REVIEW ARTICLE

Clinical Success of Iatrogenic Perforation Repair Using Mineral Trioxide Aggregate and Other Materials in Primary Molars: A Systematic Review and Meta-analysis

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Abstract

Aim: This study aimed at systematically reviewing the clinical success of repaired iatrogenic perforations using different materials in primary teeth.

Objectives: To compare mineral trioxide aggregate (MTA) with other biomaterials for the repair of iatrogenic perforations in primary molars during endodontic procedures.

Search methods: A comprehensive literature search was conducted by using three electronic databases (PubMed, Cochrane Library, Google Scholar) to identify articles that evaluated the different intervention materials for the repair of iatrogenic perforation in primary molars. Selection criteria: The articles reporting perforation repair in primary molars having clinical and radiographic success, as their outcome measures with a follow-up period of at least 1 year were included in this review. Studies and case reports with insufficient or unstated follow-up periods, in vitro, and animal studies were excluded.

Data collection and analysis: Two reviewers (SM, LM) independently screened all titles and abstracts according to the inclusion and exclusion criteria. Full texts of the selected studies were obtained for the second stage screening. The consensus was achieved by discussion with the third reviewer (AJ). Data extraction included study design, sample size, age of the patient, year of the study, follow-up period, outcome assessment criteria, material for repair, and success and failure.

Review results: A total of seven publications were included in this review. Of which, one was case series, three were case reports, and three were interventional studies. The combined success rate of MTA (80.55%) was inferior to other materials-premixed bioceramics, Atelocollagen, and calcium-enriched mixture (96.07%); the same being statistically significant ($p = 0.011$).

Conclusion: Within the limitations of our study, it can be concluded that newer biomimetic materials are superior to MTA for iatrogenic perforation repair in primary molars in terms of clinical success.

Clinical significance: This paper is a first-of-its-kind investigation comparing different materials used in the repair of perforations in primary molars. It can be a foundation for further research on the topic. In absence of any available guidelines, the above study can be applied in clinical situations with appropriate judgment and caution.

Keywords: Iatrogenic perforation repair, Mineral trioxide aggregate, Primary molars.

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Introduction

Pulp therapy in primary teeth is challenging on multiple fronts: behavioral and technical. The behavioral aspects are "forte" exclusively weaponized by a pediatric dentist. The endodontic technical challenges in primary teeth are often difficult to manage due to the small size of the oral cavity, constant movement of the tongue, painful conditions involving dentoalveolar structures. Perforation during the pulp treatment may be defined as "the mechanical or pathologic communication between root and periodontium."[1] The cause of perforation may be iatrogenic or non-iatrogenic. Non-iatrogenic perforation may occur as the result of internal/external resorption and/or large carious lesion extending into the floor of the pulp chamber.[2] The iatrogenic perforation could be the result of inadvertent and uncontrolled removal of dentin during access opening.[3]

The consequences of the root perforation, management strategy, and prognosis depend on root perforation size, location, duration of communication to the periodontium since exposure, and the level of resultant inflammation.[3]

Preservation of primary teeth until the normal eruption of permanent successor is very important for preserving arch integrity, mastication, esthetics, and speech function.[4] Preserving the primary teeth in the arch till their normal exfoliation time is the best space maintenance strategy.[5]

Perforations can be managed by two approaches, either surgical (by extraction) or by sealing the perforation site with a biocompatible material that can address the associated infection and inflammation.[6]

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Management of perforation in primary teeth differs from that in permanent teeth due to different trajectories of infection spread. The spread of lesion is in the periapical area in permanent teeth whereas, in primary teeth, it is more in the furcation area. Furcation in the primary molars is rich in accessory canals which further facilitates the rapid spread of the infection and therefore, it must have an adequate seal if perforated or otherwise.[7]

Various materials used to manage perforations in primary as well as permanent teeth have been reported in the literature to date, but none is affirmed as the ideal perforation repair material. Thus, treatments involving dental pulp in primary teeth pose a challenge not easily surmountable for any graduate or postgraduate practitioner. An ideal perforation repair material should have good sealing ability, biocompatibility, non-toxic or non-carcinogenic, bactericidal or bacteriostatic, induce osteogenesis, cementogenesis, should be dimensionally stable, insensitive to moisture or blood, easy to manipulate, and relatively inexpensive.[8]

