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Systematic review and meta analysis of first and second generation bioceramic materials in primary dentition pulpotomies

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Calcium silicate-based materials are considered the gold standard in vital pulp therapy due to their ability to induce favorable repair responses. Mineral trioxide aggregate (MTA), a first-generation bioceramic cement, has demonstrated high clinical and radiographic success rates but is associated with disadvantages such as coronal discoloration, difficult handling, and long setting time. To address these issues, second-generation bioceramic cements were developed with improved chemical composition, radiopacifiers, and handling properties. This systematic review followed the PRISMA guidelines and included a comprehensive search of PubMed, MEDLINE, CENTRAL, Web of Science, SciELO, LILACS, and TRIP databases from 2011 up to August 2023. Two independent reviewers conducted study selection, data extraction, and risk of bias assessment using the Cochrane RoB 2 tool. Meta-analysis was performed using a random-effects model to compare the clinical and radiographic success rates of first- and second-generation bioceramics in pulpotomies of primary teeth, with heterogeneity assessed using the I^2 statistic. A total of 14 studies were included, involving 1128 primary molars from 637 children. The meta-analysis revealed no statistically significant differences in clinical or radiographic success rates between first- and second-generation bioceramics across follow-up periods of up to 24 months. Both first- and second-generation bioceramics demonstrate comparable clinical and radiographic success in pulpotomies of primary teeth. The choice of material should be guided by clinical considerations and practitioner preference, as no significant differences in outcomes were observed.

Keywords Bioceramics, Deciduous teeth, Mineral trioxide aggregate, Pulpotomy

Dental pulp is responsible for the tooth vitality and can be affected by a sort of oral conditions, such as dental caries or traumatic injuries. When this tissue is affected by such condition, pulp therapy procedures aim to halter the affection of the pulp, thus maintaining the integrity and health of teeth and its surrounding supporting tissues[1,2].

Among this group of pulp treatments, pulpotomy consists of removing the coronal pulp following an extensive carious lesion[3,4] and then with the application of a capping material that often causes a non-predictable healing pulp response[3–6]. Pulpotomy is often applied in deciduous teeth and the ultimate goal is to preserve the radicular pulp intact and vital. The success of a pulpotomy relies upon multiple factors: bleeding control, complete amputation of inflamed coronal pulp, appropriate capping material, effective coronal sealing during and after treatment, and proper diagnosis of the pulpal status are critical for a successful pulpotomy in primary teeth[2,7].

One particularly important feature of pulpotomy is the pulp capping material. There has been a plethora of materials used, such as, formocresol, glutaraldehyde, ferric sulfate, zinc oxide, eugenol, and calcium hydroxide, which have been used over the years[8]. Formocresol was the most popular drug for primary teeth, yet it was

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reported to have toxic and mutagenic effects[8,9]. Ferric sulfate become then a popular alternative to formocresol and calcium hydroxide in pulpotomies, with clinical, radiological, and histological similarities to formocresol[10].

Nevertheless, to find a more biologically compatible and effective alternative to formocresol and ferric sulfate, several agents and techniques have been investigated. To overcome the side effects, new biocompatible capping agents have been developed[8–11]. The first-generation biocompatible materials, such as mineral trioxide aggregate (MTA), were made from simple mixtures of Portland cement and bismuth oxide. While they demonstrated high biocompatibility and clinical success, they presented significant drawbacks, including color instability due to bismuth oxide, difficult handling, and long setting times, which complicated their clinical application. To address these shortcomings, second-generation materials were developed using pure tricalcium silicate cement and alternative radiopacifiers to prevent discoloration (p.e. Biodentine)[12]. Additionally, these newer materials incorporated additives to improve handling properties and reduce setting times, making them more user-friendly while maintaining their biological effectiveness[11,13]. Although numerous studies have evaluated the performance of first- and second-generation bioceramics in pulpotomies, the evidence is scattered, and individual studies often have small sample sizes, varying methodologies, and inconsistent follow-up periods. A systematic review is necessary to synthesize the available evidence, provide a comprehensive comparison of the clinical and radiographic success rates of these materials, and identify potential gaps in the literature. By pooling data from multiple studies, this review aims to offer robust conclusions that can guide clinical decision-making and inform future research.

Materials and methods

Protocol and registration

The protocol for this systematic review was defined by all authors and registered at the National Institute for Health Research PROSPERO, International Prospective Register of Systematic Review (http://www.crd.york.ac.uk/PROSPERO, ID Number: CRD42024601460). We based our review design following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline[14] (Supplementary File 1).

Focused question and eligibility criteria

We aimed to answer the following PICOT question: "In primary teeth of children, how does pulpotomy with second-generation bioceramics compare to pulpotomy with MTA in terms of clinical success (sensitivity, percussion, and palpation tests) and radiographic outcomes over a follow-up period of up to 24 months?" This question is designed to explore the potential differences in effectiveness between the two materials used in pulpotomy procedures. The research question is structured according to the PICO format. The population (P) includes primary teeth in children, focusing on a pediatric dental context. The intervention (I) involves the use of second-generation bioceramics for pulpotomy, a newer material that has been developed to improve clinical outcomes. The comparison (C) is with MTA, a first-generation bioceramic material that has been widely used and studied in similar procedures. The outcomes (O) being evaluated include clinical success, assessed through sensitivity, percussion, and palpation tests, as well as the absence of radiographic signs of failure. Finally, the time frame (T) for follow-up is up to 24 months, allowing for a comprehensive evaluation of both short- and long-term results.

The following inclusion criteria were defined: (1) published between 2011 and 2023, because second-generation materials were firstly introduced in 2011; (2) human randomized and non-randomized studies of intervention; (3) studies that include full pulpotomy as an intervention; (4) with a minimum follow-up period of three months, as defined by the American Academy of Pediatric Dentistry (AAPD)[2]; (5) reporting data on clinical success and/or radiographic success.

