A Systematic Review and Meta-analysis of Regenerative Pulpotomy in the Treatment of Vital Primary Teeth

N.T. Snigdha[1,2], M.I. Karobari[3], A. Kamarudin[2,*], N.A.Samsudin[2], F. Baharin[2], N. Dziaruddin[4], A.A. Assiry[5], A.M. Luke[6,7], G.A. Scardina[8,*]

[1]Department of Dental Research, Saveetha Medical College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai 602105, Tamil Nadu, India.
[2]Paediatric Dentistry Unit, School of Dental Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian 16150, Kelantan, Malaysia.
[3]Department of Conservative Dentistry and Endodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai 600077, Tamil Nadu, India
[4]Department of Paediatric Dentistry and Orthodontics, Faculty of Dentistry, Universiti Malaya, Kuala Lumpur, Malaysia.
[5]Preventive Dental Science Department, Faculty of Dentistry, Najran University, Kingdom of Saudi Arabia.
[6]Department of Clinical Sciences, College of Dentistry, Ajman University, Ajman, UAE.
[7]Center for Medical and Bio-Allied Health Sciences Research (CMBAHSR), Ajman University, Ajman, UAE
[8]Department of Precision Medicine in Medical, Surgical and Critical Care (Me.Pre.C.C.) University of Palermo Italy.
email: alessandro.scardina@unipa.it - draimi@usm.my

DOI 10.23804/ejpd.2024.1981

Abstract

Objective To assess the clinical and radiographic success rates of regenerative pulpotomy compared to devitalising or preservative pulpotomy in treating vital pulp exposure in primary teeth.

Methods Comprehensive search with PubMed/MEDLINE, Cochrane Library, Web of Science, Google Scholar and Open Grey databases was done and two reviewers extracted the data after assessing the studies for eligibility criteria. The Cochrane Collaboration Tool and Minors Checklist assessed the quality of the selected studies. A meta-analysis was performed using RevMan ($P<0.05$).

Results Forty-nine articles were included for qualitative synthesis, of which, 44 were included in the meta-analysis. The authors found no significant differences between the clinical and radiographic failure rates of Mineral trioxide aggregate (MTA) versus formecresol (FC). MTA resulted in a success rate of 1.01 (95% CI: 0.99–1.03), 1.09 (95% CI: 0.99–1.21), 1.02 (95% CI: 0.99–1.05), 1.01(95% CI: 0.98–1.04), and 1.04-fold (95% CI: 0.97–1.11) higher than that for FC. The radiographic success rate showed a statistically significant difference favouring MTA and Ferric Sulphate comparison with a 1.2-fold (95% CI: 1.05–1.43) higher radiographic success rate for MTA at 24-months follow-up. The radiographic or clinical failure rates of Biodentine (BD) and FC or of BD and FS or CH and FC showed no substantial differences. At 6 months follow-up, BD showed 9.253-fold higher radiographic success rate as compared to FC showing a statistically significant difference (RR, 9.253, 95% CI: 1.62–55.98). Further, 24 months follow-up, CH showed 0.85-fold lower radiographic success rate as compared to FC showing a statistically significant difference (RR, 0.85 95% CI: 0.73–0.98).

Conclusion Within the limitations of the study, it can be concluded that MTA seemed to be the better alternative to FC and FS, showing a lower risk of failure and can be recommended for pulpotomy in primary teeth. BD also demonstrated promising results as a pulpotomy medicament.

KEYWORDS Endodontics; Pulpotomy; Mineral trioxide aggregate; Ferric sulfate; Formocresol.

Introduction

Pulpotomy remains the most common treatment for deep carious lesions of primary molars showing inflammation of the coronal pulp but without any signs or symptoms of radicular pulp degeneration [Cuadros-Fernández *et al.*, 2016; Maroto, Barreiro and Barbería, 2019; Fouad and Abd Al Gawad, 2019]. In this technique, after amputation of coronal pulp, the residual vital radicular pulp is treated with long-term clinically successful medicament [American Academy of Pediatric Dentistry and Stigers, 2019]. Devitalisation (mummification, cauterisation), preservation (minimal devitalisation, noninductive), or regeneration (inductive, reparative) are the different treatment objectives of pulpotomy as stated by Ranly et a.l [1994]. Devitalisation by mummification of tissue was one of the first pulpotomy approach for primary teeth [Ranly, 1994]. Over many years, formocresol (FC) was considered the gold standard and the most preferred devitalising pulpotomy medicament for primary molars [Verma et al., 2019]. FC's local and systemic complications like local pulpal inflammation/necrosis, overall cytotoxicity, mutagenic/carcinogenic consequences, systemic disorders, and immunological responses lead to concerns over its use [Milnes, 2008]. FC constitutes formaldehyde and cresol. In June 2004, the International Agency for Research on Cancer (IARC) classified formaldehyde as carcinogenic to humans, demanding for other viable substitutes to FC [Rousseau, Straif and Siemiatycki, 2005]. Glutaraldehyde for pulp fixation was proposed by Gravenmade in 1975. This di-aldehyde has a limited shelf life and a cross-linking ability superior to that of formocresol. Despite of high success rates the drawbacks in using glutaraldehyde included the cost and inadequate fixation that leaves a deficient barrier susceptible for sub base irritation resulting in internal resorption [Praveen *et al.*, 2014]. Therefore, other alternative pulpotomy procedures like preservation pulpotomy which includes materials like Zinc Oxide Eugenol, glutaraldehyde, ferric sulfate (FS) and regenerative pulpotomy technique which includes Mineral Trioxide Aggregate (MTA), Bioactive glass (BAG), Calcium hydroxide (CH), Hydroxyappetite (HA), Bone dried freezed (BDF), Bone Morphogenic proteins (BMP), recombinant protein-1 (RP1) have been introduced [Ranly, 1994; Praveen et al., 2014]. In preservative pulpotomy technique, the vitality and normal histological appearance of radicular pulp is maintained as the materials used produces negligible insult to orifice tissue. FS has reported a success rate of 60% to 97% in primary molars pulpotomy [Ibricevic and al-Jame, 2000] [Cordell *et al.*, 2021] [Sirohi *et al.*, 2017]. A ferric ion protein complex is formed by FS on contact with blood which mechanically seals the cut vessels, producing hemostasis. The protein complex also prevents the formation of blood clots and thereby minimizes

chances for inflammation and internal resorption [Sonmez, Sari and Cetinbaş, 2008]. Although high clinical success rates have been found using FS, histological findings of a few studies show that FS might produce moderate to severe inflammatory responses [Sirohi *et al.*, 2017] [Swift, Trope and Ritter, 2003]. Havale R et al compared the relative clinical and radiographic success of pulpotomies using FC, glutaraldehyde and FC over one year. They concluded that glutaraldehyde was more effective alternative to FC and FS as a pulpotomy medicament [Havale *et al.*, 2013].

The paradigm shifts from mere devitalisation to preservation to regeneration in endodontics have promoted MTA, biodentine (BD), CH, bone morphogenic protein, and collagen as an alternative vital pulp therapy medicament. Regenerative pulpotomy, called inductive pulpotomy or reparative pulpotomy stimulates the radicular pulp to heal and form a dentin-bridge/hard-tissue barrier [Praveen *et al.*, 2014]] . Recent reviews and meta-analyses done by Shirvani and Asgary [Shirvani and Asgary, 2014], Shafaee H et al [Shafaee *et al.*, 2019], and Bossu M et al [Bossù *et al.*, 2020] testified high success rates of pulpotomy with MTA and biodentine as compared to FC and FS. In contrast Anthonappa et al [Anthonappa, King and Martens, 2013] and Marghalani A et al [Marghalani, Omar and Chen, 2014] and Firoozi P et al [Firoozi, Salman and Aslaminabadi, 2022] reported no evidence that MTA and biodentine respectively were better than present materials and techniques as a pulpotomy medicament. To overcome the uncertainty in the literature this systematic review and meta-analysis were conducted to assess the clinical and radiographic success rates of regenerative pulpotomy compared to devitalisation or preservation pulpotomy in the treatment of vital pulp exposure in primary teeth.

Materials and Methods

Protocol development

The systematic review and meta-analysis is conducted and reported according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement [Moher *et al.*, 2010] and the review methods are derived from a pre-established protocol registered in PROSPERO (CRD42022319494). The research question was formulated according to the (PICO) principle [da Costa Santos, de Mattos Pimenta and Nobre, 2007]:

- P (Population) – Studies conducted on children with primary teeth with vital pulp exposure during removal of caries or due to trauma regardless of sex, age, race or socio-economic status and treated with regenerative pulpotomy as compared to devitalisation or preservation pulpotomy. Studies conducted on children with permanent teeth or on vital immature permanent teeth with open apex will be excluded.
- I (Intervention) – Studies reporting regenerative pulpotomy done using mineral trioxide aggregate (MTA), Biodentine (BD), Calcium hydroxide, bone morphogenetic protein (BMP), Calcium-enriched mixture (CEM), platelet-rich fibrin (PRF), Enriched collagen, Freeze dried bone, osteogenic protein.
- C (Comparison) – Studies reporting devitalisation or preservation pulpotomy on children with primary teeth with vital pulp exposure with minimum 1 month of follow-up.
- (Outcome) – Reporting clinical or radiographic success rates. Clinical success was defined as no pain, no abscess or fistulation, no excessive tooth mobility and no swelling. Radiographic success was considered if the teeth showed no evidence of apical and furcal radiolucency, internal or external root resorption, periodontal ligament widening, or periapical bone destruction.
- S (Study design): Clinical trials, randomized controlled studies, non-randomized comparative studies comparing the clinical and radiographic success rates of regenerative pulpotomy with devitalisation or preservation pulpotomy. Even though non-randomized studies come with certain obvious bias, we still included them as they provided additional results to reach specific conclusion. This bias arising from non-RCTs was assessed separately using appropriate tool.
- "Is there a difference in the clinical and radiographic success rates of regenerative pulpotomy as compared to devitalisation or preservation pulpotomy in the treatment of vital pulp exposure in primary teeth?" The steps of searching and selecting the articles, data collection and extraction followed for reporting this systematic review were as described by Bhor K et al [2021].

Search Strategy

A literature search was independently conducted by two reviewers (N.T.S and M.I.K) through MEDLINE and PubMed, Cochrane Library, and Web of Science from January 2000 to March 2022. Google Scholar, Greylist, and OpenGrey were used for searching the clinical trials database, cross-references and Grey literature. A combination of Medical Subject Headings (MeSH) terms and keywords presented in Table 1 were employed for the electronic search across platforms following the syntax rules of respective database.

Inclusion criteria

- Studies published in any language where English translation is possible.
- Studies comparing the clinical and radiographic success rates of regenerative pulpotomy with devitalisation or preservation pulpotomy done on vital primary teeth.
- Studies with full-text articles only will be included.

Exclusion criteria

Studies conducted on children with permanent teeth or on vital immature permanent teeth with open apex will be excluded.

- Observational study designs, case reports, case series, cross-sectional studies, and reviews.
- Studies reporting a single intervention.

Screening process

Two review authors independently (N.T.S and M.I.K) conducted the search and screening of the records as per pre-established protocol. The duplicates were removed and the titles and abstracts fulfilling the eligibility criteria were selected. Then, the relevant full-text articles selected on their titles and abstracts were read and checked for inclusion criteria. Finally, the included studies were checked for multiple publications of a single study and data extraction was done. The agreement, level between the two reviewers, calculated by Cohen's kappa (k), was 0.92 for titles and abstracts and 0.94 for full texts. Difference, if any among the two authors was resolved by the third author (A.K) after discussion.

Data extraction

Two review authors independently (N.T.S and M.I.K) extracted the data using standardised forms: author/year/ country of origin, study design, eligibility criteria specified, interventions and comparator groups, sample size, , duration of follow-up and results and conclusions. In all the included studies tooth was the unit of analysis and was randomly assigned to treatment groups.

Assessments of the risk of bias and quality

The assessment of methodological study quality was assessed using the Cochrane Collaboration Tool [de Oliveira-Neto *et al.*,

Search strategy	
Focused Question	Is there a difference in the clinical and radiographic success rates of regenerative pulpotomy as compared to devitalisation or preservation pulpotomy in the treatment of vital pulp exposure in primary teeth?
Search strategy	
Population (#1)	((("primary molar"[Text Word]) OR "deciduous molar" OR "molar"[MeSH Terms] OR molar[Text Word] OR posterior teeth [Text Word]))
Intervention (#2)	((regenerative [Text Word]) AND puplotomy[Text Word]) OR (Biodentine[Text Word])) OR "Mineral trioxide aggregate"[Text Word]) OR "Calcium hydroxid"e[Text Word] OR "Enamel matrix derivative"[Text Word] OR "hydroxyapatite crystals"[Text Word] OR Nanohydroxyapatite[Text Word] OR "ProRoot MTA"[Text Word] AND Pulpotomy[Text Word]
Comparisons (#3)	(((preservation[Text Word]) OR devitalising [Text Word])) AND pulpotomy[Text Word] ((Formocresol[Text Word] OR Gultaraldehye[Text Word] OR "Portland Cement" [Text Word]) OR "Ferric Sulphate"[Text Word] OR Tempophore [Text Word] AND Pulpotomy [Text Word]))
Outcomes (#4)	(Success [Text Word] OR Pain [Text Word] OR Clinical [Text Word] OR Radiographic [Text Word] OR Furcation [Text Word] OR Mobility [Text Word] OR Sinus [Text Word] OR Mobility [Text Word]
Study design (#5)	(Clinical trials [MeSH] OR randomized controlled studies [Text Word] OR randomized control trials [MeSH] OR randomized control clinical trial MeSH OR non-randomized control trials [Text Word] OR Quasi experimental studies [Text Word] OR before and after study design [Text Word] OR cohort studies [Text Word] OR in vivo study [Text Word])
Search Combination	#1 AND #2 AND #3 AND #4 AND #5
Database search	
Language	No restriction (Articles in English language or other language where English translation is possible.)
Electronic Databases	PubMed/MEDLINE, Cochrane Central Register of Controlled Trials, Web of Science
Period of Publication	Studies published between 1-1-2000 to 30-03-2022

TABLE 1 The search strategy and PICOS tool.