The materials suggested for repairing perforations are amalgam, RMGIC, composite, Portland cement, mineral trioxide aggregate (MTA), etc.[9] Medicaments such as calcium hydroxide, calcium hydroxide with iodoform were used traditionally to disinfect the perforation site followed by sealing with amalgam or RMGIC. Recently, biomaterials such as MTA, calcium-enriched mixture (CEM), biodentin, etc., have combined disinfectant and anti-inflammatory properties along with good sealing ability.

Although there are studies that address the clinical outcomes of repaired iatrogenic perforations with different materials; in primary teeth, there is a lack of evidence or guidelines on the management of iatrogenic perforations that may arise during the pulp therapy of primary teeth.

Hence, this paper aims to systematically review the published literature on the repair of iatrogenic perforations in primary teeth and propose recommendations on the same. The following clinical questions were formulated according to the PICO:

"Which material has higher clinical success when used for iatrogenic perforation repair in primary molars?" "How do other materials compare with MTA for the management of iatrogenic perforation in primary molars?" wherein the Population: primary molars, Intervention: MTA, Comparison: other biomaterials (Premixed bioceramics, CEM, Atelocollagen), Outcome: clinical success.

Objectives of the Study

The main objective of the study was to compare the clinical success of MTA with other biomaterials used for iatrogenic perforation repair in primary molars.

Materials and Methods

The protocol of this paper was developed using the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-P 2015). The protocol was registered with PROSPERO (University of York) with protocol number: PROSPERO CRD 420212 52753.

Criteria for Considering Studies for the Review

Inclusion Criteria

The following were the inclusion criteria:

- Types of studies—Clinical trials, Case series, Case reports.
- Types of participants—Age: 3–10 years.
- Types of interventions—Iatrogenic perforation repair using different materials with clinical success for at least 1 year.

Exclusion Criteria

The exclusion criteria included the following:

- Follow-up period was <1 year.
- Studies having no human intervention (e.g., studies on cell cultures or animal study).
- Publications in the form of letters, commentaries, or narratives.
- No specified criteria for evaluating the outcomes of treatment, or healing.

Types of Outcome Measures

Primary Outcome

The treatment was considered clinically successful if the tooth remained functionally active and with no pathological symptoms and/or signs such as the presence of pain, gingival redness, abscess, fistula, and/or pathologic mobility.

Secondary Outcome

The secondary outcome was the radiographic success of the repair measured as no radiographic sign of root resorption, the spread of infection, or evident lesion progression or stagnation.

Search Methods for Identification of Studies

A comprehensive search strategy was carried independently by two reviewers (SM and LM) using the following three search engines: PubMed, Cochrane Database, and Google Scholar. All electronic searches were last updated in January 2021. The keywords used were: "Furcal perforation primary teeth," "Iatrogenic perforation primary teeth" and different combinations of it.

Data Collection and Analysis

After the assessment of titles and abstracts in the first screening full texts of the selected studies were obtained for second stage screening independently by two reviewers (SM, LM). Any disagreements between the two were resolved by consensus discussion with the third reviewer (AJ). Studies that were selected in the second stage screening were considered for data extraction, which was done using a data collection form specially designed to record important details of each study (see Table 1).

Data Extraction and Management

For each study, the following data were recorded:

Author(s), year of publication, number of events, methods: (study design), participants: (setting where participants were recruited), demographic characteristics (age, gender), intervention: (type of material used for repair), details of outcome assessment: (clinical success and failure rates) (Table 1).

Assessment of Risk of Bias in Included Studies

Two review authors (SM and LM) independently carried out the risk of bias assessment following the domain of MINORS[15] index for nonrandomized interventional studies. The evaluations were compared and inconsistencies were discussed and resolved by the third reviewer (AJ).

Measurements of Treatment Effect

For the main outcome variable, the treatment effect was estimated in terms of clinical and radiographic success as mentioned before in the inclusion criteria.