As exclusion criteria we defined: (1) in vitro studies on human and animals; (2) systematic reviews, case series, case studies; (3) non-intervention studies, i.e., only one material used for treatment is evaluated, (4) articles involving other types of pulp treatment, (5) studies conducted in permanent teeth.

Search strategy and study selection

The search and inclusion of studies was conducted by two independent reviewers (MA, JN) in electronic five platforms PubMed via MEDLINE, The Cochrane Library, Lilacs, ScienceDirect, and BMC Public Health databases up to June 2023 was undertaken. An additional search for unconventional literature was considered using the OpenGrey (http://www.opengrey.eu/) and Mednar (http://www.mednar.com/) databases so that additional articles that may be relevant can be included in this synthesis. To identify relevant studies, we used the following key words and MeSH terms "((dentistry, pediatric) [MeSH terms]) OR (children, dentistry for [MeSH terms]) OR (Pulpotomies [MeSH terms]) OR (Primary teeth [MeSH terms]) OR (pulp, dental [MeSH terms]) (caries, dental [MeSH terms]) OR (pediatrics) OR (primary tooth) OR (pulpotomy))AND((agent, pulp capping [MeSH terms]) OR (cement, dental [MeSH terms]) OR (bioceramic OR Mineral Trioxide Aggregate OR biodentine))"; no language restrictions were imposed.

Two reviewers (MA, JN) independently reviewed all titles and abstracts sought and assessed the retrieved full texts of possibly eligible studies. If the same results on the same subjects were reported in more than one article, the study with the most subjects was included. Regarding measurement reproducibility purposes, inter-examiner reliability following full-text assessment was calculated via kappa statistics. Any disagreements were resolved by discussion with a third author (LBL).

Data extraction process and data items

Data extraction was performed by two reviewers independently and in duplicate (MA, JN). Any paper classified as potentially eligible by either examiner was independently screened by the reviewers. All disagreements were resolved through discussion with a third reviewer (LBL). The following information was gathered in general

description, research characteristics, methodology, and outcome measurements. The following standard information was extracted from each eligible study: Year of publication, authors, study design, population description, interventions, comparison groups, follow-up period, findings, funding, and risk of bias.

Risk of bias (RoB) assessment

Version 2 of the Cochrane Collaboration's tool for assessing the risk of bias in randomized clinical trials (RoB 2)[15] was implemented to systematically evaluate potential sources of bias in five different areas: bias arising from the randomization process, bias due to deviations from the intended interventions, bias due to missing outcome data, bias in the measurement of the outcome, and bias in the selection of the reported outcome. Each domain was assessed using signaling questions provided by the tool, which guided the judgment of risk as "low", "some concerns", or "high". Two independent reviewers conducted the assessment to ensure accuracy and minimize subjectivity, with disagreements resolved through discussion or consultation with a third reviewer. The results of the risk of bias assessment were summarized and used to inform the interpretation of the study findings[15].

Summary measures and synthesis of results

Predefined tables were created for the collection of continuous data, means and standard deviations (SD). The random effects model meta-analysis and forest plots (Supplementary File 3) were calculated in R version 3.4.1 (R Studio Team 2018) using the 'meta' package10 using the DerSimonian-Laird random effects meta-analysis. A meta-analysis of binary outcome data compares the clinical and radiographic results of bioceramics in pulpotomies of primary teeth. Heterogeneity was calculated using the I^2 test statistic ($p < 0.1$), with substantial heterogeneity considered when the I^2 statistic exceeded 50%. Estimates were reported with a 95% confidence interval (95%CI).

Subgroup analysis

To further explore potential differences in clinical and radiographic success rates, subgroup analyses were planned based on the following variables: follow-up period (3, 6, 9, 12, 18, and 24 months), type of bioceramic material (first-generation vs. second-generation), and study characteristics (e.g., geographic location, sample size, and risk of bias). These subgroup analyses aimed to identify any trends or variations in outcomes that may not be apparent in the overall meta-analysis.

For each subgroup, clinical and radiographic success rates were compared using a random-effects model to account for heterogeneity across studies. Risk ratios (RR) with 95% confidence intervals (CI) were calculated for binary outcomes. Heterogeneity was assessed using the I^2 statistic, with values greater than 50% indicating substantial heterogeneity. Subgroup analyses were conducted only when sufficient data were available to ensure meaningful comparisons.

Additionally, we planned to evaluate the influence of patient-specific factors, such as age, tooth type (primary first molars vs. second molars), and dental arch position (maxillary vs. mandibular), on the success rates. However, due to the lack of consistent reporting of these variables across studies, these analyses were not performed.

Results

Study selection

The online search yielded 997 potentially relevant publications. After removing duplicates, 981 articles were assessed against the eligibility criteria and 958 were excluded after title and/or abstract review. Of the 23 articles assessed for eligibility for full paper review, 9 articles were excluded (Supplementary File 2), with the reasons for exclusion detailed in Supplementary S1. As a result, a final number of 14 observational studies were included in the qualitative synthesis (Fig. 1). The inter-observer reliability of the full-text screening was was very high (kappa score = 0.914, 95% CI 0.894–0.925).

Studies characteristics

The characteristics of the included studies are presented in Table 1. Five studies were conducted in Turkey[13,16–19], two in Spain[20,21] and two in India[22,23] among the 14 in vivo randomized controlled clinical trials selected according to the inclusion and exclusion criteria. The remaining studies were conducted in Saudi Arabia[24], Brazil[25], South Korea[26], Iran[27], and Belgium[28].