2018] for RCTs, focusing on: random sequence generation, allocation concealment, blinding of participants, incomplete outcome data, selective reporting, and other biases. Minors' checklist was used for quality assessment of NRS. This tool involves eight items for non-comparative studies and additional four criteria for comparative studies [Slim *et al.*, 2003].

Data synthesis and Statistical analysis

Statistical analysis was performed using Review Manager (RevMan) 5.3. The dichotomous data was expressed as relative risks (RRs) at 95% confidence intervals (CIs) ($P<0.05$). The presence of any one of the clinical or radiological features mentioned in the inclusion criteria was considered an overall treatment failure. Moreover, the different types of MTA (unspecified MTA, grey MTA and white MTA) were combined, and for trials comparing two types of MTA, data for both arms were included. I2 test at $\alpha=0.10$ assessed the statistical heterogeneity and random-effects model was used for I2>50%. Subgroup analysis was conducted for different follow-up periods. Funnel plots detecting publication bias were plotted only if the studies were exceeding 10 in number for each specified outcome [Su *et al.*, 2016].

Results

Literature search and Study selection

The PRISMA statement flowchart illustrating the search results is shown in Figure 1. The initial electronic database search resulted in a total of 596 titles, after removal of duplicates 286 titles remained. Out of these 286 articles, 198 were removed after reading the titles and abstracts at the initial screening. Eighty-eight articles were selected for full-text evaluation after discussion with the reviewers. After pre-screening, application of the inclusion and exclusion criteria and handling of the PICOS principle , 49 studies remained (5 studies with inappropriate population, 29 studies with the inappropriate comparison group, three studies had inappropriate study design and two studies had inappropriate study outcomes) which were included in the qualitative analysis whereas 44 studies were included in the quantitative synthesis.

Characteristics of the included studies

The corresponding characteristics of 49: [Verma *et al.*, 2019; Cordell et al., 2021; Sirohi et al., 2017; Sonmez, Sari and Cetinbaş, 2008; Eidelman, Holan and Fuks, 2001; Agamy et al., 2004; Ebrahim, Khademi and Ghasemi, 2004; Holan, Eidelman and Fuks, 2005; Farsi et al., 2005; Naik and Hegde, 2005; Neamatollahi and Tajik, 2006; Moretti et al., 2008; Noorollahian, 2008; Sabbarini et al., 2008; Adlakha et al., 2009; Sakai et al., 2009; Subramaniam et al., 2009; Ansari and Ranjpour, 2010; Erdem et al., 2011; Godhi, Sood and Sharma, 2011; Srinivasan and Jayanthi, 2011; Airen, Shigli and Airen, 2012; Huth et al., 2012; Sushynski et al., 2012; Mettlach et al., 2013; Oliveira et al., 2013; Jayam et al., 2014; Yildiz and Tosun, 2014; Mineral Trioxide Aggregate/Ferric Sulfate Pulpotomy for Vital Primary Incisors: A Randomized Controlled Trial, 2014; Olatosi, Sote and Orenuga, 2015; Rajasekharan et al., 2017; Yildirim et al., 2016; Guven et al., 2017; Juneja and Kulkarni, 2017; Hugar et al., 2017; 'One-year outcomes of MTA and modified Portland cement pulpotpmy in primary teeth: a randomized clinical trial'; Biedma Perea et al., 2017; Shanta et al., 2017; Sunitha et al., 2017; Jamali et al., 2018; Junqueira et al., 2018; El Meligy et al., 2019; Ahuja et al., 2020; Lin and Lin, 2020; Abd Al Gawad and Hanafy, 2021; Meslmani et al., 2020; Somwanshi et al., 2021; Alzoubi et al., 2021; Elsherbini and Mossa, 2022] studies are presented in Table 2. All included studies were unicentric clinical trials published between 2001 and 2022 and were conducted in pediatric dentistry departments at universities or hospital centers across countries. Among the included studies, 42: [Verma et al., 2019; Cordell et al., 2021; Sirohi et al., 2017; Sonmez, Sari and Cetinbaş, 2008; Eidelman, Holan and Fuks, 2001; Agamy et al., 2004; Ebrahim, Khademi and Ghasemi, 2004; Holan, Eidelman and Fuks, 2005; Farsi et al., 2005; Naik and Hegde, 2005; Neamatollahi and Tajik, 2006; Moretti et al., 2008; Noorollahian, 2008; Adlakha et al., 2009; Sakai *et al.*, 2009; Subramaniam *et al.*, 2009; Ansari and Ranjpour, 2010; Erdem et al., 2011; Sabbarini et al., 2008; Srinivasan and Jayanthi, 2011; Huth et al., 2012; Sushynski et al., 2012; Mettlach et al., 2013; Oliveira et al., 2013; Jayam et al., 2014; Yildiz and Tosun, 2014; Mineral Trioxide Aggregate/Ferric Sulfate Pulpotomy for Vital Primary Incisors: A Randomized Controlled Trial, 2014; Olatosi, Sote and Orenuga, 2015; Rajasekharan et al.,

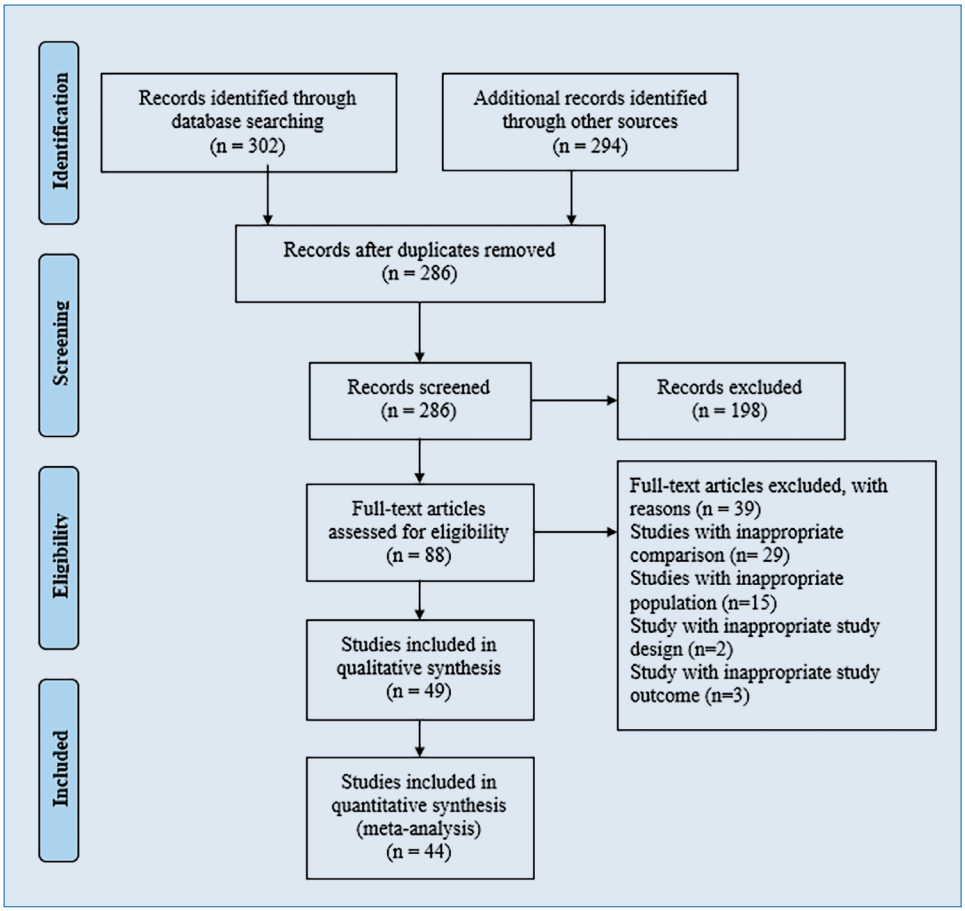


FIG.1
PRISMA flow diagram

2017; Guven et al., 2017; Juneja and Kulkarni, 2017; Hugar et al., 2017; 'One-year outcomes of MTA and modified Portland cement pulpotpmy in primary teeth: a randomized clinical trial'; Sunitha et al., 2017; Jamali et al., 2018; Junqueira et al., 2018; El Meligy et al., 2019; Ahuja et al., 2020; Meslmani et al., 2020; Alzoubi et al., 2021; Abd Al Gawad and Hanafy, 2021; Elsherbini and Mossa, 2022] were Randomized controlled trials and 7 were non-randomized trials [Godhi, Sood and Sharma, 2011; Airen, Shigli and Airen, 2012; Yildirim et al., 2016; Biedma Perea et al., 2017; Shanta et al., 2017; Lin and Lin, 2020; Somwanshi et al., 2021] . A total of 3497 carious primary molars with symptoms of provoked pain of short duration which were relieved upon removal of the stimulus and with no radiographic evidence of furcation/apical pathology and signs of physiological root resorption of children aged between 1.5 and 12 years and had follow-up period ranged from 1 month to 74 months and the dropout rates were <15%. In terms of pulpotomy technique, materials manipulation, years of experience of the clinician, final restorative materials, and outcome variables; substantial heterogeneity was observed among included studies (Table 2). The regenerative pulpotomy procedure was performed using MTA, BD, CH, and EMD as compared to FC as devitalising pulpotomy or FS, glutaraldehyde, PC, and Tempophore as a preservative pulpotomy procedure. Clinical and radiographical parameters as outcome variables were assessed by all of the included studies. Although the success criteria used across the articles were similar but were not the same. Hence, the overall clinical and radiographic success rate was considered for quantitative synthesis.

Quality Assessment

The risk of bias assessment for the included non-randomized studies is shown in Table 3. The quality assessment of 42 RCTs was performed according to the Cochrane Risk of Bias Tool. Accordingly, 15 studies showed a low potential risk of bias, 8 presented a moderate risk and 19 had a high potential risk of bias (Figure 2). Even though randomization methods were described in majority of the studies, the generation of random sequence/allocation concealment was either unclear or inappropriate. All of the included studies had a low risk of attrition bias because of no missing data. MINORS tool was used for the quality assessment of 7 non-randomised comparative studies with a score ranging from 20 to 23 (Table 3). Since all included NRS were comparative, additional four criteria were also assessed for risk of bias. Blinding of the outcome accessor was inadequate across the included studies also, only one out of the 7 included studies reported the sample size calculation.

Synthesis of results

A total of 44 studies: [Verma *et al.*, 2019;Cordell *et al.*, 2021; Sirohi *et al.*, 2017; Sonmez, Sari and Cetinbɑş, 2008; Sonmez, Sari and Cetinbaş, 2008; Eidelman, Holan and Fuks, 2001; Agamy *et al.*, 2004; Ebrahim, Khademi and Ghasemi, 2004; Holan, Eidelman and Fuks, 2005; Farsi *et al.*, 2005; Naik and Hegde, 2005; Neamatollahi and Tajik, 2006; Moretti *et al.*, 2008; Noorollahian, 2008; Sabbarini *et al.*, 2008; Sakai *et al.*, 2009; Subramaniam *et al.*, 2009; Ansari and Ranjpour, 2010; Erdem *et al.*, 2011; Godhi, Sood and Sharma, 2011; Srinivasan and Jayanthi, 2011; Airen, Shigli and Airen, 2012; Huth *et al.*, 2012; Sushynski *et al.*, 2012; Oliveira *et al.*, 2013; Jayam *et al.*, 2014; Yildiz and Tosun, 2014; *Mineral Trioxide Aggregate/Ferric Sulfate Pulpotomy for Vital Primary Incisors: A Randomized Controlled Trial*, 2014; Olatosi, Sote and Orenuga, 2015; Yildirim *et al.*, 2016; Guven *et al.*, 2017; Juneja