Table 1: Data extraction (all studies and reports)

S. no.	Author and year	Type of the study	Number of teeth (sample size) and age of participants	Material used	Control	Percentage success at 12 months follow-up	Other remarks
1	Abdelmotelb et al., 2021[10]	Mixed (*in vitro* + *in vivo*) study	76 teeth (4–7 years)	Premixed bioceramic	MTA	**Clinical:**	32 teeth successful
						MTA 86.8%	6 failed for MTA
						Premixed bioceramic 94.2%	36 teeth success
						Radiographic:	2 failed for bioceramic
						MTA 84.2%	
						Premixed bioceramic 92.1%	
2	Aldayari et al., 2019[4]	Clinical study	34 teeth (5–10 years)	MTA	–	MTA (overall)	26 teeth success
						79.3%	8 failed
							MTA
3	Masuda et al., 2011[11]	Clinical study	13 teeth (4–9 years)	Atelocollagen	–	Atelocollagen 100%	2 loss to follow-up
4	Hojjati et al., 2014[12]	Case series	3 teeth	CEM	–	–	–
			Case 1: 6 years				
			Case 2: 5 years				
			Case 3: 8 years				
5	Olieviera et al., 2008[13]	Case report	1 tooth	MTA	–	–	–
			Age: 6 years				
6	Marques et al., 2016[14]	Case report	2 teeth	MTA	–	–	–
			Case 1: 10 years				
			Case 2: 7 years				
7	Akhavan et al., 2014[2]	Case report	1 tooth	MTA	–	–	–
			Age: 9 years				

Assessment of Heterogeneity

Owing to methodological and clinical heterogeneity (due to different study designs and parameters of assessment), the effect estimate (summary statistics) estimation is required to be done with different statistical methods.

Results

Description of Studies

Table 1 presents the summary of all studies included in the review.

Results of Search

Identification of studies and selection of studies are depicted in the PRISMA flowchart of studies (Flowchart 1).

Selection of Trials

Twenty-seven articles were assessed for eligibility. Seventeen articles screened were removed because either the studies had been performed in vitro or in animals, or the follow-up period was <1 year. Seven studies were selected for the final review.

Included Studies/Articles

There were seven articles included in the final review. Out of which, three were clinical studies and four were case series and case reports. Three clinical trials which were included were conducted in Egypt (Abdelmotleb, 2020), Syria (Aldayari, 2019), and Japan (Masuda, 2011). The materials used for iatrogenic perforation repair in these studies included: MTA, pre-mixed bioceramics, CEM, Atellocollagen.

Designs and Methods

All the included clinical studies were conducted in the dental hospital set-ups.

Participants

The age of the participants ranged between 3 years and 10 years.

Interventions

Following the iatrogenic perforation, the repair was sealed with biocompatible materials (MTA, Pre-mixed bioceramics, CEM, Atellocollagen). The treated tooth was assessed clinically with a minimum of 12 months follow-up.

Outcome Measures

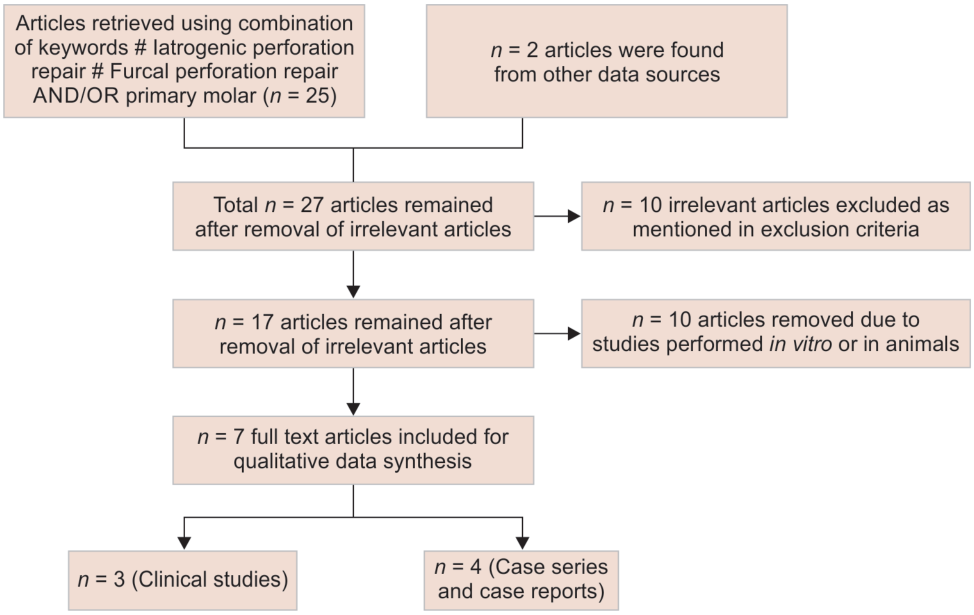
All the studies included assessed the clinical success if the tooth remained functionally active and with no pathological symptoms and/or signs such as the presence of pain, gingival redness, abscess, fistula, and/or pathologic mobility.