In all 14 studies, 1128 primary molar teeth from a total of 637 children[13,16–28] were analysed, of which 289 were female and 271 were male, with the remaining children in three studies[22–24] not identified as to sex. Of the analysed teeth, at least 259 were primary 1st molars and 291 were primary 2nd molars; however, half of the studies[17,18,21–23,26,27] did not specify which teeth were analysed. As for the dental arch, 161 are maxillary molars and 433 are mandibular molars, and half of the studies did not mention the position of the analysed tee th[16,18,21,22,25–27].

Two types of first-generation bioceramic sealers, namely ProRoot MTA and MTA Angelus were used in the included articles. Six types of second-generation bioceramic sealers, namely NeoMTA Plus, Biodentine, Ortho MTA, Bio-C Pulp, Calcium enriched mixture cement and Biofactor MTA were used in the included articles[13,16–28].

Methodological quality of the included studies

A critical appraisal and risk of bias of the included studies were independently assessed by two authors (J.N. and L.B.L.). According to the Cochrane Handbook for Systematic Reviews of Interventions, the revised tool for assessing the risk of bias in randomized trials is the Risk of Bias (RoB 2)[15] (Fig. 2). This tool provides a proposal for judging the risk of bias arising from each domain, generated by an algorithm based on the answers

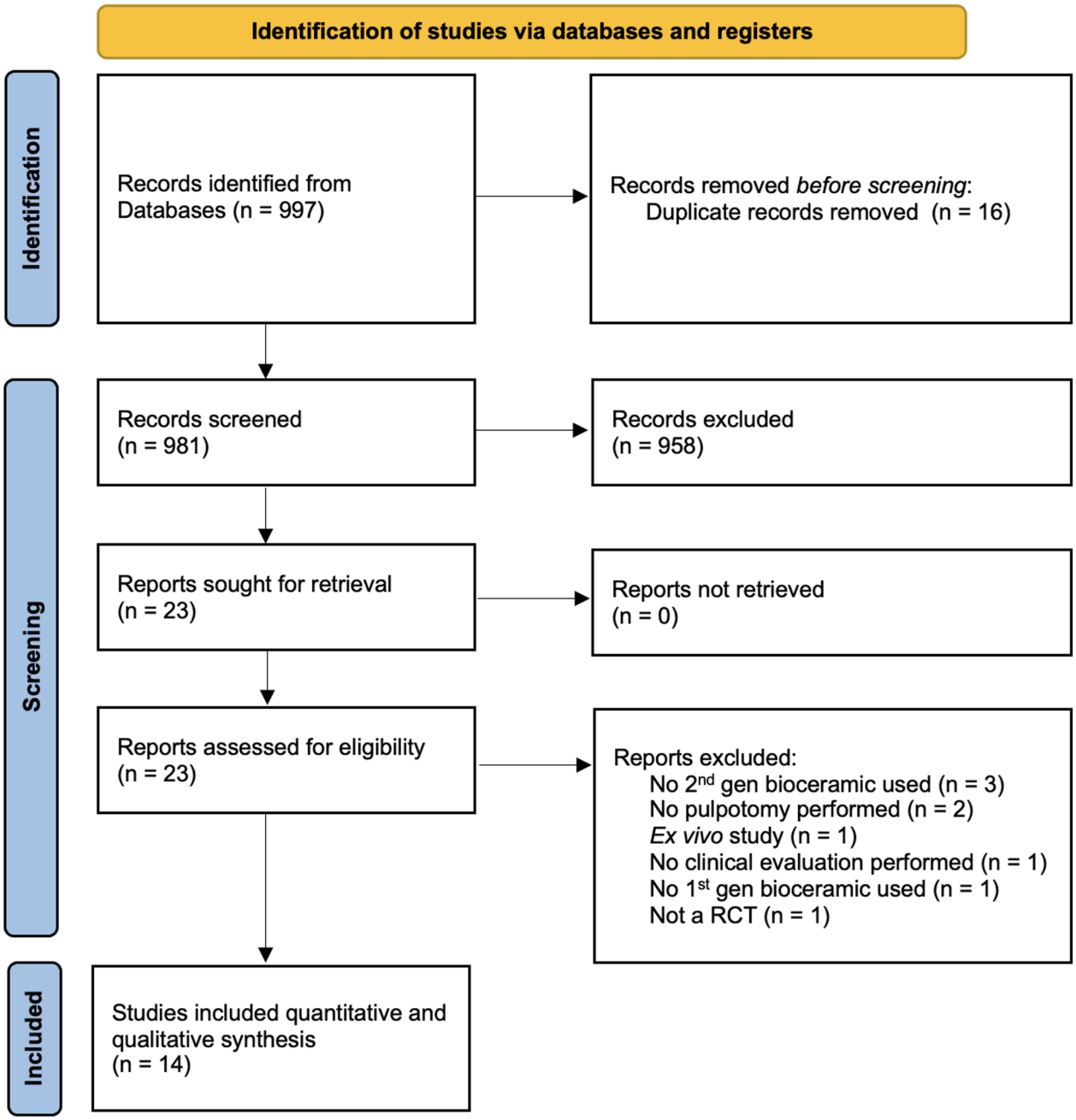

Fig. 1. PRISMA flowchart depicting the workflow of the studies selection process based.

to the signaling questions. The criteria chosen were randomized, including concealment of attribution, blinding of participants, assessment of the examiner and the result, attrition bias and reporting bias. In addition, comparability and homogeneity of the groups were the additional criteria specified for the assessment of bias:

- Low risk of bias: all criteria were met, and no more than 1 criterion was judged to be uncertain.
- Moderate risk of bias: if 2 or more criteria were judged to be uncertain and other criteria were met.
- High risk of bias was considered when 1 or more criteria were not met.

