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RESEARCH ARTICLE
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Pulpal response of primary and permanent teeth to various pulpotomy agents - A Systematic Review

S B Divya[1], M.S. Nivedhitha[2*]

[1]Department of Conservative Dentistry and Endodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai- 600077

[2]Professor, Department of Conservative dentistry and Endodontics, Saveetha Dental College and Hospitals Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-77

***Corresponding author:** M.S.Nivedhitha, Professor, Department of Conservative dentistry and Endodontics, Saveetha Dental College and Hospitals Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-77, Email: nivedhithamallisureshbabu@gmail.com

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ABSTRACT

Context: Vital pulp therapy is the treatment of choice for treating reversible pulpal injuries in both primary and permanent teeth for maintaining pulp vitality and function. Rationale of this treatment is based on the healing ability of the healthy pulp. Pulpotomy is vital pulp therapy in which a portion of vital coronal pulp tissue is removed surgically and the remaining radicular dental pulp is covered with a suitable material that protects the pulp from further injury and promotes healing.

Aim: To histologically evaluate the pulpal response of teeth treated with pulpotomy..

Methods and Material: The search identified 20 publications out of which 14 were excluded. Out of the 14 studies excluded, 3 were animal studies, 5 studies were on pulp capping and in 6 studies histological analysis was not done. The number of articles included were eight. The outcomes evaluated were dentin bridge formation, soft tissue changes, inflammatory changes. A detailed search was done in five databases namely Pubmed, Scopus, Cochrane, Lilacs and Science Direct.

Results: Within the limitations of the study, it may be concluded that biodentine had a similar effect of dentin bridge formation like MTA and both showed less pulpal response and inflammation. Formocresol, Theracal and ferric sulfate on the other hand, caused more pulpal inflammation with almost negligible dentin bridge formation.

Conclusion: MTA and Biodentine had similar results. The average follow up of various studies were 8 weeks to 6 months. In order to get more accurate results, longer follow up periods and more number of clinical trials are to be conducted.

Keywords: *pulpal response, pulpotomy, diseases, quality of life*

INTRODUCTION

Vital pulp therapy is the treatment of choice for treating reversible pulpal injuries in both primary and permanent teeth for maintaining pulp vitality and function (Asgary et al. 2018)Rationale of this treatment is based on the healing ability of the healthy pulp. Pulpotomy is vital pulp therapy in which a portion of vital coronal pulp tissue is removed surgically and the remaining radicular dental pulp is covered with a suitable material that protects the pulp from further injury and promotes healing.(Li et al. 2019) Successful pulpotomy procedure depends not only on the correct diagnosis of the inflamed dental pulp, but also on the selection of an effective and biocompatible medicament.

The ideal capping material should be bactericidal and harmless to cells and surrounding structures, promoting healing of the pulp tissue. Many different pulpotomy agents are available in the market. The most commonly used one is MTA (Mineral Trioxide Aggregate). MTA was first discovered by Mohamoud Torabinejad in 1993(Torabinejad, Parirokh, and Dummer 2018) ProRoot MTA is mainly composed of tricalcium silicate, dicalcium silicate, tricalcium aluminate, tetracalcium aluminoferrite, and bismuth oxide. When applied directly onto the pulp, MTA as a bioactive material with high sealing ability stimulates the formation of dentinal bridge and leads to pulp healing, yielding high clinical success rate (Silva et al. 2019). However, MTA has a long setting time and poor handling properties and may lead to tooth discoloration.

RetroMTA (BioMTA, Seoul, Korea) consists of calcium carbonate (60%–80% wt%), silicon dioxide (5–15 wt%), aluminum oxide (5–10 wt%), and calcium zirconia complex (20–30 wt%). This material has a setting time of 180 seconds, which can be beneficial for single-visit treatments (Bakhtiar et al. 2018).Investigating cell viability and attachment directly on human pulp cells and the release of calcium from the material were similar to those with ProRoot MTA. Additionally, the levels of vascular endothelial growth factor, angiogenin, and basic fibroblast growth factor were similar to those obtained with ProRoot MTA. When RetroMTA was evaluated in pulpotomy, continuous calcified barriers were formed in dog teeth after 4 weeks, showing that the material may be used for pulpotomy in the clinic (Kang et al. 2015) .A single clinical trial was performed with RetroMTA in 3 to 10-year-old children undergoing primary teeth pulpotomy. After 12 months, the clinical and radiographic results with RetroMTA were similar to those of MTA, indicating a very high success rate.(Divya et al. 2019)

In some countries, formocresol has been considered a low-cost alternative pulp capping material, due to its high clinical and radiographic success rates (Moretti et al. 2008). Biodentine is a tricalcium silicate–based restorative cement used for direct and indirect pulp capping. It has mechanical properties comparable to those of dentin and can be used as a dentin substitute in both the crown and root. Biodentine is bioactive and nontoxic as tested on human pulp cells and provides marginal sealing by adhering to both dentin and enamel. (Nishanthine et al. 2022)When applied directly onto the pulp in entire tooth cultures, it induced mineralization within the pulp and complete dentin bridge formation after 6 weeks in human teeth (Cuadros-Fernández et al. 2016). In addition, clinical trials have reported a high clinical success rate of pulpotomy with Biodentine comparable to that of ProRoot MTA. Clinical case reports have demonstrated a dentin bridge barrier formation when Biodentine was applied in partial pulpotomy of fractured mature teeth.(Cuadros-Fernández et al. 2016; Nowicka et al. 2013)

TheraCal is a new light-cured, resin-modified, calcium silicate–filled base/liner material designed for direct and indirect pulp capping. (Pandiyan et al. 2022)It contains 45 wt% mineral (Type III Portland cement), 10 wt% radiopaque agent, 5 wt% hydrophilic thickening agent, and 45% resin. (Bakhtiar et al. 2017)Mechanical properties analysis indicates that TheraCal has the greatest compressive and flexural strengths, whereas Biodentine has a higher stiffness and flexural modulus.(De Rossi et al. 2014)TheraCal has been reported to be toxic to pulp cells in vitro. In addition, an extensive inflammatory reaction was observed in 75% of the cases 4 weeks after TheraCal application in dog teeth, whereas a

complete dentinal bridge was formed only in 33% of the teeth.

Considering the diverse outcome finding reported by pulp capping material, it is imperative to explore and gather evidence to suggest the suitable pulpotomy agent/material.

Aim

To histologically evaluate the pulpal response of teeth treated with pulpotomy.

Research Question

What is the histologic pulp response after application of different pulpotomy material?

Null Hypothesis

Pulpotomy agents do not cause pulpal response in teeth treated with pulpotomy.