Study Id	Place of study	Sample Size I1/I2/C1/C2	Age group I1/I2/C1/C2	Type of final restoration	Pulpotomy material I1/I2/C1/C2	Follow-up period in months	Authors Conclusions
Eidelman 2001(28)	Israel	17/-/15/-	5-12	IRM and SSC	MTA/-/FC/-	6- 30	MTA showed clinical and radiographic success as a dressing material following pulpotomy in primary teeth after a short-term evaluation period
Agamy HA 2004 (29)	Egypt	24/24/24/-	4-8	IRM and SSC	Gray MTA/ White MTA/ FC/-	1, 3, 6, 12	Gray MTA is superior to both white MTA and FC as a pulp dressing for pulpotomized primary molars
Jabbarifar S et al 2004 (30)	Iran	32/-/32/-	5-8	SSC	MTA/-/FC/-	6, 12	MTA can be an alternative procedure for FC pulpotomy of primary tooth.
Holan G et al 2005 (31)	Israel	33/-/29/-	6-10	IRM and SSC	MTA/-/FC/-	4-74	MTA showed a higher long-term clinical and radiographic success rate than FC
Farsi N et al 2005 (32)	Saudi Arabia	38/-/36/-	3-8	IRM and SSC	MTA/-/FC/-	6, 12, 18, 24	MTA treated molars demonstrated significantly greater success MTA seems to be a suitable replacement for FC in pulpotomized primary teeth.
Naik S et al 2005 (33)	India	25/-/25/-	-	SSC	MTA/-/FC/-	1, 3, 6	MTA showed clinical and radiographic success as a dressing material following pulpotomy in primary teeth after a short-term evaluation period
Neamatollahi H et al 2006 (34)	Iran	45/-/45/45	3-6	SAF	MTA/-/FC/FS	3, 12	MTA is not recommended as a pulpotomy medicament in primary teeth but FS may be acceptable as an alternative to FC
Moretti A et al 2008 (35)	Brazil	14/15/14/-	5-9	GIC	MTA/CH/FC/-	3, 6, 12, 18, 24	MTA was superior to CH and equally as effective as FC as a pulpotomy dressing in primary mandibular molars
Noorollahian H 2008 (36)	Iran	30/-/30/-	5-7	SSC	MTA/-/FC/-	6, 12, 24	MTA could be used as a safe medicament for pulpotomy in cariously exposed primary molars and could be a substitute for FC.
Sabbarini J et al 2008 (37)	Jordan	15/-/15/-	4- 7	SSC	EMD/-/FC/-	2, 4, 6	The clinical and radiographic assessment of EMD pulpotomized teeth in this study offers preliminary evidence that EMD is a promising material
Sonmez D et al 2008 (13)	Turkey	15/13/15/13	4- 9	SAF MTA- ZOE	MTA/CH/FC/FS	6, 12, 18, 24	CH appeared to be clinically less appropriate than FC, FS, and MTA
Adlakha VK et al 2009 (38)	Punjab, India	30/-/30/-	4-10	SAF	paste of hydroxyapatite crystals/-/ Glutaraldehyde/-	3- 6	Hydroxyapatite crystals provided acceptable success in the study though the glutaraldehyde treated teeth showed a significantly better radiographic success.
Sakai V et al 2009 (39)	Brazil	15/-/15/-	5-9	M-GIC	MTA/-/PC/-	6, 12, 18, 24	PC may serve as an effective and less expensive MTA substitute in primary molar pulpotomies.
Subramaniam P et al 2009 (40)	India	20/-/20/-	6- 8	GIC and SS	MTA/-/FC/-	1, 6, 12, 24	MTA is a promising medicament in pediatric pulp therapy and can be recommended as a suitable alternative to the conventional pulpotomy agents
Ansari G and Ranjpour M 2010 (41)	Iran	20/-/20/-	4-9	Polycarboxylate cement with SS or SAF	MTA/-/FC/-	1, 6, 12, 24	MTA pulpotomy of primary teeth was as successful as conventional FC pulpotomies.
Erdem AP et al 2011 (42)	Turkey	25/-/25/25	5-10	SAF	MTA/-/FC/FS	6, 12, 24	No significant differences were observed, among the 3 experimental materials (MTA, FC, and FS) at 2 years follow-up.
Godhi B et al 2011 (43)	India	25/-/25/-	5- 8	IRM and SSC	MTA/-/FC/-	1, 3, 6, 12	MTA showed clinical and radiographic success as a dressing material following pulpotomy in primary teeth after a short-term evaluation period
Srinivasan D 2011 (44)	India	50/-/50/-	4- 6	GIC with SS	MTA/-/FC/-	3, 6, 9, 12	MTA is superior to FC clinically, radiographically.

TABLE 2 Characteristics of the included studies.

Airen P et al 2012 (45)	India	35/-/35/-	6- 8	IRM and SSC	MTA/-/FC/-	6, 12, 24	MTA pulpotomy has emerged as an easier line of treatment to save the premature loss of primary teeth due
Huth K et al 2012 (46)	Germany	44/-/50/50	2-8	GIC and SSC or composite	CH/-/FC/FS	6, 12, 18, 24, 36	Pulpotomies using FS revealed the best treatment outcome among the used techniques, while CH resulted in the lowest success rates after 3 years
Sushynski J et al 2012 (47)	USA	108/-/114/-	2.5- 10	IRM and SSC	GMTA/-/FC/-	6, 12, 18, 24	At the combined 6- to 24-month follow-up, Gray MTA demonstrated significantly better radiographic outcomes vs diluted FC as pulpotomy medicaments
Mettlach S et al 2013 (48)	USA	119/-/133/-	2.5- 10	SSC	GMTA/-/FC/-	6-42	Gray MTA can be considered an acceptable replacement for diluted FC when used as a medicament for primary molar pulpotomies
Oliveira TM 2013 (49)	Brazil	15/15/15/-	5- 9	RMGIC	MTA/CH/PC/-	6, 12, 24	MTA and PC may serve as effective materials for pulpotomies of primary teeth as compared to CH.
Jayam C et al 2014 (50)	India	40/-/42/-	3-7	SSC and/or GIC and SAF	MTA/-/FC/-	1, 3, 6 12, 24	MTA seems to be a promising pulpotomy medicament for future use
Yildiz E et al 2014 (51)	Turkey	41/35/29/35	5- 9	Composite resin	MTA/CH/FC/-	6, 12, 18, 24, 30	There were no clinical and radiographic differences between the four materials
Nguyen TD et al 2015 (52)	Canada	100 (no segregation of samples)	1.5- 3.5	Acid etched resin	MTA/-/FS/-	40	MTA/FS pulpotomy is an effective treatment for carious vital primary incisors.
Olatosi O et al 2015 (53)	Nigeria	25/-/25/-	4-7	SSC	MTA/-/FC/-	1, 3, 6, 9, 12	White MTA showed a higher clinical and radiographic success rate when compared to FC as a pulpotomy agent in vital primary molars
Rajasekharan S et al 2016 (54)	Belgium	25/29/27/-	3- 8	GIC and SSC	BD/ProRoot WMTA/ Tempophore/-	1, 6, 12, 18	After 18-month follow-up, there was no significant difference between BDTM in comparison with ProRoot WMTA or Tempophore
Yildirim C et al 2016 (55)	Turkey	35/35/35/35	5- 9	SSC	MTA/EMD/FC/PC	3, 6, 12, 18, 24	No statistically significant differences in clinical and radiographic success rates among the 4 groups, MTA appears to be superior to FC, Portland cement, and EMD as a pulpotomy agent in primary teeth
Guven Y et al 2017 (56)	Turkey	29/29/29/29	5- 7	SAF	BD/MTA-P/ ProRoot/ FS	6, 12, 24	The success rates of BD, MTA-P, MTA-ProRoot, and FS did not differ significantly, calcium silicate-based materials appeared to be more appropriate than FS in clinical practice
Juneja P et al 2017 (57)	India	17/17/17/-	5- 9	RMGIC and SSC	MTA/BD/FC/-	3, 6, 12 and 18	MTA and BD showed more favourable results than FC
Hugar S et al 2017 (58)	India	15/-/15/-	4- 7	IRM and SSC	light-cured CH/-/ FC/-	1, 3, 6	A comparable clinical and radiographic success rate was seen with all experimental groups as compared to FC
Mazhari F et al 2017 (59)	Iran	28/-/26/-	4–6	SSC	MTA/-/MPC/-	6, 12	Treatment success rate with MPC was comparable to MTA pulpotomy
Perea M et al 2017 (60)	Spain	138/-/74/-	2-10	SSC	MTA/-/FC/-	6- 48	There were no significant differences in clinical success rate between the two groups
Shanta KN et al 2017 (61)	Bangladesh	20/-/20/-	6-9	GIC	MTA/-/PC/-	3, 6, 12	PC can also be used as successful pulpotomy material as an effective and economic substitute of MTA
Sirohi K et al 2017 (12)	India	25/-/25/-	4- 8	Composite	BD/-/FS/-	1, 3, 6, and 9	BD can be used as a pulpotomy agent but further long-term studies are required.

TABLE 2 Characteristics of the included studies.

Sunitha B et al 2017 (62)	India	21/21/21/21		IRM and SSC	MTA/EMD/FC/ pulpotec	6, 12, 18, 24	MTA has a high success rate compared with FC, pulpotec, and EMD as pulpotomy agent.
Jamali Z et al 2018 (63)	Iran	50/-/50/-	3-6	SAF	MTA/-/FC/-	6, 12, 24	There was no significance difference between the MTA and FC group
Junqueira M et al 2018 (64)	brazil	15/-/16/-	5- 9	RMGIC	MTA/-/FS/-	3, 6, 12, 18	MTA is considered the first-choice material, FS may be a suitable alternative when treatment cost is an issue
Meligy O et al 2019 (65)		56/-/56/-	4-8	SSC	BD/-/FC/-	3,6,12	Both BD and FC pulpotomy techniques demonstrated favourable clinical and radiographic outcomes over a 12-month period without any significant difference
Verma B et al 2019 (6)	India	30/-/30/-	4-9	GIC	BD/-/FC/-	3, 6	BD used for primary teeth pulpotomy has good success rates on follow-up; and hence can be used as alternatives to FC
Ahuja S et al 2020 (66)	India	20/20/20/-	4-7	GIC and SSC	BD/MTA/FC/-	3, 6, 9	BD showed that it can be used efficiently as a pulpotomy medicament in the clinical practice.
Lin Y et al 2020 (67)	Taiwan	27/-/27/-	2-6	GIC and SSC	MTA/-/FS/-	12, 24	Similar 24-month radiographic and clinical outcomes for MTA and FS pulpotomies performed in primary molars
Meshlami W et al 2020 (68)	Syria	30/-/30/-	6-8	SSC	MTA/-/PC/-	3, 6, 12	PC can be used a as pulpotomy agent with high clinical and radiographic success rates similar to MTA
Alzoubi H et al 2021 (69)	Syria	30/-/30/-	4-9	Resin composite	White MTA/-/ White PC/-	3,6,12	White PC and White MTA were successful in 100% of the cases with no differences between the two treatments.
Cordell S et al 2021 (11)	USA	21/-/15/-	4-9	SSC	MTA/-/FS/-	6, 12	At 12 months, MTA showed superior success as a pulpotomy medicament in primary molars compared to FS
Gawad R et al 2021 (70)	Egypt	24/24/24/-	4-8	GIC and SSC	MTA/NHA/FC/-	3, 6, 12	MTA is still the material of choice for pulpotomy in primary molars
Somwanshi Y et al 2021 (71)	India	30/-/30/-	4-9	SAF and SS	MTA/-/FS/-	3, 6	FS was found to be equally effective when compared with MTA.
Elsherbini M and Mossa H 2022 (72)	Egypt	25/23/24	4-8	GIC and SSC	BD/-/FC/-	3, 6, 12	BD and 5% NaOCl indicated comparable outcomes to FC.

BD- Biodentine, C1- Comparator 1, C2- Comparator 2, CH- Calcium Hydroxide, EMD- Enamel Matrix Derivative, FC- formocresol, FS- Ferric Sulphate, GIC- Glass Ionomer Cement, I1- Intervention 1, I2- Intervention 1, IRM- Interim Restorative Material, MTA- Mineral Trioxide Aggregate, NHA- Nanohydroxy appatite, PC- Portland Cement, RMGIC- Resin Modified Glass Ionomer Cement, SAF- Silver Amalgam Filling, SSC- Stainless Steel Crown

TABLE 2 Characteristics of the included studies.

and Kulkarni, 2017; Hugar *et al.*, 2017; 'One-year outcomes of MTA and modified Portland cement pulpotpmy in primary teeth: a randomized clinical trial'; Shanta *et al.*, 2017; Sunitha *et al.*, 2017; Jamali *et al.*, 2018; Junqueira *et al.*, 2018; El Meligy *et al.*, 2019; Ahuja *et al.*, 2020; Lin and Lin, 2020; Meslmani *et al.*, 2020; Alzoubi *et al.*, 2021; Abd Al Gawad and Hanafy, 2021; Somwanshi *et al.*, 2021; Elsherbini and Mossa, 2022] were considered for quantitative synthesis . Sixteen sub-group meta-analyses were performed on the clinical and radiographic success rate of regenerative pulpotomy compared to devitalising or preservative pulpotomy.

MTA versus FC

The clinical success rate of MTA as compared to FC in tooth level unit was performed according to follow-up period. Using the random-effect model it was observed that at 1 month [Agamy *et al.*, 2004; Naik and Hegde, 2005; Jayam *et al.*, 2014; Olatosi, Sote and Orenuga, 2015] and 3 months [Agamy *et al.*, 2004; Naik and Hegde, 2005; Moretti *et al.*, 2008; Godhi, Sood and Sharma, 2011; Srinivasan and Jayanthi, 2011; Jayam *et al.*, 2014; Olatosi, Sote and Orenuga, 2015; Yildirim *et al.*, 2016; Juneja and Kulkarni, 2017; Ahuja *et al.*, 2020; Abd Al Gawad and Hanafy, 2021], MTA and FC showed no statistically significant difference with RR of 1.00 and 0% heterogeneity. At, 6 [Sonmez, Sari and Cetinbaş, 2008; Agamy *et al.*, 2004; Ebrahim, Khademi and Ghasemi, 2004; Naik and Hegde, 2005; Moretti et al., 2008; Subramaniam et al., 2009; Ansari and Ranjpour, 2010; Erdem et al., 2011; Noorollahian, 2008; Godhi, Sood and Sharma, 2011; Srinivasan and Jayanthi, 2011; Sushynski et al., 2012; Yildiz and Tosun, 2014; Jayam et al., 2014; Olatosi, Sote and Orenuga, 2015; Yildirim et al., 2016; Juneja and Kulkarni, 2017; Sunitha et al., 2017; Jamali et al., 2018; Ahuja et al., 2020; Abd Al Gawad and Hanafy, 2021], 9 [Srinivasan and Jayanthi, 2011; Olatosi, Sote and Orenuga, 2015; Ahuja et al., 2020], 12 [Sonmez, Sari and Cetinbaş, 2008; Eidelman, Holan and Fuks, 2001; Agamy et al., 2004; Ebrahim, Khademi and Ghasemi, 2004; Neamatollahi and Tajik, 2006; Moretti et al., 2008; Noorollahian, 2008; Subramaniam et al., 2009; Ansari and

	A clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the aim of the study	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	Loss to follow up less than 5%	Prospective calculation of the study size	*An adequate control group	*Contemporary groups	*Baseline equivalence of groups	*Adequate statistical analyses	Total
Godhi B et al 2011 (43)	2	2	2	2	1	2	2	0	2	2	2	2	21
Airen P et al 2012 (45)	2	2	2	2	1	2	2	0	2	2	2	2	21
Yildirim C et al 2016 (55)	2	2	2	2	0	2	2	0	2	2	2	2	20
Perea M et al 2017 (60)	2	2	2	2	1	2	2	0	2	2	2	2	21
Shanta KN et al 2017 (61)	2	2	2	2	1	2	2	0	2	2	2	2	21
Lin Y et al 2020 (67)	2	2	2	2	2	2	2	0	2	2	2	2	22
Somwanshi Y et al 2021 (71)	2	2	2	2	1	2	2	2	2	2	2	2	23

*The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The global ideal score being 16 for non-comparative studies and 24 for comparative studies. *For study with control group*

TABLE 3 Methodological index for non-randomized studies (MINORS).