As can be seen in Fig. 2, of the included studies, the risk of bias is estimated to be low in 5 of the articles[18,21,22,24,27]. The risk of bias is moderate in 5 of the articles[16,19,20,23,28]. The remaining 4 studies have a high risk of bias[13,17,25,26]. Domains D1 and D3 (randomization process and missing outcome data, respectively) are of greater concern than domains D2 and D4 (deviations from the intended interventions and measurement of the outcome, respectively). No concerns were found for domain D5 (selection of the reported result) (Fig. 3).

These findings highlight that while a significant proportion of the included studies demonstrated a low or moderate risk of bias, concerns remain regarding the randomization process (D1) and missing outcome

Author (Year) (Country)	Study design	Population description	Interventions	Control Group	Comparison groups	Follow-up period	Outcomes	Findings	Funding details	Risk of Bias
Alsanouni et al. [24] (2019) (Saudi Arabia)	RCT	4 to 8 years old 80 teeth 15 1st maxillary molars; 25 1st mandibulary molars; 17 2nd maxillary molars; 23 2nd mandibulary molars	Pulpotomies in primary molars deep caries approximating or reaching the pulp. Hemostasis with sterile cotton pellets. Final coronal restoration with s stainless steel crown using glass-ionomer luting cement	ProRoot MTA	NeoMTA Plus	3, 6 and 12 month	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	NeoMTA Plus showed a high percent success similar to MTA at 12 months; NeoMTA Plus is a potential pulpotomy medicament for primary teeth	Research Grant Provided by the College of Dentistry, King Saud University, Riyadh, Saudi Arabia; there was no funding for the materials ProRoot MTA and NeoMTA Plus	Not determined / not used
Bani et al. [13] (2017) (Turkey)	RCT	4 to 9 years old 64 teeth 34 1st mandibulary molars; 30 2nd mandibulary molars 15 males, 17 females	Pulpotomies in primary molars deep proximal carious lesions on symmetric mandibular teeth requiring pulp treatment Hemostasis achieved with light pressure from a moistened sterile cotton pellet Final coronal restoration with s stainless steel crown using glass-ionomer luting cement	MTA	Biodentine	6, 12, 18 and 24 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	Biodentine and MTA did not differ significantly in their clinical and radiographic success after 24 months. The clinical success rates at 24 months were identical for Biodentine and MTA (96.8%). The radiographic success rates at 24 months were 93.6% for Biodentin and 87.1% for MTA	Not Reported	Not determined / not used
Carti et al. [16] (2017) (Turkey)	RCT	5 to 9 years old 50 teeth 27 1st molars, 23 2nd molars 13 males, 12 females	Pulpotomies in primary molars deep caries approximating or reaching the pulp. Hemostasis achieved with light pressure from a moistened sterile cotton pellet. Final coronal restoration with s stainless steel crown using glass-ionomer luting cement	MTA	Biodentine	1, 3, 6 and 12 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	There was no statistically significant difference between clinical success rates. According to the results of this study, both MTA and Biodentine can be used as pulpotomy agents, but more long-term studies with larger samples size are required	Research Grant Supported by CUBAP	Not determined / not used
Çelik et al. [17] (2018) (Turkey)	RCT	5 to 9 years old 50 mandibular molars 24 males, 20 females	Pulpotomies in primary molars deep caries approximating or reaching the pulp Hemostasis achieved with light pressure from a moistened sterile cotton pellet Final coronal restoration with s stainless steel crown	MTA	Biodentine	3, 6, 12, 18 and 24 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	Biodentine and MTA had similar success rates at the end of the 24-month follow-up period. Based on this finding, the shorter setting time and easier handling of Biodentine may make it a preferred alternative to MTA. However, clinical trials with longer follow-up periods are required before any conclusive recommendations can be made	Not Reported	Not determined / not used