Alternate Hypothesis

Pulpotomy agents cause pulpal response in teeth treated with pulpotomy.

Pico

Population- Pulpotomy treated primary and permanent teeth

Intervention- Other pulpotomy agents
Comparison- MTA
Outcome- Dentin Bridge Formation
Pulpal Tissue Organisation
Pulpal Inflammation.

MATERIALS AND METHODS

The reporting of this systematic review was guided by the standards of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Statement.

Search strategy and Sources- A detailed search was done in five databases namely Pubmed, Scopus, Cochrane, Lilacs and Science Direct. The search queries were formulated in the databases with PICO format.

Search number	Search terms	Results	Time
#7	(((#1) AND (#3)) AND (#4)) AND (#5)	50	23:13:30
#4	(((((((dentin bridge formation) OR (hard tissue barrier formation)) OR (soft tissue inflammation)) OR (pulpal tissue inflammation)) OR (soft tissue organisation)) OR (pulpal tissue organisation)) OR (pulp tissue inflammation)) OR (pulp tissue organisation)	15,110	23:08:52
#5	((((((((((calcium hydroxide)) OR (other pulpotomy agents)) OR (other pulpotomy agent)) OR (bioceramic agent)) OR (bioceramic agents)) OR (formocresol)) OR (Theracal)) OR (Biodentine)) OR (iRoot BP)) OR (iRoot SP)) OR (Portland cement)) OR (Modified portland cement)	4948	23:12:14
#2	((((((((((other pulpotomy agents) OR (pulpotomy agents)) OR (formocresol)) OR (biodentine)) OR (theracal)) OR (iRoot BP)) OR (iRoot SP)) OR (portland cement)) OR (modified portland cement)) OR calcium hydroxide	21,891	23:01:20

J Popul Ther Clin Pharmacol Vol 30(10):e442–e460; 08 May 2023.

#3	((MTA) OR (ProRoot MTA)) OR (RetroMTA)	11,182	23:02:38
#1	(((((((pulpotomy treated teeth) OR (pulpotomy treated tooth)) OR (vital pulp therapy)) OR (vital pulp therapy treated tooth)) OR (pulpotomy treated molar)) OR (pulpotomy treated premolar)) OR (vital pulp therapy treated teeth)) OR (pulpotomy treated primary teeth)) OR (pulpotomy treated primary tooth)) OR (pulpotomy treated permanent tooth)) OR (pulpotomy treated permanent teeth)	2225	22:56:28

Search	Actions	Details	Query	Results	Time
#7	•••	>	Search: **(((#1) AND (#6)) AND (#3)) AND (#4)**	50	23:13:30
#6	•••	>	Search: **Calcium hydroxide OR(((((((Other pulpotomy agents) OR (Pulpotomy agents)) OR (formocresol)) OR (Biodentine)) OR (Theracal)) OR (i Root BP)) OR (i Root SP)) OR (Portland cement)) OR (Modified Portland cement)**	21,891	23:12:14
#5	•••	>	Search: **(((#1) AND (#2)) AND (#3)) AND (#4)**	35	23:10:55
#4	•••	>	Search: **(((((((Dentin bridge formation) OR (hard tissue barrier formation)) OR (soft tissue inflammation)) OR (pulpal tissue inflammation)) OR (Pulpal tissue organisation)) OR (soft tissue organisation)) OR (pulp tissue inflammation)) OR (pulp tissue organisation)**	15,110	23:08:52
#3	•••	>	Search: **((MTA) OR (proRoot MTA)) OR (RetroMTA)**	11,182	23:02:38
#2	•••	>	Search: **(((((((Other pulpotomy agents) OR (Pulpotomy agents)) OR (formocresol)) OR (Biodentine)) OR (Theracal)) OR (i Root BP)) OR (i Root SP)) OR (Portland cement)) OR (Modified Portland cement)**	14,758	23:01:20
#1	•••	>	Search: **((((((((((Pulpotomy treated teeth) OR (Pulpotomy treated tooth)) OR (vital pulp therapy)) OR (vital pulp therapy treated tooth)) OR (pulpotomy treated molar)) OR (pulpotomy treated premolar)) OR (pulpotomy treated primary tooth)) OR (pulpotomy treated primary teeth)) OR (pulpotomy treated permanent teeth)) OR (pulpotomy treated permanent tooth) OR (Vital pulp therapy treated teeth)**	2,225	22:56:28

Eligibility Criteria

Inclusion Criteria

Only studies which are Randomized Clinical Trials.

Pulpotomy performed in primary or permanent teeth.

Partial or full pulpotomy performed.

Only studies in which teeth with closed apices were considered.

Exclusion Criteria

Review articles, case reports, in vitro studies.

Animal studies.

Studies in which MTA was not used as one of the pulpotomy agents.

Studies in which teeth with open apices were considered.

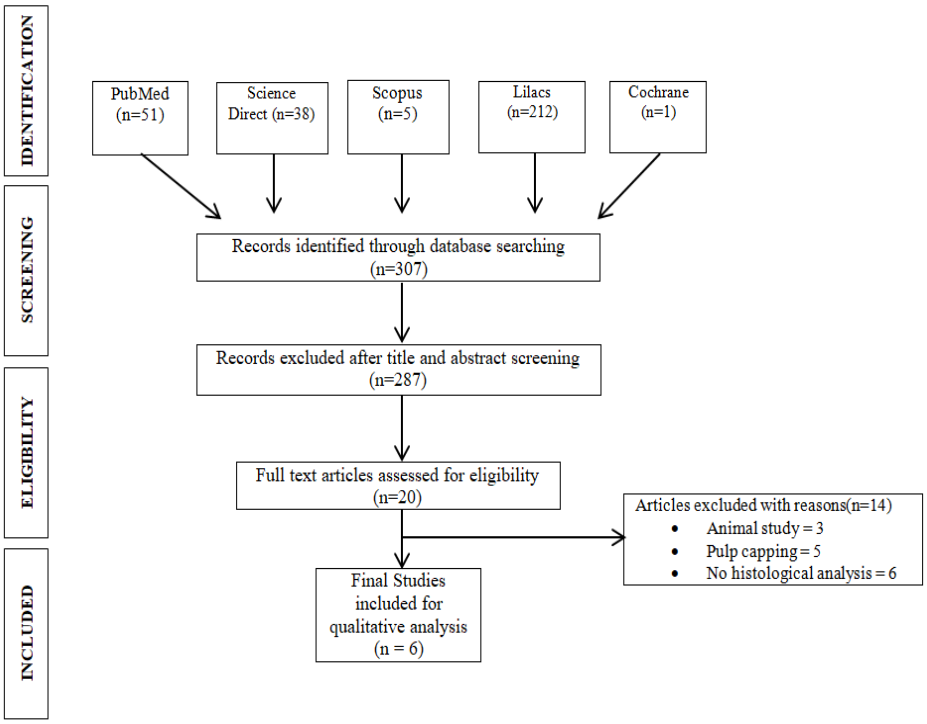
Pulpotomy performed on incisors.