Ranjpour, 2010; Erdem et al., 2011; Godhi, Sood and Sharma, 2011; Srinivasan and Jayanthi, 2011; Airen, Shigli and Airen, 2012; Sushynski et al., 2012; Jayam et al., 2014; Yildiz and Tosun, 2014; Olatosi, Sote and Orenuga, 2015; Yildirim et al., 2016; Juneja and Kulkarni, 2017; Sunitha et al., 2017; Jamali et al., 2018; Abd Al Gawad and Hanafy, 2021], 18 [Sonmez, Sari and Cetinbaş, 2008; Moretti et al., 2008; Sushynski et al., 2012; Yildiz and Tosun, 2014; Yildirim et al., 2016; Juneja and Kulkarni, 2017; Sunitha et al., 2017] and 24 [Sonmez, Sari and Cetinbaş, 2008; Moretti et al., 2008; Noorollahian, 2008; Subramaniam et al., 2009; Ansari and Ranjpour, 2010; Erdem et al., 2011; Airen, Shigli and Airen, 2012; Sushynski et al., 2012; Yildiz and Tosun, 2014; Yildirim et al., 2016;Sunitha et al., 2017;Jamali et al., 2018] months follow-up MTA resulted in a success rate of 1.01, 1.09, 1.02, 1.02, 1.04-fold higher than that for FC (RR, 1.01; 95% CI: 0.99–1.03; P=0.19), (RR, 1.09; 95% CI: 0.99–1.21; P=0.09), (RR, 1.02; 95% CI: 0.99–1.05; P=0.17), (RR, 1.01; 95% CI: 0.98–1.04; P=0.42) and (RR, 1.04; 95% CI: 0.97–1.11; P=0.24) showed no statistically significant difference with 0%, 42%, 45%, 9% and 70% heterogeneity, respectively (Fig. 3). The radiographic success rate of MTA as compared to FC in tooth level unit was performed according to follow-up period, using random-effect model it was observed that at 1 [Agamy et al., 2004; Naik and Hegde, 2005; Jayam et al., 2014; Olatosi, Sote and Orenuga, 2015] 3 [Agamy et al., 2004; Naik and Hegde, 2005; Moretti et al., 2008; Godhi, Sood and Sharma, 2011; Srinivasan and Jayanthi, 2011; Jayam et al., 2014; Olatosi, Sote and Orenuga, 2015; Yildirim et al., 2016; Juneja and Kulkarni, 2017; Ahuja et al., 2020; Abd Al Gawad and Hanafy, 2021], 6 months [Sonmez, Sari and Cetinbaş, 2008; Agamy *et al.*, 2004; Ebrahim, Khademi and Ghasemi, 2004;Naik and Hegde, 2005; Moretti *et al.*, 2008; Noorollahian, 2008; Subramaniam *et al.*, 2009; Ansari and Ranjpour, 2010; Erdem *et al.*, 2011; Godhi, Sood and Sharma, 2011; Srinivasan and Jayanthi, 2011; Jayam *et al.*,2014; Yildiz and Tosun, 2014; Olatosi, Sote and Orenuga, 2015; Yildirim *et al.*, 2016; Juneja and Kulkarni, 2017; Sunitha *et al.*, 2017; Jamali *et al.*, 2018; Ahuja *et al.*, 2020; Abd Al Gawad and Hanafy, 2021] and 9 [Srinivasan and Jayanthi, 2011; Olatosi, Sote and Orenuga, 2015; Ahuja *et al.*, 2020], MTA and FC (RR, 1.02; 95% CI: 0.97–1.07; P=0.48), (RR, 1.00; 95% CI: 0.98–1.02; P=0.99), (RR, 1.02; 95% CI: 0.97–1.07; P=0.48), (RR, 1.04; 95% CI: 1.00–1.09; P=0.05) and (RR, 1.21; 95% CI: 0.93–1.56; P=0.15), showed no statistically significant difference with 12%, 0%, 65% and 74% heterogeneity, respectively. At 12 [Sonmez, Sari and Cetinbaş, 2008; Eidelman, Holan and Fuks, 2001; Agamy *et al.*, 2004; Ebrahim, Khademi and Ghasemi, 2004; Neamatollahi and Tajik, 2006; Moretti *et al.*, 2008; Noorollahian, 2008; Subramaniam *et al.*, 2009; Ansari and Ranjpour, 2010; Erdem *et al.*, 2011; Godhi, Sood and Sharma, 2011; Srinivasan and Jayanthi, 2011; Airen, Shigli and Airen, 2012; Sushynski *et al.*, 2012; Jayam *et al.*, 2014; Yildiz and Tosun, 2014; Olatosi, Sote and Orenuga, 2015; Yildirim *et al.*, 2016; Juneja and Kulkarni, 2017; Sunitha *et al.*, 2017; Jamali *et al.*, 2018; Abd Al Gawad and Hanafy, 2021], 18 [Sonmez, Sari and Cetinbaş, 2008; Moretti *et al.*, 2008; Sushynski *et al.*, 2012; Yildiz and Tosun, 2014; Yildirim *et al.*, 2016; Juneja and Kulkarni, 2017; Sunitha *et al.*, 2017] and 24 [Sonmez, Sari and Cetinbaş, 2008; Moretti *et al.*, 2008; Noorollahian, 2008; Subramaniam *et al.*, 2009; Ansari and Ranjpour, 2010; Erdem *et al.*, 2011; Airen,

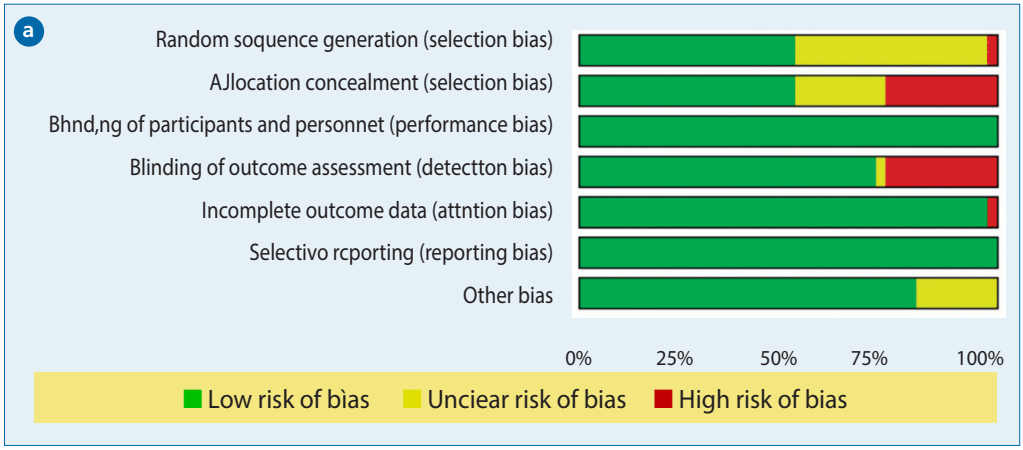
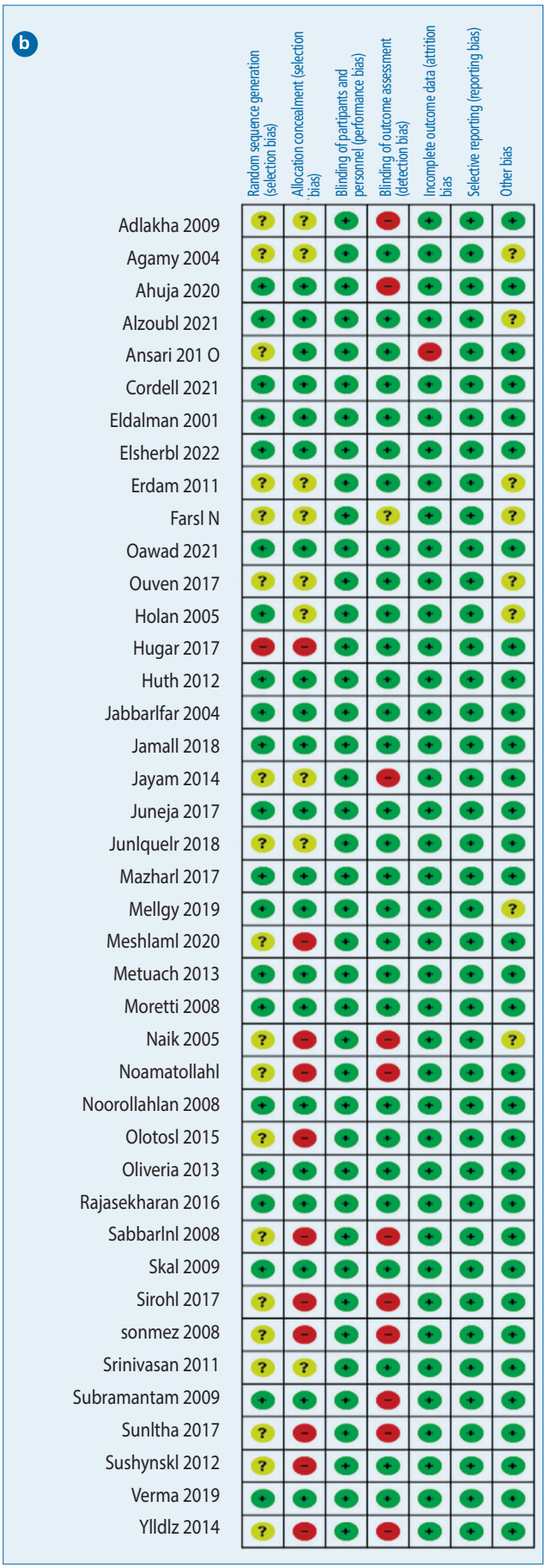


FIG 2
Risk of Bias **a.** Graph and **b.** Summary.



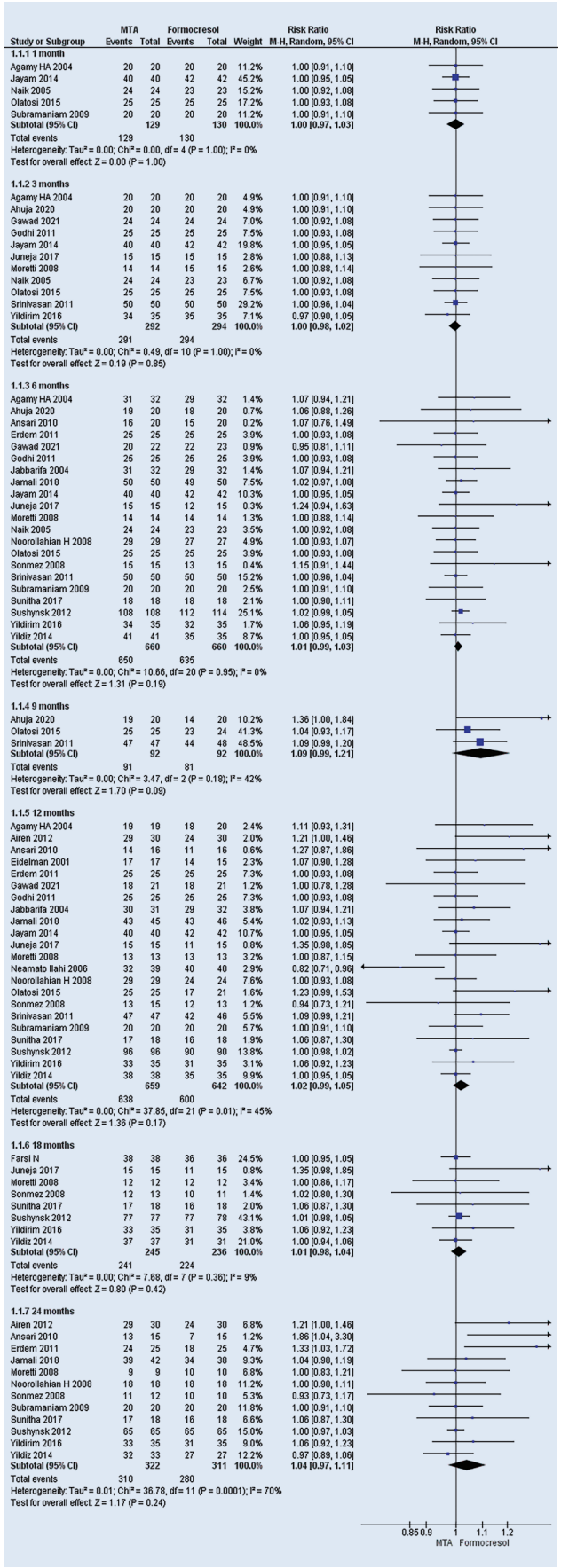


FIG 3 Forest plot for MTA versus FC – Clinical outcome.