Continued

Author (Year) (Country)	Study design	Population description	Interventions	Control Group	Comparison groups	Follow-up period	Outcomes	Findings	Funding details	Risk of Bias
Cuadros-Fernández et al. [20] (2015) (Spain)	RCT	4 to 9 years old 90 teeth 24 1st maxillary molars; 24 1st mandibulary molars; 18 2nd maxillary molars; 24 2nd mandibulary molars 35 males, 33 females	Pulpotomies in symptomatic-free primary molars deep caries approximating or reaching the pulp. Hemostasis achieved with light pressure from a moistened sterile cotton pellet Final coronal restoration with s stainless steel crown using glass-ionomer luting cement	MTA	Biodentine	6 and 12 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	Clinical success rate in the MTA Group after 12 months was 92%, whereas the clinical success rate in the Biodentine Group after 12 months was 97%. MTA yielded a radiographic success of 97% (38/39) and Biodentine yielded a radiographic success of 95%	Not Reported	Not determined / not used
Guven et al. [18] (2017) (Turkey)	RCT	5 to 7 years old 116 molars 19 males, 10 females	Pulpotomies in at least four primary molars deep proximal carious lesions mandibular teeth requiring pulp treatment Hemostasis achieved with light pressure from a moistened sterile cotton pellet. Final coronal restoration with amalgam restoration	ProRoot MTA	MTA-Plus Biodentine	6, 12 and 24 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	This study found no statistically significant differences among pulpotomy techniques	The authors have no financial conflicts of interest in any way with the products, materials, or suppliers used in this article	Not determined / not used
Kang et al. [26] (2015) (South Korea)	RCT	3 to 10 years old 151 molars 60 males, 42 females	Pulpotomies in primary molars deep caries approximating or reaching the pulp. Hemostasis achieved with light pressure from a moistened sterile cotton pellet Final coronal restoration with s stainless steel crown	ProRoot MTA	RetroMTA	3, 6 and 12 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	Similarly high success rates, with no significant differences between the clinical and radiographic outcomes of pulpotomy in primary molars treated with MTA or RetroMTA. The clinical success rates of MTA and RetroMTA were 100% at the 12-month follow-up. There were more radiographic failures in the RetroMTA group than in the MTA group	Supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI12C1061). All authors have no financial and personal relation ships that could influence their work	This study was subject to several limitations that should be addressed. First, the participants were followed up by investigators who were part of the clinical staff. Even though the treated teeth were evaluated fairly according to the set study criteria, clinician bias cannot be completely excluded. In addition, as several clinicians performed the pulpotomies, there was a high risk of bias when making different clinical decisions
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Author (Year) (Country)	Study design	Population description	Interventions	Control Group	Comparison groups	Follow-up period	Outcomes	Findings	Funding details	Risk of Bias
Kusum et al. [2] (2015) (India)	RCT	3 to 10 years old 90 molars	Pulpotomies in symptomatic-free primary molars deep caries approximating or reaching the pulp Hemostasis achieved with light pressure from a moistened sterile cotton pellet Final coronal restoration with glass-ionomer cement	MTA	Biodentine	3, 6 and 9 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	Clinical outcome of Biodentine is comparable to that of MTA at both 6 and 9 months follow up period. Furthermore, the radiographic outcome of Biodentine was statistically not different, compared to MTA. These findings suggest the potential of Biodentine for being used as a pulpotomy medicament in primary teeth	Not Reported	Were recognize some factors as minor limitations which might be curtailed in future studies. One of them is the consideration of changes in the regenerative ability of dental pulp that varies with age. This variable can be controlled by narrowing the age range of the subjects. However, this might result in practical difficulty of getting an adequate sample size
Lima et al. [25] (2020) (Brazil)	RCT	3 to 10 years old 70 molars 18 males, 15 females	Pulpotomies in primary molars deep caries approximating or reaching the pulp. Hemostasis achieved with light pressure from a moistened sterile cotton pellet Final coronal restoration with composite resin	MTA Angelus	Bio-C Pulpo	1, 3, 6 and 12 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	Both MTA and Bio-C Pulpo pulpotomy medicaments are appropriate options for pulpotomies in primary teeth, with high clinical and radiographic success rates. However, more long-term studies are required to test the new Bio-C Pulpo medicament	Not Reported	Not determined / not used
Malekafzali et al. [27] (2011) (Iran)	RCT	4 to 8 years old 80 molars 23 males, 17 females	Pulpotomies in primary molars deep caries approximating or reaching the pulp. Hemostasis achieved with light pressure from a moistened sterile cotton pellet Final coronal restoration with s stainless steel crown or amalgam, depending on the cavity size	MTA	CEM cement	6, 12 and 24 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	The results revealed 100% clinical success rates for both biomaterials during the trial. 91% and 97% radiographic success rates were achieved for MTA and CEM at one-year, respectively; this was not statistically significant	Research Grant This trial was supported by Iran National Science Foundation and Iranian Center for Endodontic Research, Shahid Beheshti Medical University, Tehran, Iran	As the type of the two biomaterials was water-based, the clinician was unaware of the pulp capping agent used, therefore eliminating researcher's cognitive bias in this trial
Oznurhan et al. [19] (2020) (Turkey)	RCT	6 to 9 years old 24 2nd mandibular molar 5 males, 7 females	Pulpotomies in second primary molars deep caries approximating or reaching the pulp Hemostasis achieved with light pressure from a moistened sterile cotton pellet Final coronal restoration with s stainless steel crown using glass-ionomer luting cement	ProRoot MTA	BIOfactor MTA	1, 3, 6 and 12 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	No statistically significant differences between MTA and BIOfactor MTA in first 6 months. However, in 12 months follow-up, MTA had statistically significant higher clinical	Research Grant Supported by the Scientific Research Project Fund Cumhuriyet University	Not determined / not used

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Author (Year) (Country)	Study design	Population description	Interventions	Control Group	Comparison groups	Follow-up period	Outcomes	Findings	Funding details	Risk of Bias
Rajasekharan et al. [28] (2016) (Belgium)	RCT	3 to 8 years old 80 teeth 9 1st maxillary molars, 21 2nd maxillary molars, 19 1st mandibulary molars, 31 2nd mandibulary molars 22 males, 59 females	Pulpotomies in primary molars under general anesthesia deep caries approximating or reaching the pulp. Hemostasis achieved with light pressure with cotton pellet. Final coronal restoration with s stainless steel crown using glass-ionomer luting cement	ProRoot MTA	Biodentine	1, 6, 12 and 18 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	No significant difference between the materials use and the clinical or radiographic success after 6, 12 or 18 months. Biodentine appears to be an effective pulpotomy agent for the treatment of carious deciduous molars	The authors of the present study do not have any financial interest in the commercial products used	Not determined / not used
Togaru et al. [23] (2016) (India)	RCT	4 to 9 years old 90 teeth	Decayed primary molars indicated for pulpotomy Hemostasis achieved with light pressure from a moistened sterile cotton pellet Final coronal restoration with s stainless steel crown	MTA	Biodentine	3, 6, 9 and 12 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	Pulpotomy with MTA and Biodentine is a reliable biological method for pulp treatment of primary teeth. Mineral trioxide aggregate and Biodentine have been considered as most favorable materials of choice for pulpotomy in primary teeth as they have shown a high success rate of 95.5%, for the period of observation	Not Reported	Not determined / not used
VilellaPastor et al. [21] (2021) (Spain)	RCT	4 to 9 years old 90 teeth 35 males, 33 females	Primary molars with pulpal caries and/or dental trauma leading to pulp exposure without clinical evidence of pulp degeneration (irreversible pulpitis or pulp necrosis) Hemostasis achieved with light pressure from a moistened sterile cotton pellet Final coronal restoration with s stainless steel crown	MTA	Biodentine	6, 12, 18 and 24 months	Clinically successful in the absence of spontaneous pain, tenderness to percussion or palpation; soft tissue swelling; sinus tract or fistula; or pathologic tooth mobility. Radiographically successful in the absence of widening of the periodontal ligament space; furcal or periapical radiolucency; or pathological external or internal root resorption	Biodentine and MTA demonstrated similar long-term results in primary molar pulp capping procedures at 24 months follow-up. These two materials had high clinical and radiographic success rates, showing no statistically significant differences between them	Not Reported	Not determined / not used

Table 1. Characteristics of the included studies.

data (D3), which could potentially impact the reliability of the results. The absence of concerns in domain D5 (selection of the reported result) suggests that reporting bias is unlikely to have influenced the findings. Overall, the variability in the risk of bias across studies underscores the need for cautious interpretation of the results, particularly for studies with moderate to high risk of bias.