Selection of studies

The selected studies were analysed based on the inclusion/exclusion criteria and imported to a reference managing software. After removal of duplicates, the title and abstract of the remaining records were screened independently for eligibility.

PRISMA flow chart

Kindly use recommended the PRISMA flow chart



List of Excluded studies

S no.	Author/ Year	Reason
1.	Lee et al. 2016	Animal study
2.	Lopes et al. 2019	Animal study
3.	Prabhakar et al. 2019	Animal study
4.	Caicedo et al. 2006	Pulp capping
5.	Nair et al. 2008	Pulp capping
6.	Sawicki et al. 2008	Pulp capping
7.	Alicja et al. 2013	Pulp capping
8.	Hegde et al. 2017	Pulp capping
9.	Moroto et al. 2007	No histological analysis done
10.	Moretti et al. 2008	No histological analysis done
11.	Vivien et al. 2009	No histological analysis done
12.	Cameron et al. 2010	No histological analysis done
13.	Silva et al. 2019	No histological analysis done
14.	Mariano et al. 2020	No histological analysis done

Outcome measures
Variables of interest table

S no.	Variables of Interest (Based on histological analysis)
1.	Dentin bridge formation
2.	Pulpal Inflammation
3.	Soft tissue organization

Data Extraction

Data of the included studies was extracted using a customized data extraction form. Data extracted consisted of the following:

Article identification information – Authors, and Publication year, Type of Study

Baseline demographic data – Age, Sex of participants.

Study Characteristics – Sample size, tooth on which pulpotomy was performed, Follow-up period, groups and number to teeth per group.

Outcome of Interest – Dentin Bridge Formation, Soft tissue organisation, pulpal inflammation. (Kindly explain, which outcome measure (continuous or dichotomous or any other values) were collected)

Description of studies

The search identified 20 publications out of which 14 were excluded. Out of the 14 studies excluded, 3 were animal studies, 5 studies were on pulp capping and in 6 studies histological analysis was not done.

TABLE 1: General Information of included studies

No	Author/ Year	Type of study	Age group	Sample size (N/n)	Type of teeth	Study group
1)	Daya Srinivasan et al. 2011	Randomized Clinical Trial	4 to 6 years	10/4+4+2	Deciduous canines	Group1- MTA Group2- Formocresol Group3- Carious teeth
2)	Dipti Bhagat et al. 2016	Randomized Clinical Trial	12 to 18 years	30/15	Premolars	Group 1-MTA Group2- Portland Cement
3)	Bakhtiar et al. 2017	Randomized Clinical Trial	18 to 32 years	27/9	Maxillary & Mandibular 3rd molars	Group1-MTA Group2-Theracal Group3-Biodentine
4)	Bakhtiar et al. 2018	Randomized Clinical Trial	18 to 32 years	22/11	Maxillary and Mandibular 3rd molars	Group1-ProRoot MTA Group2-RetroRoot MTA
5)	Marina Azevedo et al. 2018	Randomized Clinical Trial	5 to 9 years	31/16+15	Primary Maxillary and Mandibular molars	Group1-MTA Group2- Ferric sulfate
6)	Meslmani et al. 2020	Randomized Clinical Trial	7.5 to 9 years	60/30	Primary maxillary and Mandibular molars	Group1-MTA Group2-Modified Portland Cement

Characteristic table of Included articles

No	Author/ Year	Groups	Type of teeth/N	Pulp Therapy performed	Follow up period	Scoring criteria	Soft tissue organization	Pulpal Inflammation	Dentin Bridge Formation	Conclusion
1.	Daya Srinivasan et al. 2011	Group1-MTA Group2-Formocresol Group3-Carious teeth	Deciduous canines /10	Pulpotomy	6 months	No specific criteria	1)MTA →Pulp stones were more numerous in pulp compared to Formocresol. 2)Formocresol →Pulp stones were less numerous in pulp than MTA	1)MTA →Less inflammatory cells infiltrate the pulp. 2)Formocresol →More inflammatory cell infiltrates the pulp.	1)MTA →Amorphous eosinophilic layer of dentin bridge formation seen. 2) Formocresol →No dentin bridge formation seen	MTA had better biological properties and better dentin bridge formation capacity than formocresol.
2.	Dipti Bhagat et al. 2016	Group 1-MTA Group2-Portland Cement	Premolar/30	Pulpotomy	6 months	Cox et al. criteria	1)MTA- →7 teeth scored 1 →2 teeth scored 2 →6 teeth scored 3 2)Portland Cement- →8 teeth scored 1 →7 teeth scored 3	1) MTA →11 teeth scored 1 →4 teeth scored 2 2) Portland Cement →10 teeth scored 1 →5 teeth scored 2	1) MTA →7 teeth scored 1 →2 teeth scored 2 →6 teeth scored 3 2) Portland Cement →8 teeth scored 1 7 scored 3	Portland cement may serve as effective and less expensive MTA substitute

3.	Bakhtiar et al. 2017	Group1-MTA Group2-Theracal Group3-Biodentine	Maxillary and Mandibular 3rd molars/ 27	Partial Pulpotomy	8 weeks	Nowicka et al. criteria	1) MTA →Pulpal organization normal in 33.3% →Local pulp tissue disorganisation seen in 2 cases →complete pulp disorganisation in 44.4% 2) Theracal →Pulpal organization normal in 11.11% →Local pulp tissue disorganisation seen in 6 cases →complete pulp disorganisation in 22.2%. 3) Biodentine →Pulpal organization normal in 66.67% →Local pulp tissue disorganisation seen in 3 cases →complete pulp disorganisation in none.	Pulpal inflammation was absent in all the three groups after 8 weeks	1) MTA Hard tissue formation in the form of complete dentin bridge. 56% 2) Theracal Complete dentin bridge formation in 11% of cases. 3) Biodentine All the teeth showed hard tissue formation in the form of a complete dentin bridge. Dentin bridge was thicker than that formed in MTA	Biodentine was more reliable followed by proRoot MTA as a partial pulpotomy agent. This study did not support the use of Theracal as a partial pulpotomy agnt.