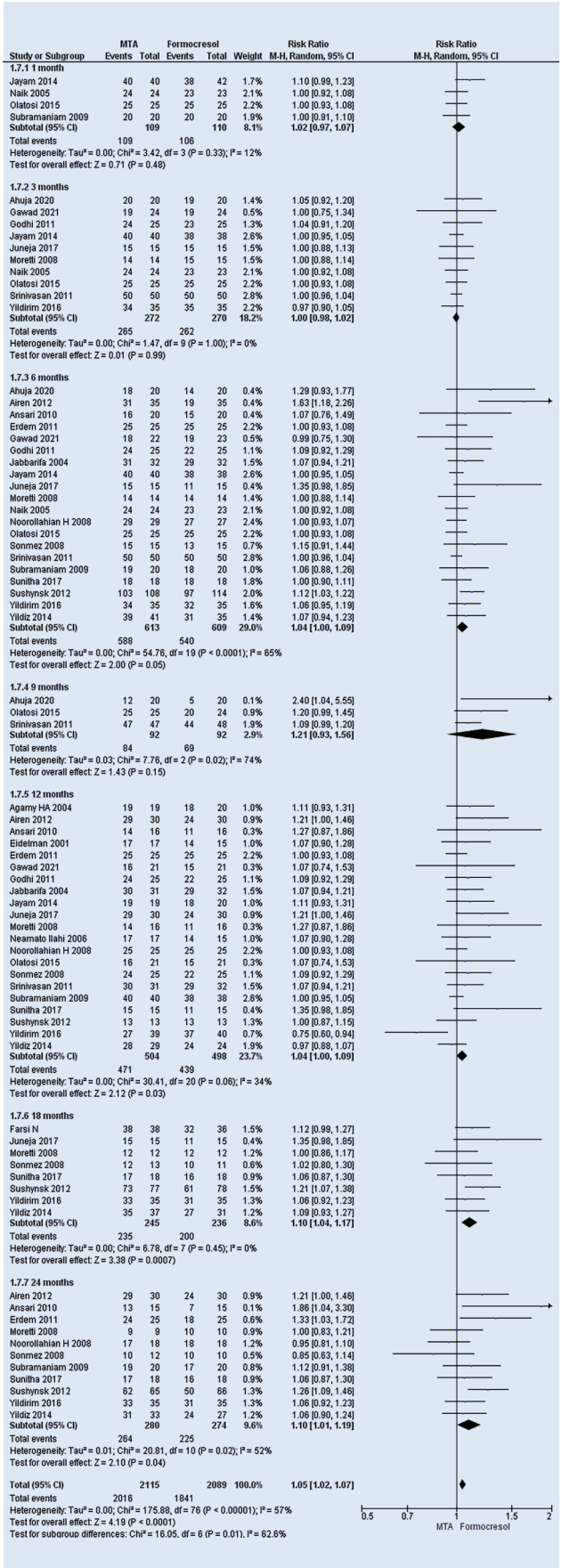


FIG 4 Forest plot for MTA versus FC – Radiographic outcome.

Shigli and Airen, 2012; Sushynski *et al.*, 2012; Yildiz and Tosun, 2014; Yildirim *et al.*, 2016; Sunitha *et al.*, 2017; Jamali *et al.*, 2018] months follow-up MTA resulted in a success rate of 1.04, 1.10 and 1.10-fold higher than that for FC (RR, 1.04; 95% CI: 1.00–1.09; P=0.03), (RR, 1.10; 95% CI: 1.04–1.17; P=0.0007) and (RR, 1.10; 95% CI: 1.01–1.19; P=0.04 showed statistically significant difference with 34%, 0% and 52% heterogeneity, respectively favouring the MTA pulpotomy (Fig. 4).

MTA versus FS

The clinical and radiographic success rate of MTA as compared to FS in tooth level unit was performed according to follow-up period, using random-effect model. It was observed that at 3 [Junqueira *et al.*, 2018; Somwanshi *et al.*, 2021], 6 [Cordell *et al.*, 2021; Sonmez, Sari and Cetinbaş, 2008; Ansari and Ranjpour, 2010; Yildiz and Tosun, 2014; Junqueira *et al.*, 2018; Somwanshi *et al.*, 2021], 12 [Cordell *et al.*, 2021; Sonmez, Sari and Cetinbaş, 2008; Neamatollahi and Tajik, 2006 ;Erdem *et al.*, 2011; Yildiz and Tosun, 2014; Junqueira *et al.*, 2018; Lin and Lin, 2020] and 18 [Sonmez, Sari and Cetinbaş, 2008; Yildiz and Tosun, 2014; Junqueira *et al.*, 2018; Lin and Lin, 2020] months, MTA and FS showed no statistically significant difference in the success rate. At 24 months [Sonmez, Sari and Cetinbaş, 2008; Erdem *et al.*, 2011; Yildiz and Tosun, 2014] follow-up, the value of RR was greater than one (RR, 1.19; 95% CI: 0.97–1.46, P=0.09), implying that clinical success of MTA was 1.19-fold higher as compared to FS in spite of the diamond favouring FS group. This difference was not statistically significant with 45% heterogeneity. Similarly, radiographic success rate showed statistically significant difference favouring MTA with the success rate 1.2-fold higher than FS (RR, 1.22; 95% CI: 1.05–1.43, P=0.01) even though the diamond favoured FS group and 0% heterogeneity (Fig.5).

MTA versus PC

The clinical and radiographic success rate of MTA as compared to PC in tooth level unit was performed according to follow-up period, using the random-effect model, no statistically significant difference was observed that at 3 [Yildiz and Tosun, 2014; Shanta *et al.*, 2017; Meslmani *et al.*, 2020; Alzoubi *et al.*, 2021; Meslmani *et al.*, 2020], 6 [Sakai *et al.*, 2009;Oliveira *et al.*, 2013; Yildiz and Tosun, 2014; 'One-year outcomes of MTA and modified Portland cement pulpotpmy in primary teeth: a randomized clinical trial'; Shanta *et al.*, 2017; Meslmani *et al.*, 2020; Alzoubi *et al.*, 2021; Meslmani *et al.*, 2020] ,12 [Sakai *et al.*, 2009;Oliveira *et al.*, 2013;Yildiz and Tosun, 2014; 'One-year outcomes of MTA and modified Portland cement pulpotpmy in primary teeth: a randomized clinical trial'; Shanta *et al.*, 2017, Meslmani *et al.*, 2020; Alzoubi *et al.*, 2021; Meslmani *et al.*, 2020], 18 [Sakai *et al.*, 2009; Yildiz and Tosun, 2014] and 24 months [Sakai *et al.*, 2009; Oliveira *et al.*, 2013; Yildiz and Tosun, 2014] follow-up (Fig. 6).

BD versus FC

The clinical and radiographic success rate of BD as compared to FC in tooth level unit was performed according to follow-up period, using the random-effect model, no statistically significant difference was observed that at 3 (Juneja and Kulkarni, 2017;El Meligy *et al.*, 2019; Elsherbini and Mossa, 2022; Ahuja *et al.*, 2020] , 6 [Juneja and Kulkarni, 2017; El Meligy *et al.*, 2019; Elsherbini and Mossa, 2022] and 12 [Juneja and Kulkarni, 2017; El Meligy *et al.*, 2019; Elsherbini and Mossa, 2022]. At 6 months follow-up, the value of RR was greater than one (RR, 9.253; 95% CI: 1.62–55.98, P=0.01), implying that BD showed 9.253-fold higher radiographic success rate as compared to FC showing a statistically significant difference and 0% heterogeneity (Fig. 7). Though these

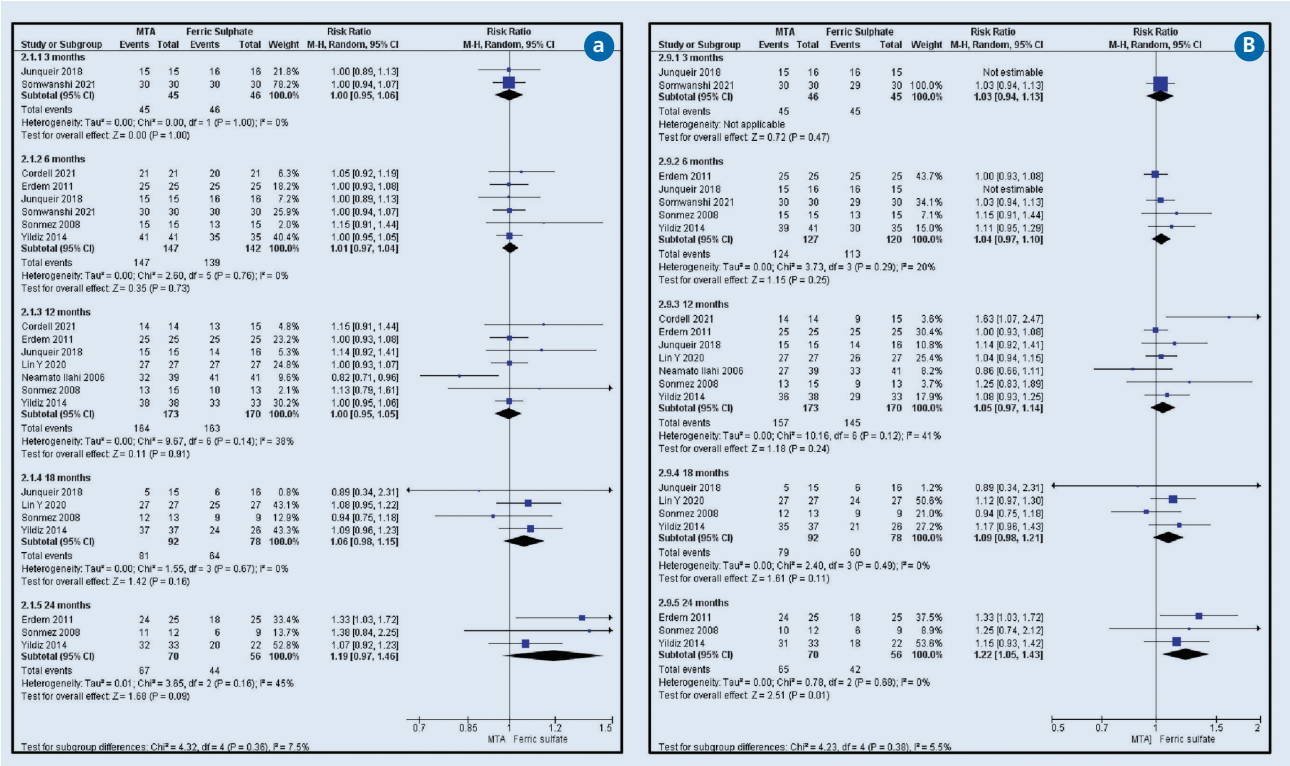


FIG 5 Forest plot for MTA versus FS a. Clinical success and b. Radiographic success.

results are statistically significant, the confidence interval for RR is too wide indicating uncertainty in the interpretation of results as wide CI suggests high dispersion in the data.

BD versus FS

The clinical and radiographic success rate of BD as compared to FS in tooth level unit at 6 months [Sirohi *et al.*, 2017; Guven *et al.*, 2017] follow-up period, using the random-effect model, showed no statistically significant difference (Fig. 7).

CH versus FC

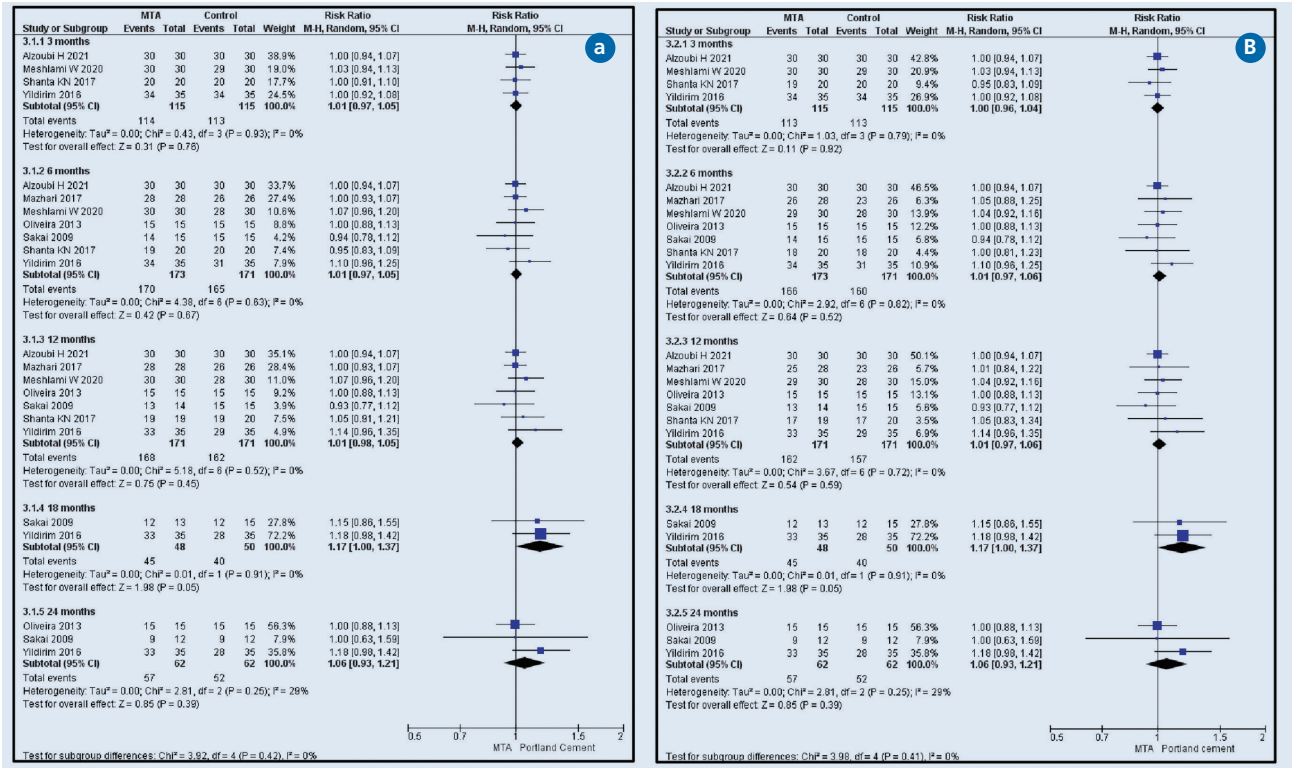


FIG 6 Forest plot for MTA versus PC a. Clinical success and b. Radiographic success.