Outcome measures

A meta-analysis of binary outcome data compared clinical and radiographic results at different follow-up months. Tables 2 and 3 show the clinical success of second-generation bioceramics based on MTA and Biodentine, respectively, compared with the MTA group in pulpotomies of primary teeth. Forest plots can be accessed in the Supplementary File 3.

1st generation bioceramics (MTA) versus 2nd generation bioceramics (MTA-based)

The studies comparing the clinical and radiographic success of MTA and MTA-based bioceramics were divided into subgroups according to the months of follow-up (3, 6, 12, and 24 months). Success rates were presented according to risk ratio (RR), confidence interval, *p*-value, and heterogeneity between studies (Table 2).

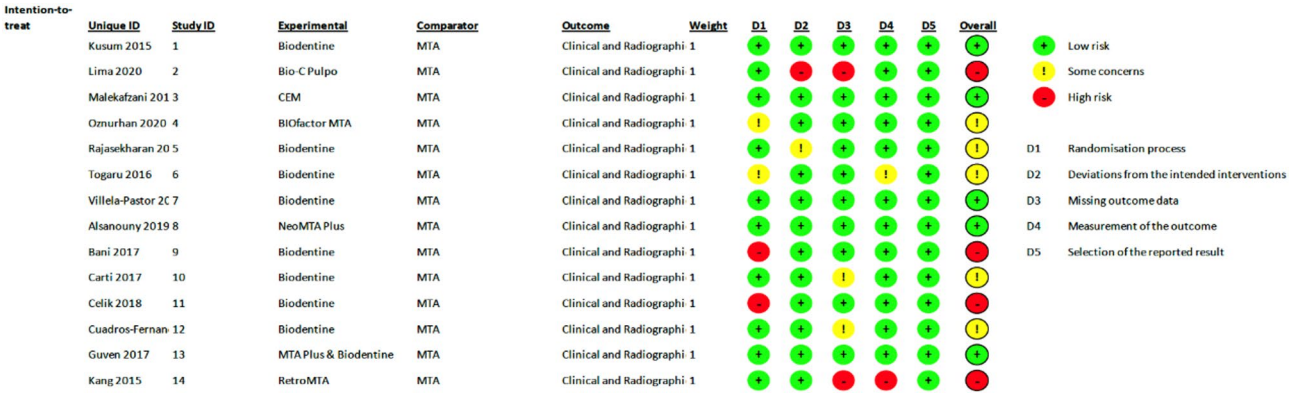

Fig. 2. Risk of bias assessment of included studies.

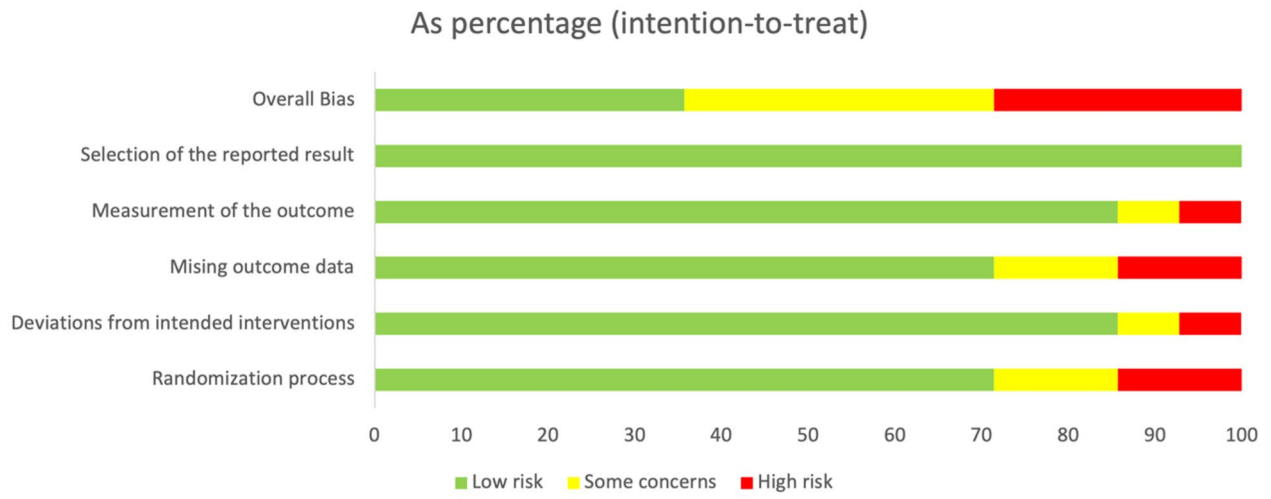

Fig. 3. General risk of bias.