4.	Bakhtiar et al. 2018	Group1-ProRoot MTA Group2-RetroRoot MTA	Maxillary and Mandibular 3rd molars /22	Partial Pulpotomy	8 weeks	Nowicka et al. criteria	1)ProRoot MTA →Normal pulp organisation or limited disorganisation in 8 cases out of 11 →Complete disorganisation in 3 cases out of 11. 2) Retro MTA →Normal pulp organisation or limited disorganisation in 4 cases out of 11. →Complete disorganisation in 7 cases out of 11.	Pulpal inflammation was absent in both the groups after 8 weeks	1)ProRoot MTA →Incomplete dentin bridge formation seen in 4 cases out of 11. →Complete dentin bridge formation seen in 7 cases out of 11. 2) RetroMTA →Incomplete dentin bridge formation seen in 7 cases out of 11. →Complete dentin bridge formation seen in 4 cases out of 11.	Retro MTA shows more pulp disorganisation, incomplete dentin bridge formation which may be a potential drawback for RetroMTA.

5.	Marina Azevedo et al. 2018	Group1-MTA Group2-Ferric sulfate	Primary Maxillary and Mandibularmolars/31	Pulpotomy	Teeth at regular exfoliation period was extracted.	No specific criteria	1)Sound loose connective tissue with odontoblasts seen in MTA 2)Sound loose connective tissue seen in ferric sulfate.	No inflammatory cell infiltrate in both the groups	1) MTA showed a hard tissue barrier surrounded by odontoblasts over the pulp stumps. 2) Ferric Sulfate showed no such barrier formation and changes.	Both MTA and 15.5% ferric sulfate are effective as pulpotomy agents but first choice must be MTA.
6.	Meslmani et al. 2020	Group1-MTA Group2-Modified Portland Cement	Primary maxillary and Mandibular molars/60	Pulpotomy	2 months	Shayegan et al. criteria	1)MTA →Slight disruption in soft tissue organisation by 30%. →Moderate disruption in soft tissue organisation by 70%. 2)MPC →Slight disruption in soft tissue organisation by 50%. →Moderate disruption in soft tissue organisation by 50%.	1)MTA →No inflammation by 80% →Low grade inflammation by 20% 2)MPC →No inflammation by 90% →Low grade inflammation by 10%.	1) MTA →Incomplete formation by 60% →Beginning of formation by 20% →No evidence of formation by 20% 2)MPC →Incomplete formation by 30% →Beginning of formation by 40% →No evidence of formation by 30%	Both the materials were biocompatible with little excellence of MTA in terms of dentin bridge formation.

Quality Assessment and Level of Evidence

Should be based on study design of included studies whereas evidence level is synthesize for each outcome assessed here.

The assessment of the methodology was conducted using Cochrane Collaboration's Risk of Bias Assessment Tool - Review Manager (5.4.1). Domains that were assessed was as follows

Random sequence generation

Allocation Concealment

Blinding of participants and personnel

Blinding of the outcome assessment

Incomplete outcome data

Selective reporting

Other sources of bias

Each domain was rated as "low-risk", "high risk" or "unclear risk". The level of evidence of each of the included studies was also assessed according to the Oxford Centre for Evidence-based Medicine, 2009.

Risk of Bias

Table of Risk of Bias Major Criteria

No	Author/Year	Randomization	Allocation Concealment	Assessor Blinding	Drop outs described	Risk of Bias
1.	Daya Srinivasan et al. 2011	Yes	No	Yes	Yes	Low
2.	Dipti Bhagat et al. 2016	Yes	Yes	Yes	Unclear	Low
3.	Bakhtiar et al. 2017	Yes	No	Yes	Unclear	Moderate
4.	Bakhtiar et al. 2018	Yes	No	Yes	Unclear	Moderate
5.	Marina Azevedo et al. 2018	Yes	No	Yes	Yes	Low
6.	Meslmani et al. 2020	Yes	No	Unclear	No	High

Table of Risk of Bias Minor Criteria

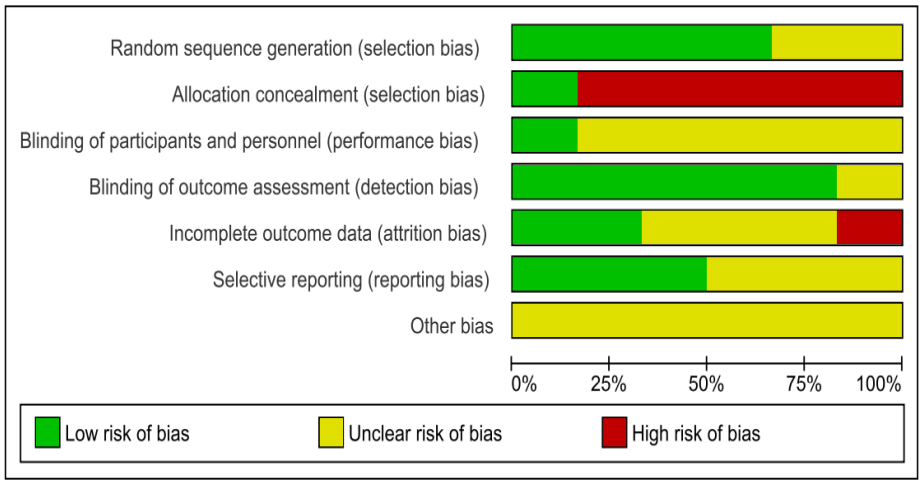
No.	Author	Sample Justified	Baseline Comparison	I/E Criteria	Method Error
1.	Daya Srinivasan et al. 2011	Yes	Yes	Yes	No
2.	Dipti Bhagat et al. 2016	Yes	Yes	Yes	Yes
3.	Bakhtiar et al. 2017	Yes	No	No	Yes
4.	Bakhtiar et al. 2018	Yes	No	No	Yes
5.	Marina Azevedo et al. 2018	Yes	Yes	Yes	No
6.	Meslmani et al. 2020	Yes	No	Yes	No