Risk of Bias in Included Studies [MINORS Index for Nonrandomized Clinical Trials]

MINORS is a valid instrument designed to assess the methodological quality of nonrandomized surgical studies, whether comparative or non-comparative.

The following domains were assessed: 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

Flowchart 1: Study flow diagram



the study, loss to follow-up <5%, prospective calculation of the study size.

Additional criteria for the comparative study: An adequate control group, contemporary groups, baseline equivalence of groups, adequate statistical analysis.

Each domain in the tool is scored as 0 (not reported); 1 (reported but inadequate); 2 (reported and adequate).

The global ideal score being 16 for non-comparative studies and 24 for comparative studies. The studies included in this review consisted of one study (Abdelmotleb et al., 2021) with a comparative group and two studies were interventional (Aldayari et al., 2019 and Masuda et al., 2011). The interpretation of the score was done as in Tables 2 and 3).

A study conducted by Abdlemotleb et al. (2020) had low risk, Aldayari et al. (2019) had moderate risk and Masuda et al. (2011) had a high risk of bias (Table 3).

Table 2: MINOR score interpretation

MINOR score	*Category*	*Risk of bias*
16 or 24	A	Low
>12–<16	B	Moderate
<12 or <20	C	High

Effects of Intervention

The percentage success and failure of each material (MTA vs other materials) from interventional studies were calculated and compared using Chi-square; the p-value < 0.05 was considered statistically significant.

Of the total number of teeth treated in the MTA group (72), 80.55% (58) were successful compared to 96.07% (49) teeth of the total number of teeth (51) treated with other materials. This was statistically significant $p = 0.011$ (Table 4).

The comparison made above was further extended to include case reports. Of the total number of teeth treated in the MTA group

Table 3: Overall risk of bias

S. no.	*Domain*	*Abdlemotleb et al. (2021)*	*Aldayari et al. (2019)*	*Masuda et al. (2011)*
1	A clearly stated aim	*2*	*2*	*0*
2	Inclusion of consecutive patients	2	2	0
3	Prospective collection of data	2	2	2
4	Endpoints appropriate to the aim of the study	2	2	0
5	Unbiased assessment of the study endpoint	0	0	0
6	Follow-up period appropriate to the aim of the study	2	2	2
7	Loss to follow-up <5%	2	2	2
8	Prospective calculation of the study size	2	2	0
Additional criteria for comparative study				
9	An adequate control group	2		
10	Contemporary groups	2		
11	Baseline equivalence of groups	2		
12	Adequate statistical analysis	2		
Total score		22/24	14/16	6/16

(76), 81.5% (62) were successful compared to 96.29% (51) teeth of the total number of teeth (54) treated with other materials. This was statistically significant $p = 0.012$ (Table 5).

Mineral trioxide aggregate had a higher risk of failure compared to other materials (RR = 4.958, CI = 1.117–20.876) (Table 6).

In the Numbers-Needed-to-Treat/Harm comparison with other materials, for 6.44 the cases treated with MTA had provided one failure (NNH 6.44, CI = 26.51–3.66, ARR = 0.155). This was statistically significant (Table 6).