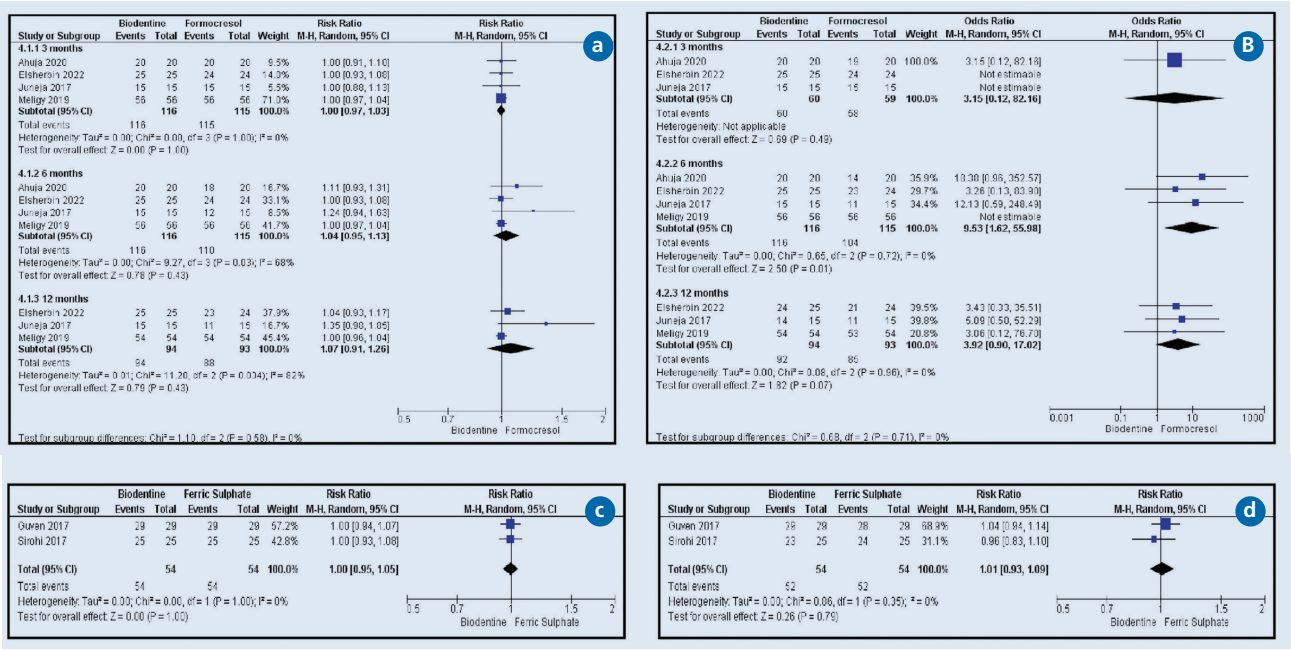


FIG 7 Forest plot for Biodentine versus FS and FC; a. Clinical success and b. Radiographic success.

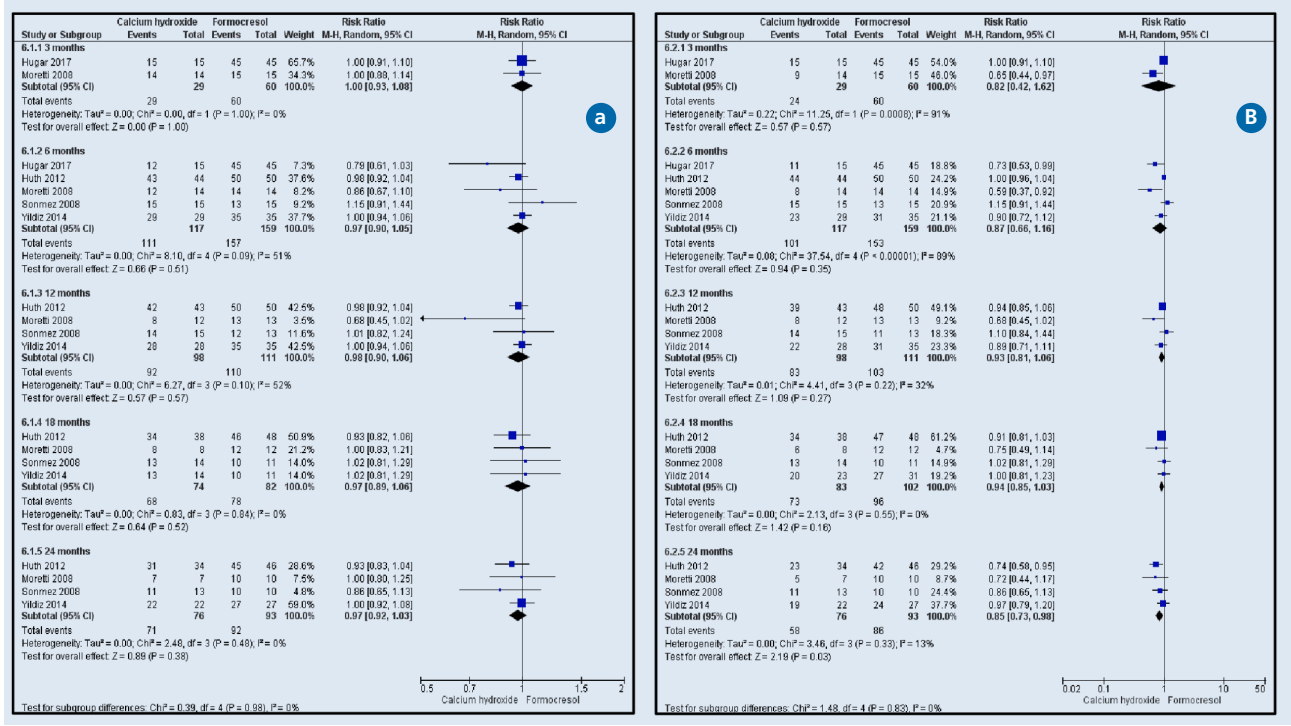


FIG. 8 Forest plot for CH versus FC a. Clinical success and b. Radiographic success

The clinical and radiographic success rate of CH as compared to FC in tooth level unit was performed according to follow-up period, using random-effect model, no statistically significant difference was observed that at 3 (Moretti *et al.*, 2008; Adlakha *et al.*, 2009) , 6 [Sonmez, Sari and Cetinbaş, 2008; Moretti *et al.*, 2008; Yildiz and Tosun, 2014; Huth *et al.*, 2012], 12 [Sonmez, Sari and Cetinbaş, 2008; Moretti *et al.*, 2008; Yildiz and Tosun, 2014, Huth *et al.*, 2012], 18 [Sonmez, Sari and Cetinbaş, 2008; Moretti *et al.*, 2008; Huth *et al.*, 2012; Yildiz and Tosun, 2014]and 24 [Sonmez, Sari and Cetinbaş, 2008; Huth *et al.*, 2012; Moretti *et al.*, 2008; Yildiz and Tosun, 2014] months except, at 24 months follow-up, the value of RR was less than one (RR, 0.85; 95% CI: 0.73–0.98, P=0.03), implying that CH showed 0.85-fold lower radiographic success rate as compared to FC showing a statistically significant difference and 13% heterogeneity favouring FC pulpotomy (Fig. 8).

CH versus FS

The clinical and radiographic success rate of CH as compared to FS in tooth level unit at 6 (Sonmez, Sari and Cetinbaş, 2008; Huth *et al.*, 2012; Yildiz and Tosun, 2014], 12 [Sonmez, Sari and Cetinbaş, 2008; Huth et al., 2012; Yildiz and Tosun, 2014], 18 [Sonmez, Sari and Cetinbaş, 2008; Huth et al., 2012; Yildiz and Tosun, 2014] and 24 [Sonmez, Sari and Cetinbaş, 2008; Huth et

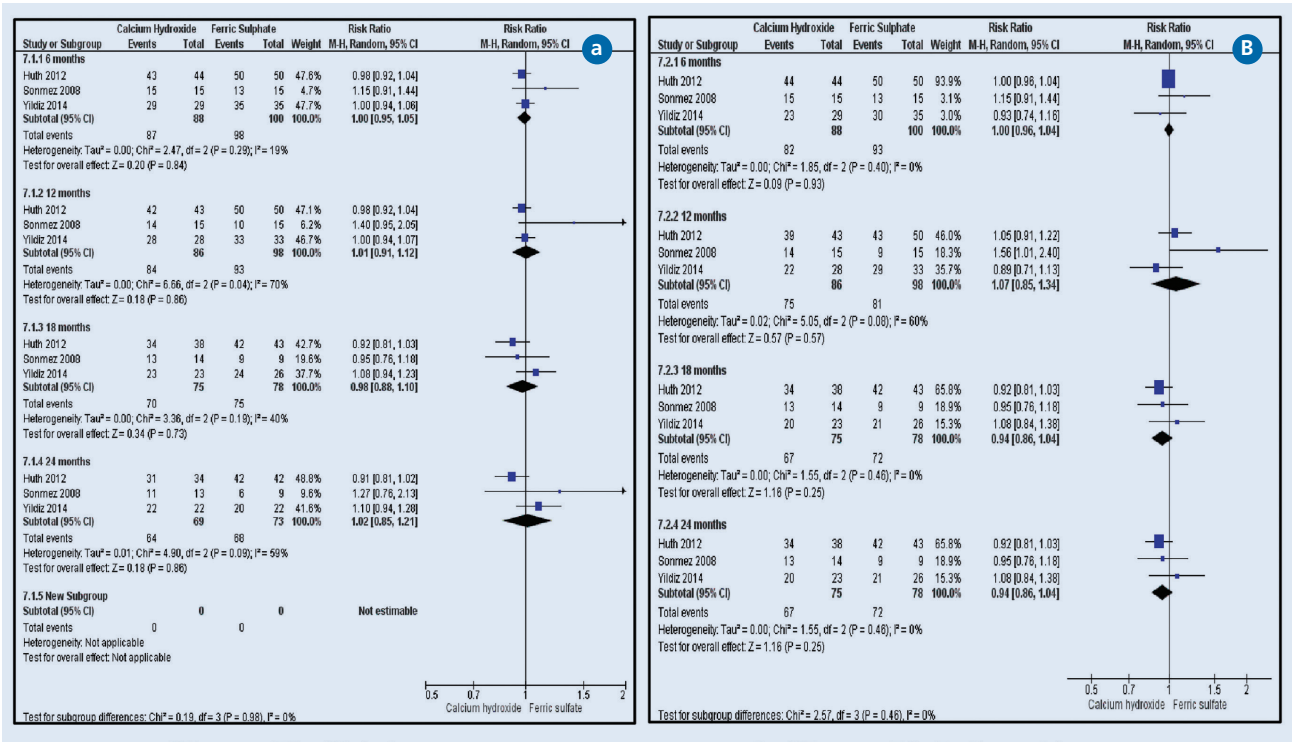


FIG. 9 Forest plot for CH versus FS a. Clinical success and b. Radiographic success.

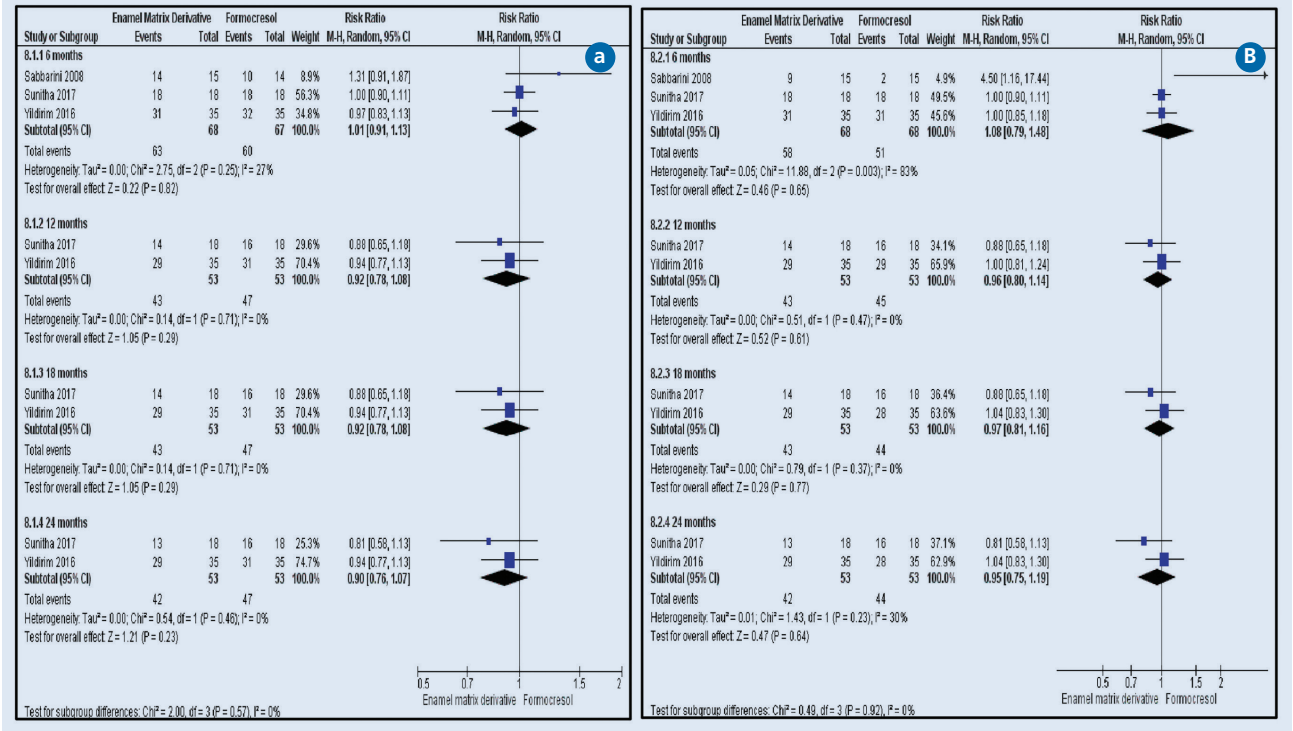


FIG. 10. Forest plot for EMD versus FC a. Clinical success and b. Radiographic success.

al., 2012; Yildiz and Tosun, 2014] months follow-up period, using random-effect model, did not show statistically significant difference between groups (Fig. 9).