Table of Risk of Bias for RevMan

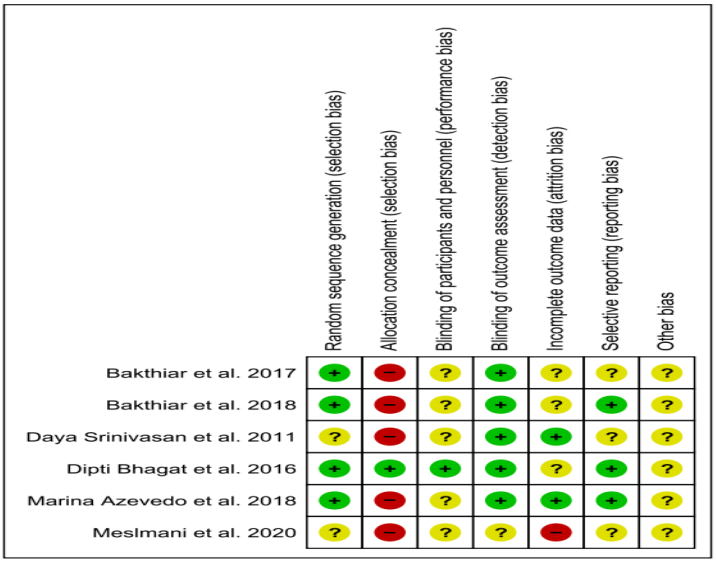
No	Author/Year	Randomization	Allocation Concealment	Blinding of participants, personnels	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
1.	Daya Srinivasan et al. 2011	Unclear	No	No	Yes	Yes	Unclear
2.	Dipti Bhagat et al. 2016	Yes	Yes	Yes	Yes	Unclear	Unclear
3.	Bakhtiar et al. 2017	Yes	No	No	Yes	Unclear	Unclear
4.	Bakhtiar et al. 2018	Yes	No	No	Yes	Unclear	Unclear

5.	Marina Azevedo et al. 2018	Yes	No	Unclear	Yes	Yes	Unclear
6.	Meslmani et al. 2020	Unclear	No	No	Unclear	No	Unclear

Risk of Bias summary



Risk of Bias graph



Level of evidence of included studies

S no.	Author/ Year	Study Design	Level of evidence
1.	Daya Srinivasan et al. 2011	Randomized Clinical Trial	Level 1b
2.	Dipti Bhagat et al. 2016	Randomized Clinical Trial	Level 1b
3.	Bakhtiar et al. 2017	Randomized Clinical Trial	Level 2b
4.	Bakhtiar et al. 2018	Randomized Clinical Trial	Level 2b

5.	Marina Azevedo et al. 2018	Randomized Clinical Trial	Level 1b
6.	Meslmani et al. 2020	Randomized Clinical Trial	Level 2b

DISCUSSION

The objective of this systematic review was to histologically evaluate pulpal response of teeth treated with pulpotomy using various pulpotomy agents. Number of studies included was 6. All of them were randomized clinical trials.The teeth selected for pulpotomy were primary or permanent canines,premolars and molars.(Subramanyam and Somasundaram 2020)The age group of participants ranged from 4 years to 32years. Follow up period ranged from 8 weeks to 6 months. 2 studies had a follow up period of 6 months. 2 studies followed up for 8 weeks,1 study for 2 months, 1 study followed up till the natural exfoliation time of the tooth.

In two studies, maxillary and mandibular 3rd molars were studied, in 2 studies primary maxillary and mandibular molars were studied,in one study premolars and in one other study, deciduous canines were studied. Partial pulpotomy was performed in 2 studies.Different scoring criteria were used like Cox et al., Nowicka et al., (Nowicka et al. 2013)Shayegan et al(Shayegan, Petein, and Abbeele 2008)

Various pulpotomy agents, formaldehyde-based materials, electrosurgery, lasers, glutaraldehyde, haemostatic medicaments, zinc oxide eugenol, bone morphogenic protein (BMP), collagen and calcium involving, dentin bridge inducing materials, have been recommended from the past to the present. The first pulpotomy agent used for primary teeth, introduced by Sweet, was formocresol (FC), which fixes and mummifies the tissue completely. However, the ideal pulpotomy treatment should leave the radicular pulp vital and healthy and completely enclosed within an odontoblast-lined dentin chamber. calcium hydroxide (CH) was the first medication that induced dentin bridge formation in pulpotomies.Another alternative pulpotomy agent, ferric sulphate (FS), a haemostatic medicament, has been used because it might minimize the chances for inflammation and thereby prevent internal resorption (IR). In 1995, Torabinejad et al. described mineral trioxide aggregate (MTA) a biocompatible, dentin bridge inducing material and was used as a pulpotomy agent.In all the included studies, MTA was commonly used as a pulpotomy agent.Other agents used were formocresol,ferric sulphate, modified Portland cement, theracal, biodentine, RetroMTA, ProRoot MTA.

Daya srinivasan et al. compared MTA with that of formocresol.MTA showed less infiltration of inflammatory cells into the pulp, and also amorphous dentin bridge formation was seen in MTA group and no dentin bridge formation was seen in formocresol.According to the author, MTA showed better biological and better dentin bridge formation than formocresol.Histological findings confirm that formocresol has no reparative ability and its action is limited as a fixative agent (Srinivasan and Jayanthi 2011; Bhagat et al. 2016).Studies in literature have been stated which conducted study on MTA and formocresol as pulpotomy agents.In a study by Nematollahi et al., comparison was between MTA and formocresol, no significant difference was found between the two groups clinically and radiographically(Nematollahi et al. 2018).A study conducted by Olatosi et al., MTA was compared with formocresol and MTA performed better than formocresol both clinically and radiographically(Olatosi, Sote, and Orenuga 2015).Similar results to Daya Srinivasan were given in a study conducted by Ansari et al.(Ansari and Ranjpour 2010) but the only difference being that histological analysis was not done by Ansari et al.

Dipti Bhagat et al. compared MTA with that of Portland cement. MTA has portland cement as one of its major constituents.(Janani, Teja, and Ajitha 2021)Comparing portland cement with that of MTA showed similar results for both the groups. So portland cement can be used as a substitute for MTA in a cost effective way. Despite the specifications and advantages of Portland Cement, it has some undesirable

properties like long setting time and radio translucency. Therefore, the researchers have focused on improving those specifications (Bhagat et al. 2016).Similar study was conducted by Vivien et al in 2009(Sakai et al. 2009) which showed similar results to Bhagat et al. but histological analysis was not done. Portland cement was tried as pulp capping agent.In a study conducted by Erfanparast et al, portland cement based material Theracal was used as direct pulp capping agent and it showed considerable results(Erfanparast, Iranparvar, and Vafaei 2018).Portland cement was also tried as indirect pulp capping material(Petrou et al. 2014)

Melsmani et al. compared MTA with Modified portland cement.Grey Portland Cement has been used in this research (W et al. 2020). This Portland Cement Contains the same components of MTA. However, the lime has been added to the Portland Cement during manufacturing procedure for delaying setting time. For using this material in this research, the lime had been excluded without modifying the cement's specifications.(Nandakumar and Nasim 2020) And the Accelerator, Calcium Chloride,had been added by 10% of the mix and the Radiopaque Zirconium Oxide had been added by 30% of the mix. (Bhagat et al. 2016; W et al. 2020)This material was sterilized by Gamma rays by cooperation with the Nuclear power Agency.