Months	*n*	RR	95% CI	T	T^2	I^2	z	*p*-value
Clinical								
3	4	1.00	0.97–1.03	0.00	0.00	0.0	− 0.17	0.8656
6	6	1.00	0.97–1.02	0.00	0.00	0.0	− 0.14	0.8918
12	6	1.01	0.98–1.04	0.00	0.00	26.6	0.49	0.6276
24	2	0.99	0.83–1.17	0.00	0.00	58.3	− 0.13	0.8986
Radiographic								
3	4	1.00	0.97–1.03	0.00	0.00	0.0	− 0.17	0.8656
6	6	1.00	0.97–1.02	0.00	0.00	0.0	− 0.14	0.8918
12	6	1.01	0.98–1.04	0.00	0.00	26.6	0.49	0.6276
24	2	0.99	0.83–1.17	0.00	0.00	58.3	− 0.13	0.8986

Table 2. Clinical and radiographic evaluation of 1st generation bioceramics (MTA) vs. 2nd generation bioceramics (MTA-based). n - number of studies; RR - risk ratio; T - tau; z - z value.

The studies comparing the clinical and radiographic success of MTA and MTA-based bioceramics were divided into subgroups according to follow-up periods (3, 6, 12, and 24 months). The results are summarized in Table 2.

Clinical Success:

Months	*n*	RR	95% CI	T	T^2	I^2	z	*p*-value
Clinical								
3	4	1.00	0.97–1.03	0.00	0.00	0.0	0.00	1.0000
6	9	1.00	0.98–1.02	0.00	0.00	0.0	0.02	0.9879
9	2	0.98	0.95–1.02	0.00	0.00	0.0	– 0.87	0.3832
12	8	1.01	0.99–1.03	0.00	0.00	0.0	0.80	0.4220
18	4	0.99	0.95–1.02	0.00	0.00	0.0	– 0.76	0.4494
24	4	0.99	0.95–1.03	0.00	0.00	0.0	– 0.68	0.4961
Radiographic								
3	4	1.00	0.96–1.03	0.00	0.00	0.0	– 0.18	0.8544
6	9	1.00	0.98–1.02	0.00	0.00	0.0	– 0.34	0.7318
9	2	1.00	0.95–1.05	0.00	0.00	0.0	0.00	1.0000
12	8	1.00	0.97–1.03	0.00	0.00	0.0	– 0.16	0.8707
18	4	1.01	0.94–1.09	0.04	0.00	20.4	0.24	0.8096
24	4	0.96	0.90–1.03	0.00	0.00	7.5	– 1.11	0.2678

Table 3. Clinical and radiographic evaluation of 1st generation bioceramics (MTA) vs. 2nd generation bioceramics (Biodentine). n - number of studies; RR - risk ratio; T - tau; z - z value.

At 3 months: RR = 1.00 (95% CI: 0.97–1.03), I^2= 0%, p = 0.8656.
At 6 months: RR = 1.00 (95% CI: 0.97–1.02), I^2= 0%, p = 0.8918.
At 12 months: RR = 1.01 (95% CI: 0.98–1.04), I^2 = 26.6%, p = 0.6276.
At 24 months: RR = 0.99 (95% CI: 0.83–1.17), I^2= 58.3%, p = 0.8986.

Radiographic Success:

At 3 months: RR = 1.00 (95% CI: 0.97–1.03), I^2 = 0%, p = 0.8656.
At 6 months: RR = 1.00 (95% CI: 0.97–1.02), I^2 = 0%, p = 0.8918.
At 12 months: RR = 1.01 (95% CI: 0.98–1.04), I^2 = 26.6%, p = 0.6276.
At 24 months: RR = 0.99 (95% CI: 0.83–1.17), I^2 = 58.3%, p = 0.8986.

There were no statistically significant differences in the studies comparing MTA with MTA-based bioceramics at the significance levels ($p < 0.05$) over the months of follow-up, both clinically and radiographically. The heterogeneity (I^2 was less than 50%, except for the 24-month clinical control, where the heterogeneity value was 58%.

1st generation bioceramics (MTA) versus 2nd generation bioceramics (Biodentine)
The studies comparing the clinical and radiographic success of MTA and Biodentine were divided into subgroups according to the months of follow-up (3, 6, 9, 12, 18, and 24 months). Success rates were presented according to RR, confidence interval, p-value, and heterogeneity between studies (Table 3).

The studies comparing the clinical and radiographic success of MTA and Biodentine were divided into subgroups according to follow-up periods (3, 6, 9, 12, 18, and 24 months). The results are summarized in Table 3.

Clinical Success:

At 3 months: RR = 1.00 (95% CI: 0.97–1.03), I^2 = 0%, p = 1.0000.
At 6 months: RR = 1.00 (95% CI: 0.98–1.02), I^2 = 0%, p = 0.9879.
At 9 months: RR = 0.98 (95% CI: 0.95–1.02), I^2 = 0%, p = 0.3832.
At 12 months: RR = 1.01 (95% CI: 0.99–1.03), I^2 = 0%, p = 0.4220.
At 18 months: RR = 0.99 (95% CI: 0.95–1.02), I^2 = 0%, p = 0.4494.
At 24 months: RR = 0.99 (95% CI: 0.95–1.03), I^2 = 0%, p = 0.4961.

Radiographic Success:

At 3 months: RR = 1.00 (95% CI: 0.96–1.03), I^2 = 0%, p = 0.8544.
At 6 months: RR = 1.00 (95% CI: 0.98–1.02), I^2 = 0%, p = 0.7318.
At 9 months: RR = 1.00 (95% CI: 0.95–1.05), I^2 = 0%, p = 1.0000.
At 12 months: RR = 1.00 (95% CI: 0.97–1.03), I^2 = 0%, p = 0.8707.
At 18 months: RR = 1.01 (95% CI: 0.94–1.09), I^2 = 20.4%, p = 0.8096.
At 24 months: RR = 0.96 (95% CI: 0.90–1.03), I^2 = 7.5%, p = 0.2678.

According to the significance values ($p < 0.05$), there were no statistically significant differences over the months of follow-up, both clinically and radiographically, in the studies comparing MTA with Biodentine. The heterogeneity (I^2 was less than 50% over the months.