EMD versus FC

The clinical and radiographic success rate of EMD as compared to FC in tooth level unit at 6 [Sabbarini *et al.*, 2008; Yildiz and Tosun, 2014; Sunitha *et al.*, 2017], 12 [Yildiz and Tosun, 2014; Sunitha *et al.*, 2017], 18 [Yildiz and Tosun, 2014; Sunitha *et al.*, 2017], and 24 [Yildiz and Tosun, 2014; Sunitha *et al.*, 2017] months follow-up period, using the random-effect model, did not show a statistically significant difference between groups (Fig. 10).

Publication bias for studies included on MTA compared with FC at different follow-ups was evaluated using a funnel plot (Fig. 11-12). The funnel plot showed asymmetry at the apex from the centre line having more studies on the right side as compared to

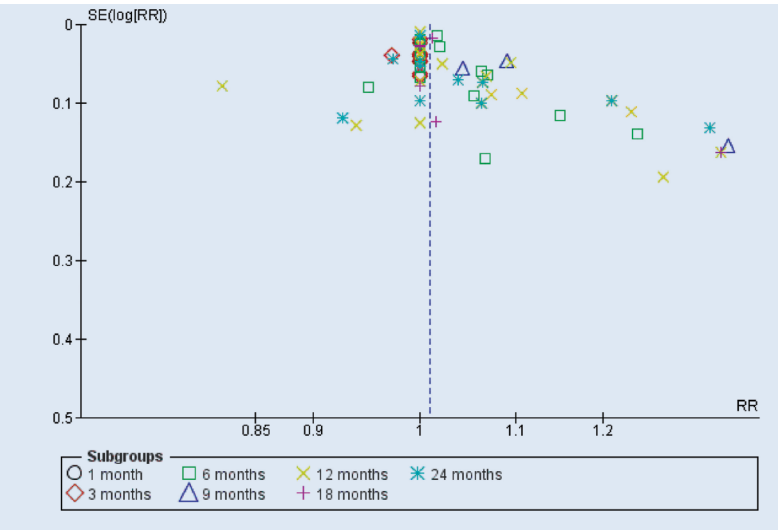


FIG. 11 Funnel plot for MTA versus FC – Clinical outcome.

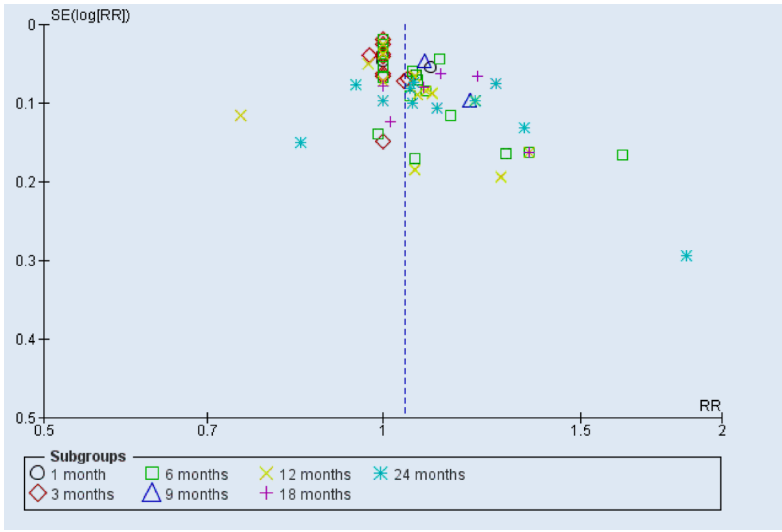


FIG.12 Funnel plot for MTA versus FC – Radiographic outcome.

the left, representing missing publications with nonsignificant results.

Discussion

The outcome of pulpotomy is mostly resolute by the medicament used. Procedures and materials used in pulpotomy treatment have advanced from devitalising to preservative and regenerative treatments. Due to a lack of agreement regarding an ideal pulpotomy medicament, the present systematic review and meta-analysis aimed to establish a preferred medicament to be used in the regenerative pulpotomy as compared to devitalising or preservative pulpotomy technique of primary teeth affected by deep caries. The review included 49 studies (42 RCT and 7 NRS) published from 2001 to 2022 and conducted in several countries. The included patients age ranged from 1.5–12 years across genders. Hence, the results of this systematic review are applicable to a varied paediatric population range with asymptomatic deep coronal caries. The primary teeth with evidence of periapical pathology, internal or external root resorption and physiologic root resorption of more than one-third of the root length were excluded in the studies, thus minimising the selection bias. Although, the clinical technique performed for different medicaments used was different, most of the studies followed the manufactures instruction for manipulation of the materials, thus reducing the clinical heterogeneity among procedures. Croll and Killian recommended that a Stainless-Steel Crown (SSC) should be placed after a pulpotomy to eliminate the potential for microleakage, marginal breakdown, or a subsequent bacterial influx in the pulp. Two of the included studies restored the teeth with SSC followed by amalgam and Glass Ionomer Cement [Cordell *et al.*, 2021; Croll and Killian, 1992].

The efficacy of pulpotomy medicaments was assessed by clinical success rate and radiographical success rate at minimum of 1 month of follow-up period in this systematic review. The score assessment's goal was to label all treated teeth as "success" or "failure" based on isolated signs and symptoms. The clinical and radiological success rate served as the base for the meta-analysis of the extracted data from 44 studies fulfilling the inclusion criteria. The meta-analysis generates pooled estimate of the effects across studies by statistically pooling the data. [Brandt *et al.*, 2011]. Random-effects model was used to address the methodological heterogeneity detected in terms of study site and setting, clinical expertise, pulpotomy technique and follow-up period. Different regenerative pulpotomy materials were compared separately with devitalising or preservative pulpotomy materials. MTA was compared clinical and radiographically separately with FC, FS, PC. The results of the meta-analysis for comparison between MTA and FC and PC showed that MTA yielded a better performance after 12, 18, and 24 months of evaluation but the results were not statistically significant. These similar results between the MTA, FC and PC could be attributed to the positive pulpal response, the high potential healing ability and the high regenerative power associated with the use of MTA and PC preserving the primary pulp vital and healthy leading to dentine bridge formation and the high bactericidal and fixative power of FC which is similar to the systematic review conducted by Bossù M et al. [2020].

The comparison of MTA and FS also revealed similar findings showing a statistically significant radiographic success rate in MTA after 24 months of evaluation, concluding that MTA is better material than to FS. Based on the quantitative synthesis results, it can be concluded that there is no superiority of one material over the other and MTA and PC can be used in primary teeth pulpotomy. BD new biocompatible, bioactive material stimulates dentine regeneration by inducing odontoblast differentiation from pulp progenitor cells. The quantitative comparison of BD with FC revealed that the clinical success rate of BD and FC are comparable but the radiographical success rate show statistically significant results post 6 months follow-up evaluation suggesting that BD is a promising alternative to FC which are similar to the results of the systematic review conducted by Shafaee et al [2019]. Ferric sulphate has gained popularity not only as a haemostatic agent but also as a pulpotomy medicament for primary molars. The comparison of BD with FS showed non-significant difference between the two groups; however, BD showing a high overall success rate compared with FS [Sirohi *et al.*, 2017; Guven *et al.*, 2017]. Similar to the previous systematic review and a meta-analysis conducted by Bossù et al. [2020] and Lin et al [2014], the present review confirmed that CH seemed to be the most ineffective material for pulpotomies of primary teeth when compared with FC and FS at all follow-up points. However, our systematic review also evaluated the regenerative materials used for pulpotomy such as MTA, PC, EMD. The comparison of EMD with FC also revealed similar results as that of CH. Also, its high price, and the required storage conditions are its disadvantages [Yildirim *et al.*, 2016].

Nevertheless, the present review is not without limitations. It was not possible to completely avoid the clinical heterogeneity among the included studies. Although subgroup analysis was

considered for the follow-up period, the lack of unequivocal standard procedures resulted in an imprecise comparison of data. The sample size of the included studies was small, thus lacking statistical power. Small sample size also affected confidence interval of study in some comparisons. Hence the results should be interpreted with caution. Both the clinical and radiographical parameters were clubbed as overall success or failure of the procedure. Intra-group comparison of medication was not performed. Hence, a comparison between MTA and BD and between FC and FS could not be made.

An overall high risk of bias was detected, mainly blinding of outcome assessment followed by allocation concealment for the included studies Also, scoring for blinding of participants and personnel was compromised. High quality study design and uniform clinical and radiographical protocols are needed to assess the performances of pulpotomy medicaments used in deciduous teeth.

Conclusions

Within the limitations of the current systematic review, MTA seemed to be the better alternative to FC and FS, showing a lower risk of failure and can be recommended for pulpotomy in primary teeth. BD also demonstrated promising results as a pulpotomy medicament. In order to improve the quality of future studies, it would be advisable to conduct RCTs with large sample sizes, standardized protocols, long follow-ups, and high quality to reduce the risk of bias and to confirm these outcomes.

Declaration Section

Availability of data and materials

The datasets used and analyzed during the current study are included within the paper.

Competing Interests

The authors declare that they have no competing interests.

Funding

This research received no external funding.

References

› Abd Al Gawad,RY and Hanafy, R.M.H. (2021) 'Success rate of three capping materials used in pulpotomy of primary molars: A randomized clinical trial', *The Saudi dental journal*, 33(7), pp. 560–567.
› Adlakha, V.K. *et al.* (2009) 'A comparative evaluation of hydroxyapatite crystals and glutaraldehyde as agents for pulpotomy in deciduous molars', *International journal of clinical pediatric dentistry*, 2(1), pp. 13–22.
› Agamy, H.A. *et al.* (2004) 'Comparison of mineral trioxide aggregate and formocresol as pulp-capping agents in pulpotomized primary teeth', *Pediatric dentistry*, 26(4), pp. 302–309.
› Ahuja, S. *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', *International journal of clinical pediatric dentistry*, 13(2), pp. 167–173.
› Airen, P., Shigli, A. and Airen, B. (2012) 'Comparative evaluation of formocresol and mineral trioxide aggregate in pulpotomized primary molars--2 year follow up', *The Journal of clinical pediatric dentistry*, 37(2), pp. 143–147.
› Alzoubi, H. *et al.* (2021) 'Clinical and Radiographic Evaluation of Using White Portland Cement and MTA in Pulpotomy Primary Anterior Teeth: A Randomized, Split-Mouth, Controlled Clinical Trial with 12 Months Follow-Up', 8(9), pp. 4195–4200.
› American Academy of Pediatric Dentistry and Stigers, J. (2019) *The Reference Manual of Pediatric Dentistry: Definitions, Oral Health Policies, Recommendations, Endorsements, Resources*. American Academy of Pediatric Dentistry.
› Ansari, G. and Ranjpour, M. (2010) 'Mineral trioxide aggregate and formocresol pulpotomy of primary teeth: a 2-year follow-up', *International endodontic journal*, 43(5), pp. 413–418.
› Anthonappa, R.P., King, N.M. and Martens, L.C. (2013) 'Is there sufficient evidence to support the long-term efficacy of mineral trioxide aggregate (MTA) for endodontic therapy in primary teeth?', *International endodontic journal*, 46(3), pp. 198–204.
› Bhor, K.B. *et al.* (2021) 'Effectiveness of oral health educational interventions on oral health of visually impaired school children: A systematic review and meta-analysis', *Special care in dentistry: official publication of the American Association of Hospital Dentists, the Academy of Dentistry for the Handicapped, and the American Society for Geriatric Dentistry*, 41(3), pp. 291–308.
› Biedma Perea, M. *et al.* (2017) 'Clinical and radiographic evaluation of white MTA versus formocresol pulpotomy: A 48-month follow-up study', *American journal of dentistry*, 30(3), pp. 131–136.
› Bossù, M. *et al.* (2020) 'Different Pulp Dressing Materials for the Pulpotomy of Primary Teeth: A Systematic Review of the Literature', *Journal of clinical medicine research*, 9(3). Available at: https://doi.org/10.3390/jcm9030838.
› Brandt, R.G. *et al.* (2011) 'The pulpal anesthetic efficacy of articaine versus lidocaine in dentistry: a meta-analysis', *Journal of the American Dental Association* , 142(5), pp. 493–504.
› Cordell, S. *et al.* (2021) 'A Randomized Controlled Trial Comparing the Success of Mineral Trioxide Aggregate and Ferric Sulfate as Pulpotomy Medicaments for Primary Molars', *Journal of dentistry for children* , 88(2), pp. 120–128.
› da Costa Santos, C.M., de Mattos Pimenta, C.A. and Nobre, M.R.C. (2007) 'The PICO strategy for the research question construction and evidence search', *Revista latino-americana de enfermagem*, 15(3), pp. 508–511.
› Croll, T.P. and Killian, C.M. (1992) 'Zinc oxide-eugenol pulpotomy and stainless steel crown restoration of a primary molar', *Quintessence international* , 23(6), pp. 383–388.
› Cuadros-Fernández, C. *et al.* (2016) 'Short-term treatment outcome of pulpotomies in primary molars using mineral trioxide aggregate and Biodentine: a randomized clinical trial', *Clinical oral investigations*, 20(7), pp. 1639–1645.
› Ebrahim, J., Khademi, A. and Ghasemi, D. (2004) 'Success rate of formocresol pulpotomy versus Mineral Trioxide Aggregate in human primary molar tooth', *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*, 9, pp. 55–58.
› Eidelman, E., Holan, G. and Fuks, A.B. (2001) 'Mineral trioxide aggregate vs. formocresol in pulpotomized primary molars: a preliminary report', *Pediatric dentistry*, 23(1), pp. 15–18.
› El Meligy, O.A.E.S. *et al.* (2019) 'BiodentineTM versus formocresol pulpotomy technique in primary molars: a 12-month randomized controlled clinical trial', *BMC oral health*, 19(1), p. 3.
› Elsherbini, M. and Mossa, H. (2022) 'Clinical & radiographic assessment of the relative efficacy of 1:5 concentration of Buckley's Formocresol, 5% Sodium hypochlorite (NaOCl) and BiodentineTM in pulpotomies for primary molars: A randomized controlled clinical trial', *Egyptian dental journal*, 68(1), pp. 47–62.
› Erdem, A.P. *et al.* (2011) 'Success rates of mineral trioxide aggregate, ferric sulfate, and formocresol pulpotomies: a 24-month study', *Pediatric dentistry*, 33(2), pp. 165–170.
› Farsi, N. *et al.* (2005) 'Success of mineral trioxide aggregate in pulpotomized primary molars', *The Journal of clinical pediatric dentistry*, 29(4), pp. 307–311.
› Firoozi, P., Salman, B.N. and Aslaminabadi, N. (2022) 'Clinical and radiographic comparison of Biodentine and Formocresol: an updated meta-analysis with trial sequential analysis', *European archives of paediatric dentistry: official journal of the European Academy of Paediatric Dentistry*, 23(6), pp. 855–867.
› Fouad, W.A. and Abd Al Gawad, R.Y. (2019) 'Is Biodentine, as successful as, mineral trioxide aggregate for pulpotomy of primary molars? A split-mouth clinical trial', *Tanta Dental Journal*, 16(2), p. 115.
› Godhi, B., Sood, P.B. and Sharma, A. (2011) 'Effects of mineral trioxide aggregate and formocresol on vital pulp after pulpotomy of primary molars: An in vivo study', *Contemporary clinical dentistry*, 2(4), pp. 296–301.
› Guven, Y. *et al.* (2017) 'Success Rates of Pulpotomies in Primary Molars Using Calcium Silicate-Based Materials: A Randomized Control Trial', *BioMed research international*, 2017, p. 4059703.
› Havale, R. *et al.* (2013) 'Clinical and radiographic evaluation of pulpotomies in primary molars with formocresol, glutaraldehyde and ferric sulphate', *Oral health and dental management*, 12(1), pp. 24–31.
› Holan, G., Eidelman, E. and Fuks, A.B. (2005) 'Long-term evaluation of pulpotomy in primary molars using mineral trioxide aggregate or formocresol', *Pediatric dentistry*, 27(2), pp. 129–136.
› Hugar, S.M. *et al.* (2017) 'Comparative Evaluation of Clinical and Radiographic