The results in the study showed both the materials were comparable but little excellence by MTA in terms of dentin bridge formation

Biodentine is a tricalcium silicate–based restorative cement used for direct and indirect pulp capping. It has mechanical properties comparable to those of dentin . Biodentine is bioactive and nontoxic as tested on human pulp cells and provides marginal sealing by adhering to both dentin and enamel.When applied directly onto the pulp in entire tooth cultures, it induced mineralization within the pulp and complete dentin bridge formation after 6 weeks in human teeth.(Hegde et al. 2017) TheraCal is a new light-cured, resin-modified, calcium silicate–filled base/liner material designed for direct and indirect pulp capping. It contains 45% weight mineral (type III Portland cement), 10 wt% radiopaque agent, 5 wt% hydrophilic thickening agent, and 45% resin. (Prabakar et al. 2020)Mechanical properties analysis indicates that TheraCal has the greatest compressive and flexural strengths, whereas Biodentine has a higher stiffness and flexural modulus.Bakhtiar et al. in 2017 reported a study on MTA in comparison with Theracal and Biodentine as pulpotomy agents. Various aspects like soft tissue organisation, pulpal inflammation and dentin bridge formation were evaluated. Biodentine showed thicker and more continuous dentin bridge formation followed by MTA and least by theracal.Also biodentine showed better biological properties than theracal.The author did not recommend the use of theracal as a pulpotomy agent(Bakhtiar et al. 2017)Literature shows many studies on biodentine. Biodentine was compared as pulpotomy agent with that of MTA and showed comparable results(Çelik et al. 2019).Another such study in which no significant difference was found between MTA and biodentine.(Carti and Oznurhan 2017).It was also tried in vital pulp therapy(Awawdeh et al. 2018) and as direct pulp capping agent(Brizuela et al. 2017).In all these studies, biodentine showed comparable results with MTA.

Mineral trioxide aggregate (MTA) is a water-based material used for endodontic treatment and pulp capping. It is made of tricalcium silicate, tricalcium aluminate, and bismuth oxide and tetracalcium aluminoferrite. ProRoot MTA (Dentsply Tulsa Dental,Tulsa, OK) sets in moisture and significantly reduces bacterial invasion with a high sealing ability. Additionally, several studies have shown its biocompatibility and its capacity to stimulate dentin bridge formation faster than calcium hydroxide. This explains why ProRoot application for treating pulp wounds

leads to high success rates in clinical procedures. (Ravikumar et al. 2018)However, MTA has a long setting time and poor handling properties and results in tooth discoloration because of the presence of bismuth oxide as a radiopacifier in its composition (Nguyen et al. 2017; Kang et al. 2015)RetroMTA (BioMTA, Seoul, Korea) consists of calcium carbonate (60%–80% wt%), silicon dioxide (5–15 wt%), aluminum oxide (5–10 wt%), and calcium zirconia complex (20–30 wt%). This material has a setting time of 180

seconds, which can be beneficial for single-visit treatments.Bakhtiar et al. in 2018 reported a study in which ProRoot MTA was compared with RetroMTA.Though the setting time of RetroMTA was favourable, it showed more pulp disorganisation and more incomplete dentin bridge formation compared with that of ProRoot MTA.This may be a potential drawback for RetroMTA (Bakhtiar et al. 2018)

Successful pulpotomy procedure depends not only on the correct diagnosis of the inflamed dental pulp, but also on the selection of an effective and biocompatible medicament.The ideal capping material should be bactericidal and harmless to cells and surrounding structures, promote healing of the pulp tissue and not interfere with the physiologic root resorption.Different pulpotomy agents have been tried in order for evaluate if they are clinically effective,biologically safe and at the same time cost effectiveness was considered. In some countries, ferric sulfate has been considered a low-cost alternative pulp capping material, due to its high clinical and radiographic success rates. The reaction of ferric sulfate with blood results in a ferric ion-protein complex, which mechanically blocks the capillary orifices, favoring the hemostasis (Nguyen et al. 2017)

Marina et al. in 2018 reported a study comparing white MTA with that of 15.5% ferric sulfate as a pulpotomy agent.The results showed that ferric sulfate was biologically comparable with MTA but dentin bridge formation was not very much evident with ferric sulfate.So, the first choice of use must be MTA and ferric sulfate was considerable though, according to the author. Though many pulpotomy agents were studied, MTA still proved to show better biological and better reparative dentin formation ability compared to other agents.(Shayegan, Petein, and Abbeele 2008) Biodentine was another material which showed similar properties as MTA

Nowicka et al. criteria	
Intensity of pulp inflammation	
Scoring	Feature
1	Absent or few inflammatory cells
2	Mild,< 10 inflammatory cells
3	Moderate, 10-25 inflammatory cells
4	Severe, > 25 inflammatory cells
Extent of pulp inflammation	
Scoring	Feature
1	Absent
2	Mild, inflammatory cells present only next to site of pulp exposure
3	Moderate,Inflammatory cells observed in part of coronal pulp
4	Severe,All coronal pulp is infiltrated
Pulp tissue organization and morphology	
Scoring	Feature
1	Normal pulp organization

2	Disorganization of pulp beneath the cavity
3	Disorganization of entire pulp

Dentin Bridge Thickness

Scoring	Feature
1	>0.25mm
2	0.1 to 0.25mm
3	<0.1mm
4	No bridge formation

Cox et al. criteria

Inflammatory cell response

Scoring	Feature
1	None or few scattered inflammatory cells present in the pulp beneath the exposure site
2	Polymorphonuclear leukocytes (acute) or mononuclear lymphocyte (chronic) in an inflammatory lesion.
3	Severe inflammatory lesion appearing as an abscess or dense infiltrate involving one third or more the coronal pulp
4	Completely necrotic pulp

Soft Tissue Organization

Scoring	Feature
1	Normal or almost normal tissue morphology below the exposure site and throughout the pulp
2	Lack of normal tissue morphology below the exposure site, with deeper pulp tissue appearing normal
3	Loss of general pulp morphology and cellular organization below the exposure site
4	Necrosis in at the coronal third of the pulp

Dentinal Bridge Formation

Scoring	Feature
1	New barrier tissue directly adjacent to some portion of the restorative material
2	New dentin bridge some distance from the material interface

3	No evidence of any dentin tissue formation in any of the tissue sections

Vital pulp therapy is a growing field.There is a marked development in this field with new materials coming up.However, the advantages and disadvantages of all these materials must be evaluated clinically.Hence, randomised clinical trials and systematic reviews with longer follow up periods are necessary to understand these material properties and put them to clinical practice.

