	High	Low	Low	Low	Low
M.A. Qudeimat (2007)	Low	Unclear	Unclear	Unclear	Low	Low	Low
Asgary Saeed (2013)	Low	Low	Low	Low	Low	Low	Low
Ali Nosrat (2013)	Low	Low	High	Low	Low	Low	Low
Deepa Keswani (2014)	Low	Low	High	Low	Low	Low	Low
Chung-Min Kang et al. (2017)	Low	Low	Unclear	Low	Low	Low	Low
Nessrin A. Taha (2017)	Low	Low	Unclear	Low	Low	Low	Low
Beste Özgür (2017)	Low	Low	Unclear	Low	Low	Low	Low
Hanmanth Reddy Eppa (2018)	Low	Unclear	High	Unclear	Low	Low	Low

A. Random sequence generation (selection bias)
B. Allocation concealment (selection bias)
C. Blinding of participants and personnel (performance bias)
D. Blinding of outcome assessment (detection bias)
E. Incomplete outcome data (attrition bias)
F. Selective reporting (reporting bias)
Other bias