Success of Formocresol, Propolis, Turmeric Gel, and Calcium Hydroxide on Pulpotomized Primary Molars: A Preliminary Study', *International journal of clinical pediatric dentistry*, 10(1), pp. 18–23.
› Huth, K.C. *et al.* (2012) 'Long-term effectiveness of four pulpotomy techniques: 3-year randomised controlled trial', *Clinical oral investigations*, 16(4), pp. 1243–1250.
› Ibricevic, H. and al-Jame, Q. (2000) 'Ferric sulfate as pulpotomy agent in primary teeth: twenty month clinical follow-up', *The Journal of clinical pediatric dentistry*, 24(4), pp. 269–272.
› Jamali, Z. *et al.* (2018) 'Randomized Controlled Trial of Pulpotomy in Primary Molars using MTA and Formocresol Compared to 3Mixtatin: A Novel Biomaterial', *The Journal of clinical pediatric dentistry*, 42(5), pp. 361–366.
› Jayam, C. *et al.* (2014) 'Evaluation and comparison of white mineral trioxide aggregate and formocresol medicaments in primary tooth pulpotomy: clinical and radiographic study', *Journal of the Indian Society of Pedodontics and Preventive Dentistry*, 32(1), pp. 13–18.
› Juneja, P. and Kulkarni, S. (2017) 'Clinical and radiographic comparison of biodentine, mineral trioxide aggregate and formocresol as pulpotomy agents in primary molars', *European archives of paediatric dentistry: official journal of the European Academy of Paediatric Dentistry*, 18(4), pp. 271–278.
› Junqueira, M.A. *et al.* (2018) 'Clinical, Radiographic and Histological Evaluation of Primary Teeth Pulpotomy Using MTA And Ferric Sulfate', *Brazilian dental journal*, 29(2), pp. 159–165.
› Lin, P.-Y. *et al.* (2014) 'Primary molar pulpotomy: a systematic review and network meta-analysis', *Journal of dentistry*, 42(9), pp. 1060–1077.
› Lin, Y.-T. and Lin, Y.-T.J. (2020) 'Success rates of mineral trioxide aggregate, ferric sulfate, and sodium hypochlorite pulpotomies: A prospective 24-month study', *Journal of the Formosan Medical Association = Taiwan yi zhi*, 119(6), pp. 1080–1085.
› Marghalani, A.A., Omar, S. and Chen, J.-W. (2014) 'Clinical and radiographic success of mineral trioxide aggregate compared with formocresol as a pulpotomy treatment in primary molars: a systematic review and meta-analysis', *Journal of the American Dental Association* , 145(7), pp. 714–721.
› Maroto, M., Barreiro, S. and Barbería, E. (2019) 'Portland cement as pulp dressing agent in pulpotomy treatment of primary molars: a 12-month clinical study', *European journal of paediatric dentistry: official journal of European Academy of Paediatric Dentistry*, 20(1), pp. 23–26.
› Meslmani, W. *et al.* (2020) 'The efficacy of Portland cement as a pulpotomy agent in deciduous teeth', *Pediatric Dental Journal*, 30(2), pp. 99–105.
› Mettlach, S.E. *et al.* (2013) 'Comparison of mineral trioxide aggregate and diluted formocresol in pulpotomized human primary molars: 42-month follow-up and survival analysis', *Pediatric dentistry*, 35(3), pp. E87–94.
› Milnes, A.R. (2008) 'Is formocresol obsolete? A fresh look at the evidence concerning safety issues', *Pediatric dentistry*, 30(3), pp. 237–246.
› *Mineral Trioxide Aggregate/Ferric Sulfate Pulpotomy for Vital Primary Incisors: A Randomized Controlled Trial* (2014). Available at: https://search.proquest.com/openview/4ff617a1cb197764f08b6e60b33eea96/1?pq-origsite=gscholar&cbl=18750.
› Moher, D. *et al.* (2010) 'Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement', *International journal of surgery* , 8(5), pp. 336–341.
› Moretti, A.B.S. *et al.* (2008) 'The effectiveness of mineral trioxide aggregate, calcium hydroxide and formocresol for pulpotomies in primary teeth', *International endodontic journal*, 41(7), pp. 547–555.
› Naik, S. and Hegde, A.H. (2005) 'Mineral trioxide aggregate as a pulpotomy agent in primary molars: an in vivo study', *Journal of the Indian Society of Pedodontics and Preventive Dentistry*, 23(1), pp. 13–16.
› Neamatollahi, H. and Tajik, A. (2006) 'Comparison of clinical and radiographic success rates of pulpotomy in primary molars using formocresol, ferric sulfate and mineral trioxide aggregate (MTA)'. Available at: https://www.sid.ir/paper/297715/fa.
› Noorollahian, H. (2008) 'Comparison of mineral trioxide aggregate and formocresol as pulp medicaments for pulpotomies in primary molars', *British dental journal*, 204(11), p. E20.
› Olatosi, O.O., Sote, E.O. and Orenuga, O.O. (2015) 'Effect of mineral trioxide aggregate and formocresol pulpotomy on vital primary teeth: a clinical and radiographic study', *Nigerian journal of clinical practice*, 18(2), pp. 292–296.
› de Oliveira-Neto, O.B. *et al.* (2018) 'Risk of bias assessment of systematic reviews regarding dental implant placement in smokers: An umbrella systematic review', *The Journal of prosthetic dentistry*, 120(2), pp. 198–203.
› Oliveira, T.M. *et al.* (2013) 'Clinical, radiographic and histologic analysis of the effects of pulp capping materials used in pulpotomies of human primary teeth', *European archives of paediatric dentistry: official journal of the European Academy of Paediatric Dentistry*, 14(2), pp. 65–71.
› 'One-year outcomes of MTA and modified Portland cement pulpotpmy in primary teeth: a randomized clinical trial' (no date). Available at: https://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope=site&authtype=crawler&jrnl=23224150&AN=125555234&h=IfZ0KHP2MMuptHOmBmtU9qK5uyCKcuwiuABpAsm2Co%2BxWGPzG%2FFV7cRkoKJXV%2BHPvNMMiH1Dc74QRHyT58yQMg%3D%3D&crl=c.
› Praveen, N.H.K. *et al.* (2014) 'Pulpotomy medicaments: continued search for new alternatives-a review', *Oral health and dental management*, 13(4), pp. 883–890.
› Rajasekharan, S. *et al.* (2017) 'Efficacy of three different pulpotomy agents in primary molars: a randomized control trial', *International endodontic journal*, 50(3), pp. 215–228.
› Ranly, D.M. (1994) 'Pulpotomy therapy in primary teeth: new modalities for old rationales', *Pediatric dentistry*, 16(6), pp. 403–409.
› Rousseau, M.-C., Straif, K. and Siemiatycki, J. (2005) 'IARC carcinogen update', *Environmental health perspectives*, pp. A580–1.
› Sabbarini, J. *et al.* (2008) 'Comparison of enamel matrix derivative versus formocresol as pulpotomy agents in the primary dentition', *Journal of endodontia*, 34(3), pp. 284–287.
› Sakai, V.T. *et al.* (2009) 'Pulpotomy of human primary molars with MTA and Portland cement: a randomised controlled trial', *British dental journal*, 207(3), p. E5; discussion 128–9.
› Shafaee, H. *et al.* (2019) 'Comparison of the success rate of a bioactive dentin substitute with those of other root restoration materials in pulpotomy of primary teeth: Systematic review and meta-analysis', *Journal of the American Dental Association* , 150(8), pp. 676–688.
› Shanta, K.N. *et al.* (2017) 'Clinical and radiographic efficacy of portland cement as pulpotomy material in human primary molar', *Bangladesh Medical Research Council bulletin*, 43(2), pp. 71–76.
› Shirvani, A. and Asgary, S. (2014) 'Mineral trioxide aggregate versus formocresol pulpotomy: a systematic review and meta-analysis of randomized clinical trials', *Clinical oral investigations*, 18(4), pp. 1023–1030.
› Sirohi, K. *et al.* (2017) 'Comparison of Clinical and Radiographic Success Rates of Pulpotomy in Primary Molars using Ferric Sulfate and Bioactive Tricalcium Silicate Cement: An in vivo Study', *International journal of clinical pediatric dentistry*, 10(2), pp. 147–151.
› Slim, K. *et al.* (2003) 'Methodological index for non-randomized studies (minors): development and validation of a new instrument', *ANZ journal of surgery*, 73(9), pp. 712–716.
› Somwanshi, Y. *et al.* (2021) 'Comparative Evaluation of the Success Rate of Pulpotomy in Primary Molars Using Ferric Sulphate (FS) and Mineral Trioxide Aggregate (MTA): A Clinical and Radiographic Study', *Journal of Pharmaceutical Research International*, pp. 356–363.
› Sonmez, D., Sari, S. and Cetinbaş, T. (2008) 'A Comparison of four pulpotomy techniques in primary molars: a long-term follow-up', *Journal of endodontia*, 34(8), pp. 950–955.
› Srinivasan, D. and Jayanthi, M. (2011) 'Comparative evaluation of formocresol and mineral trioxide aggregate as pulpotomy agents in deciduous teeth', *Indian journal of dental research: official publication of Indian Society for Dental Research*, 22(3), pp. 385–390.
› Subramaniam, P. *et al.* (2009) 'Mineral trioxide aggregate as pulp capping agent for primary teeth pulpotomy: 2 year follow up study', *The Journal of clinical pediatric dentistry*, 33(4), pp. 311–314.
› Su, N. *et al.* (2016) 'Efficacy and safety of articaine versus lidocaine for irreversible pulpitis treatment: A systematic review and meta-analysis of randomised controlled trials', *Australian endodontic journal: the journal of the Australian Society of Endodontology Inc*, 42(1), pp. 4–15.
› Sunitha, B. *et al.* (2017) 'Clinical and Radiographic Evaluation of Four Different Pulpotomy Agents in Primary Molars: A Longitudinal Study', *International journal of clinical pediatric dentistry*, 10(3), pp. 240–244.
› Sushynski, J.M. *et al.* (2012) 'Comparison of gray mineral trioxide aggregate and diluted formocresol in pulpotomized primary molars: a 6- to 24-month observation', *Pediatric dentistry*, 34(5), pp. 120–128.
› Swift, E.J., Jr, Trope, M. and Ritter, A.V. (2003) 'Vital pulp therapy for the mature tooth – can it work?', *Endodontic topics*, 5(1), pp. 49–56.
› Verma, B. *et al.* (2019) 'Comparative evaluation of success of pulpotomy in primary molars treated with Formocresol, Pulpotec and Biodentine-6 month follow up study', *Int J Appl Dent Sci*, 5, pp. 77–82.
› Yildirim, C. *et al.* (2016) 'Clinical and Radiographic Evaluation of the Effectiveness of Formocresol, Mineral Trioxide Aggregate, Portland Cement, and Enamel Matrix Derivative in Primary Teeth Pulpotomies: A Two Year Follow-Up', *The Journal of clinical pediatric dentistry*, 40(1), pp. 14–20.
› Yildiz, E. and Tosun, G. (2014) 'Evaluation of formocresol, calcium hydroxide, ferric sulfate, and MTA primary molar pulpotomies', *European journal of dentistry*, 8(2), pp. 234–240.