CONCLUSION

The aim of the systematic review was to evaluate the pulpal response of teeth treated with pulpotomy. Within the limitations of the study, it may be concluded that biodentine had a similar effect of dentin bridge formation like MTA and both showed less pulpal response and inflammation. Formocresol, Theracal and ferric sulfate on the other hand, caused more pulpal inflammation with almost negligible dentin bridge formation.However, the overall quality of articles included in the study was moderate.The average follow up of various studies were 8 weeks to 6 months. In order to get more accurate results, longer follow up periods and more number of clinical trials are to be conducted.

REFERENCES

1. Ansari, G., and M. Ranjpour. 2010. “Mineral Trioxide Aggregate and Formocresol Pulpotomy of Primary Teeth: A 2-Year Follow-Up.” International Endodontic Journal 43 (5): 413–18.
2. Asgary, Saeed, Raheleh Hassanizadeh, Hassan Torabzadeh, and Mohammad Jafar Eghbal. 2018. “Treatment Outcomes of 4 Vital Pulp Therapies in Mature Molars.” Journal of Endodontia 44 (4): 529–35.
3. Awawdeh, Lama, Aladdin Al-Qudah, Hanan Hamouri, and Rosalie Jean Chakra. 2018. “Outcomes of Vital Pulp Therapy Using Mineral Trioxide Aggregate or Biodentine: A Prospective Randomized Clinical Trial.” Journal of Endodontia 44 (11): 1603–9.
4. Bakhtiar, Hengameh, Pouyan Aminishakib, Mohammad Reza Ellini, Fereshteh Mosavi, Fatemeh Abedi, Samar Esmailian, Ehsan Esnaashari, et al. 2018. “Dental Pulp Response to RetroMTA after Partial Pulpotomy in Permanent Human Teeth.” Journal of Endodontia 44 (11): 1692–96.
5. Bakhtiar, Hengameh, Mohammad Hossein Nekoofar, Pouyan Aminishakib, Fatemeh Abedi, Fereshteh Naghi Moosavi, Ehsan Esnaashari, Arash Azizi, et al. 2017. “Human Pulp Responses to Partial Pulpotomy Treatment with TheraCal as Compared with Biodentine and ProRoot MTA: A Clinical Trial.” Journal of Endodontia 43 (11): 1786–91.
6. Bhagat, Dipti, Ravi Kadur Sunder, Shashikiran Nandihalli Devendrappa, Amit Vanka, and Nidhi Choudaha. 2016. “A Comparative Evaluation of ProRoot Mineral Trioxide Aggregate and Portland Cement as a Pulpotomy Medicament.” Journal of the Indian Society of Pedodontics and Preventive Dentistry 34 (2): 172–76.
7. Brizuela, Claudia, Andrea Ormeño, Carolina Cabrera, Roxana Cabezas, Carolina Inostroza Silva, Valeria Ramírez, and Montse Mercade. 2017. “Direct Pulp Capping with Calcium Hydroxide, Mineral Trioxide Aggregate, and Biodentine in Permanent Young Teeth with Caries: A Randomized Clinical Trial.” Journal of Endodontia 43 (11): 1776–80.
8. Carti, O., and F. Oznurhan. 2017. “Evaluation and Comparison of Mineral Trioxide Aggregate and Biodentine in Primary Tooth Pulpotomy: Clinical and Radiographic Study.” Nigerian Journal of Clinical Practice 20 (12): 1604–9.
9. Çelik, Burcu Nihan, Merve Safa Mutluay, Volkan Arıkan, and Şaziye Sarı. 2019. “The Evaluation of MTA and Biodentine as a Pulpotomy Materials for Carious Exposures in Primary Teeth.” Clinical Oral Investigations 23 (2): 661–66.
10. Cuadros-Fernández, C., A. I. Lorente Rodríguez, S. Sáez-Martínez, J. García-Binimelis, I. About, and M. Mercadé. 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): 1639–45.
11. De Rossi, Andiara, Lea Assed Bezerra Silva, Patrícia Gatón-Hernández, Manoel Damião Sousa-Neto, Paulo Nelson-Filho, Raquel Assed Bezerra Silva, and Alexandra Mussolino de Queiroz. 2014. "Comparison of Pulpal Responses to Pulpotomy and Pulp Capping with Biodentine and Mineral Trioxide Aggregate in Dogs." Journal of Endodontia 40 (9): 1362–69.
12. Divya, S., Ganesh Jeevanandan, S. Sujatha, E. M. G. Subramanian, and Vignesh Ravindran. 2019. "Comparison of Quality of Obturation and Post-Operative Pain Using Manual vs Rotary Files in Primary Teeth - A Randomised Clinical Trial." Indian Journal of Dental Research: Official Publication of Indian Society for Dental Research 30 (6): 904–8.
13. Erfanparast, L., P. Iranparvar, and A. Vafaei. 2018. "Direct Pulp Capping in Primary Molars Using a Resin-Modified Portland Cement-Based Material (TheraCal) Compared to MTA with 12-Month Follow-up: A Randomised Clinical Trial." European Archives of Paediatric Dentistry: Official Journal of the European Academy of Paediatric Dentistry 19 (3): 197–203.
14. Hegde, Swaroop, B. Sowmya, Sylvia Mathew, Shilpa H. Bhandi, Shruthi Nagaraja, and K. Dinesh. 2017. "Clinical Evaluation of Mineral Trioxide Aggregate and Biodentine as Direct Pulp Capping Agents in Carious Teeth." Journal of Conservative Dentistry: JCD 20 (2): 91–95.
15. Janani, Krishnamachari, Kavalipurapu Venkata Teja, and P. Ajitha. 2021. "Cytotoxicity of Oregano Essential Oil and Calcium Hydroxide on L929 Fibroblast Cell: A Molecular Level Study." Journal of Conservative Dentistry: JCD 24 (5): 457–63.
16. Kang, C-M, S-H Kim, Y. Shin, H-S Lee, J-H Lee, G. T. Kim, and J. S. Song. 2015. "A Randomized Controlled Trial of ProRoot MTA, OrthoMTA and RetroMTA for Pulpotomy in Primary Molars." Oral Diseases 21 (6): 785–91.
17. Li, Yuanyuan, Bingdong Sui, Christian Dahl, Brian Bergeron, Peter Shipman, Lina Niu, Jihua Chen, and Franklin R. Tay. 2019. "Pulpotomy for Carious Pulp Exposures in Permanent Teeth: A Systematic Review and Meta-Analysis." Journal of Dentistry 84 (May): 1–8.
18. Moretti, A. B. S., V. T. Sakai, T. M. Oliveira, A. P. C. Fornetti, C. F. Santos, M. A. A. M. Machado, and R. C. C. Abdo. 2008. "The Effectiveness of Mineral Trioxide Aggregate, Calcium Hydroxide and Formocresol for Pulpotomies in Primary Teeth." International Endodontic Journal 41 (7): 547–55.
19. Nandakumar, Mahalakshmi, and Iffat Nasim. 2020. "Effect of Intracanal Cryotreated Sodium Hypochlorite on Postoperative Pain after Root Canal Treatment - A Randomized Controlled Clinical Trial." Journal of Conservative Dentistry: JCD 23 (2): 131–36.
20. Nematollahi, Hossein, Homa Noorollahian, Ali Bagherian, Mahsa Yarbakht, and Samane Nematollahi. 2018. "Mineral Trioxide Aggregate Partial Pulpotomy Versus Formocresol Pulpotomy: A Randomized, Split-Mouth, Controlled Clinical Trial with 24 Months Follow-Up." Pediatric Dentistry 40 (3): 184–89.
21. Nguyen, Trang D., Peter L. Judd, Edward J. Barrett, Nicole Sidhu, and Michael J. Casas. 2017. "Comparison of Ferric Sulfate Combined Mineral Trioxide Aggregate Pulpotomy and Zinc Oxide Eugenol Pulpectomy of Primary Maxillary Incisors: An 18-Month Randomized, Controlled Trial." Pediatric Dentistry 39 (1): 34–38.
22. Nishanthine, Cruz, Revathi Miglani, Indira R, Saravanan Poorni, Manali Ramakrishnan Srinivasan, Ali Robaian, Nassreen Hassan Mohammad Albar, et al. 2022. "Evaluation of Fluoride Release in Chitosan-Modified Glass Ionomer Cements." International Dental Journal 72 (6): 785–91.
23. Nowicka, Alicja, Mariusz Lipski, Mirosław Parafiniuk, Katarzyna Sporniak-Tutak, Damian Lichota, Anita Kosierkiewicz, Wojciech Kaczmarek, and Jadwiga Buczkowska-Radlińska. 2013. "Response of Human Dental Pulp Capped with Biodentine and Mineral Trioxide Aggregate." Journal of Endodontia 39 (6): 743–47.
24. Olatosi, O. O., E. O. Sote, and O. O. Orenuga. 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): 292–96.
25. Pandiyan, Indumathy, Sakthi D. Sri, Meignana Arumugham Indiran, Pradeep Kumar Rathinavelu, Jayashri Prabakar, and S. Rajeshkumar. 2022. "Antioxidant, Anti-Inflammatory Activity of Thymus Vulgaris-Mediated Selenium Nanoparticles: An in Vitro Study." Journal of Conservative Dentistry: JCD 25 (3): 241–45.
26. Petrou, Marina Agathi, Fadi Alhaddad Alhamoui, Alexander Welk, Mohammed Basel Altarabulsi, Mohammed Alkilzy, and Christian