Meta-analysis with a forest plot using a fixed-effects model based on risk ratios and CI was attempted; however, the RR (CI) could not be estimated for two studies (Aldayari et al., 2019 and Masuda et al., 2011). The summary statistics based on only one study (Abdelmotleb et al., 2021) revealed RR 0.89 in favor of other materials compared to MTA with the CI (0.76–1.04); the same being statistically insignificant (Fig. 1).

Discussion

Endodontic mishaps such as iatrogenic perforation, file separation, ingestion of dental instruments are unexpected complications that can occur while performing pulpal therapy in primary teeth; however, their prevalence is not known.[16] The iatrogenic perforations occur due to lack of experience, inadequate knowledge about the anatomy and morphology. These unexpected mishaps hinder the clinical success of the tooth invariably leading to failures.

Previously, the management of furcal perforations were extractions, but now there has been a paradigm shift from extraction-oriented practice to sealing the perforation to preserve the strategically important primary teeth.[10] These strategically important primary teeth (primary canines and primary second molars) help stabilize the occlusion, guide the growth and development of jaws and permanent teeth. Therefore, it is important to attempt to preserve the primary teeth with questionable prognosis until a certain age or for a certain period.[17]

Repair of iatrogenic perforation of primary molars is one of the critical situations during pulp therapy.[10] To repair the perforation site, several materials such as amalgam, tricalcium phosphate (TCP), hydroxyapatite, gutta-percha, calcium hydroxide, zinc oxide-eugenol-based cement (IRM and Super-EBA), glass ionomer cement, composite resins, resin-glass ionomer hybrids, demineralized freeze-dried bone, and MTA have been used over the years.[9]

The main question addressed in this review was how successful would MTA be to other materials for an iatrogenic perforation repair in primary molars.

In absence of well-randomized and controlled trials, we decided to make a sense of currently available evidence, both qualitatively and quantitatively.

As per the Cochrane Handbook of Systematic Reviews [2019], for studies with heterogeneity, different analyzes could be carried out. In the present study, we, therefore, performed: a direct comparison

Table 4: Comparison of MTA vs other materials (only studies)

Groups	*Success*	*Failure*	*Total nos of teeth treated (N)*	*% of success*	*Chi-square*	*p-value*
MTA	58	14	72	80.55	6.36	0.011*
Other materials	49	2	51	96.07		

***Significant**

Table 5: Comparison of MTA vs other materials (inclusive case reports)

Groups	*Success*	*Failure*	*Total nos of teeth treated (N)*	*% of success*	*Chi-square*	*p-value*
MTA	62	14	76	81.5	6.36	0.012*
Other materials	52	2	54	96.29		

***Significant**

Table 6: Comparison of MTA vs other materials in terms of NNH/ARR

Groups	*Risk ratio*	*CI*	*NNT*	*CI*	*ARR*	*p-value*
MTA	4.958	1.177–20.876	6.44	26.513–3.66	0.155	0.0290
Other materials						

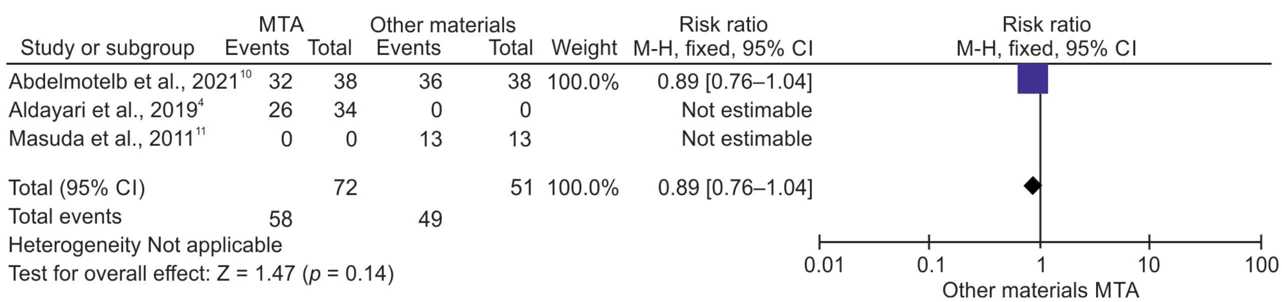


Fig. 1: Forest plot 1: Fixed-effect model

using the Chi-square test; relative risk [CI], NNT [CI], and summary statistic estimation using the forest plot.