Additional analysis

No further analysis was performed due to heterogeneity between studies. Also, because there were no statistically significant differences in all groups ($p < 0.05$), the analysis of sex, tooth type, or arch position was not performed.

Discussion

This systematic review and meta-analysis aimed to compare the clinical and radiographic success rates of first- and second-generation bioceramic materials in pulpotomies of primary teeth. The results demonstrated no statistically significant differences between the two generations of materials across all follow-up periods, both clinically and radiographically. These findings suggest that both first- and second-generation bioceramics are effective options for pulpotomy procedures in primary teeth. However, the implications of these results warrant further discussion, particularly in the context of the materials' properties, study methodologies, and clinical applications.

The comparable success rates observed between first- and second-generation bioceramics may be attributed to their shared fundamental properties. Both materials are calcium silicate-based, which promotes biocompatibility, induces mineralization, and supports the formation of a dentin bridge. Mineral trioxide aggregate (MTA), the prototypical first-generation bioceramic, has been extensively studied and is considered a gold standard in vital pulp therapy. However, its limitations, such as discoloration, difficult handling, and long setting time, have driven the development of second-generation bioceramics like Biodentine and NeoMTA Plus. These newer materials incorporate modifications, such as alternative radiopacifiers and improved handling properties, which address some of MTA's shortcomings. Despite these advancements, the lack of significant differences in clinical and radiographic outcomes suggests that these improvements may not necessarily translate into superior biological performance in pulpotomies of primary teeth.

The absence of significant differences could also be influenced by the relatively short follow-up periods in some studies. While the regenerative capacity of the pulp in primary teeth is well-documented, longer follow-up periods are necessary to assess the durability of the materials' effects, particularly as primary teeth approach exfoliation. Additionally, the heterogeneity in study designs, sample sizes, and operator experience may have contributed to the observed results. For instance, the 24-month follow-up for MTA versus MTA-based bioceramics showed moderate heterogeneity ($I^2 = 58\%$), which could reflect variations in clinical protocols or patient populations.

The findings of this review align with previous systematic reviews that have reported high success rates for both MTA and Biodentine in pulpotomies of primary teeth. For example, a Cochrane review by Smaïl-Faugeron et al. (2014) highlighted the effectiveness of MTA compared to other materials, while more recent studies have emphasized the comparable performance of Biodentine. However, this review provides a more focused comparison between first- and second-generation bioceramics, offering a nuanced understanding of their relative performance. Unlike earlier reviews, this study also incorporates a detailed risk of bias assessment and evaluates the methodological quality of included studies, which strengthens the reliability of the findings.

The risk of bias assessment revealed that only five studies had a low risk of bias, while the remaining studies exhibited moderate to high risks. Methodological issues, such as inadequate randomization, lack of blinding, and variability in outcome reporting, were common. These biases have clinical relevance, as they may influence the reported success rates and limit the generalizability of the findings. For instance, the lack of blinding in some studies could introduce observer bias, particularly in the assessment of clinical outcomes like pain or swelling. Additionally, the use of different operators in some trials may have introduced variability in technique, further complicating the interpretation of results. Future studies should prioritize rigorous methodological designs, including standardized protocols and blinding, to minimize bias and enhance the validity of their findings.

Strengths and limitations

This review has several strengths. It adhered to the PRISMA guidelines, included a comprehensive search strategy across multiple databases, and employed a robust meta-analytic approach to synthesize data. The inclusion of both randomized and non-randomized studies allowed for a broader evaluation of the available evidence. Furthermore, the detailed risk of bias assessment provides valuable insights into the quality of the included studies.

However, there are limitations that should be acknowledged. First, the relatively small number of included studies and their methodological heterogeneity may limit the generalizability of the findings. Second, the follow-up periods in some studies were insufficient to assess long-term outcomes, particularly as primary teeth approach exfoliation. Third, the variability in operator experience and clinical protocols across studies may have influenced the results. Finally, the lack of data on certain variables, such as patient age, tooth type, and arch position, precluded subgroup analyses that could have provided additional insights.

Clinical implications and future directions

The findings of this review suggest that both first- and second-generation bioceramics are viable options for pulpotomy in primary teeth, with no significant differences in clinical or radiographic success rates. Clinicians should consider factors such as handling properties, setting time, and cost when selecting a material, as these practical considerations may influence the ease and efficiency of the procedure.

Future research should focus on addressing the limitations identified in this review. Long-term, multicenter randomized controlled trials with standardized protocols are needed to provide more definitive evidence. Additionally, studies should explore the impact of patient-specific factors, such as age and pulp status, on the performance of bioceramic materials. Finally, the development of new materials should prioritize not only improved handling and physical properties but also enhanced biological performance.

Conclusion

First- and second-generation bioceramics have comparable clinical and radiographic success rates in pulpotomies of primary teeth. The level of evidence is still far from ideal and future studies should address the methodological limitations identified in this review.

in the clinical and radiographic success rates of in pulpotomies of primary teeth. Both materials demonstrated high success rates, supporting their use as effective options for vital pulp therapy. The choice between first- and second-generation bioceramics should be guided by clinical considerations and practitioner preference. Future studies should aim to address the methodological limitations identified in this review and provide more robust evidence to inform clinical decision-making.

Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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Author contributions

Conceptualization, J.A.N.; methodology, J.A.N. and M.A.D.; validation, L.B.L.; formal analysis, J.A.N. and L.B.L.; investigation, J.A.N. and L.B.L.; resources, J.J.M.; writing—original draft preparation, J.A.N. and M.A.D.; writing—review and editing, J.J.M. and T.P.; supervision, J.J.M. and T.P.; project administration, J.J.M. All authors have read and agreed to the published version of the manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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