H Splieth. 2014. “A Randomized Clinical Trial on the Use of Medical Portland Cement, MTA and Calcium Hydroxide in Indirect Pulp Treatment.” Clinical Oral Investigations 18 (5): 1383–89.

27. Prabakar, Jayashri, Meignana A. Indiran, Pradeep Kumar, Srisakthi Dooraikannan, and Ganesh Jeevanandan. 2020. “Microleakage Assessment of Two Different Pit and Fissure Sealants: A Comparative Confocal Laser Scanning Microscopy Study.” International Journal of Clinical Pediatric Dentistry 13 (Suppl 1): S29–33.
28. Ravikumar, Dhanalakshmi, Mahesh R, Sharna Ningthoujam, Waikhom Robindro, Gayathri R, and Vishnu Priya V. 2018. “Genotypic Characterization of Streptococcus Mutans in Child-Mother Pair-A PCR Based Study.” Journal of Oral Biology and Craniofacial Research 8 (3): 225–30.
29. Sakai, Vivien Thiemy, A. B. S. Moretti, T. M. Oliveira, A. P. C. Fornetti, C. F. Santos, M. A. A. M. Machado, and R. C. C. Abdo. 2009. “Pulpotomy of Human Primary Molars with MTA and Portland Cement: A Randomised Controlled Trial.” British Dental Journal 207 (3): E5; discussion 128–29.
30. Shayegan, Amir, Michel Petein, and Astrid Vanden Abbeele. 2008. “Beta-Tricalcium Phosphate, White Mineral Trioxide Aggregate, White Portland Cement, Ferric Sulfate, and Formocresol Used as Pulpotomy Agents in Primary Pig Teeth.” Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics 105 (4): 536–42.
31. Silva, Lidiane Lucas Costa E., Leopoldo Cosme-Silva, Vivien Thiemy Sakai, Camila Soares Lopes, Ana Paula Pereira da Silveira, Rafael Tobias Moretti Neto, João Eduardo Gomes-Filho, Thais Marchini Oliveira, and Ana Beatriz da Silveira Moretti. 2019. “Comparison between Calcium Hydroxide Mixtures and Mineral Trioxide Aggregate in Primary Teeth Pulpotomy: A Randomized Controlled Trial.” Journal of Applied Oral Science: Revista FOB 27 (May): e20180030.
32. Srinivasan, Daya, and M. Jayanthi. 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): 385–90.
33. Subramanyam, Divya, and Sujatha Somasundaram. 2020. “Clinical and Radiographic Evaluation of Aloe Vera vs Formocresol as a Pulpotomy Medicament in Primary Molars: A Double Blinded Randomized Controlled Trial.” International Journal of Clinical Pediatric Dentistry 13 (2): 138–43.
34. Torabinejad, M., M. Parirokh, and P. M. H. Dummer. 2018. “Mineral Trioxide Aggregate and Other Bioactive Endodontic Cements: An Updated Overview - Part II: Other Clinical Applications and Complications.” International Endodontic Journal 51 (3): 284–317.
35. W, Meslmani, W. Meslmani, MSc Department of Pediatric Dentistry, faculty of dentistry, Damascus University, Al-Mazzeh St. Damascus, and Syria. 2020. “Evaluation of Modified Portland Cement versus Mineral Trioxide Aggregate as a Pulpotomy Agent in Primary Molars: Histological Study.” International Journal of Dentistry and Oral Science. https://doi.org/10.19070/2377-8075-20000145.