The overall success for MTA (80.55%) was inferior to other materials (96.05%). Although MTA may be considered a gold standard material used for repair of furcal perforation, several regenerative materials have recently evolved to seal such perforations with higher claims of success.[10–12,18]

Mineral trioxide aggregate was introduced by Macwan C et al.[19] When we pooled our results, it amplified the use of recently emerged newer materials. Mineral trioxide aggregate has a wide array of applications in endodontic therapy, due to its excellent biocompatible properties on periodontal as well as pulpal tissue.[20,21] Mineral trioxide aggregate promotes periradicular tissue regeneration, and it differs from other materials in its ability to promote cementum regeneration, thus facilitating the regeneration of the periodontal apparatus.[22]

Premixed bioceramics are recently developed materials that have been preferred to MTA in terms of their usability, handling properties, regenerative properties, inductive properties, and tissue compatibility.[23]

Atellocollagen, which is extracted from collagen molecules after being treated with pepsin, is considered to be a proper biomaterial since the main antigenic telopeptide regions are excluded. Atelocollagen has been used as a biocompatible material for skin reconstruction and has also been applied to oral membranes. In addition, atelocollagen sponges have been used in extraction sockets as hemostasis.[24]

Calcium-enriched mixture cement, due to its alkaline pH, has a better antibacterial effect compared to MTA.[11,25] Calcium-enriched mixture cement releases calcium and phosphate ions[26] and then forms hydroxyapatite not only in simulated body tissue fluid but also in normal saline solution; the latter is unlikely with MTA.[27]

The new regenerative materials further help overcome the limitations of MTA such as poor handling properties due to a grainy mix; a long time to set and its cost in-effectiveness.[10,19]

The recent biomimetic materials can be used for an iatrogenic perforation repair in primary teeth due to their superior properties of inducing, proliferation, and differentiation of stem cells thus enhancing healing and repair.[5,10,18,28,29] Our study tends to support the claims.

Limitations

We found inconsistency in reporting such mishaps, follow-up duration, and postoperative assessment of success. Perforations, being mishaps, could not possibly be studied using the "randomized controlled trials" study design. Thus, the available literature was in the form of nonrandomized comparisons, case series, and case reports. The inclusion of different study designs in a meta-analysis is unwarranted; however, to make the best sense of information, we accessed all relevant literature. We also used different methods of inferential statistical comparisons. In the published literature, there is a tendency to under-report failures of the management mishaps such as iatrogenic perforation repair; therefore, the percentage success could be higher than in the real-life.

The cost implications with respect to materials used may also affect the choices for treatment; however, we could not study that aspect owing to lack of information.

Conclusion

All the materials used to repair an iatrogenic perforation repair showed clinical success, with the newer biomimetic materials (Premixed bioceramics, Atellocollagen, CEM) appearing to be superior to MTA; the quality of evidence being low.

Recommendations

Based on the results of our study, we recommend preferential use of newer biomimetic materials and MTA as appropriate in the iatrogenic perforation repair in primary molars. More primary research is needed to substantiate our claim.

Clinical Significance

This paper is a first-of-its-kind investigation comparing different materials used in the repair of perforations in primary molars. It can be a foundation for further research on the topic. In absence of any available guideline, the above inference can be applied in clinical situations with appropriate judgment and caution.

Abbreviations

LM, Laresh Mistry; AJ, Ashwin Jawdekar; SM, Sahili Mungekar Markandey; MTA, mineral trioxide aggregate; CEM, calcium-enriched mixture; RMGIC, resin modified glass ionomer cement; PICO, population intervention comparison outcome; PRISMA, preferred reporting items for systematic reviews and meta-analyses; CI, confidence interval; NNT, number needed to treat; NNH, number needed to harm.

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