

The use of bioactive cements in the endodontic treatment of the deciduous and permanent dentition: a systematic review

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Abstract

Abstract: Bioactive cements are indicated in many treatments of pediatric dentistry. The present study aims to analyze the efficacy of bioactive cements, in endo-pedodontics, both in deciduous dentition (vital teeth) and in permanent dentition (vital and necrotic teeth with immature apex), comparing them with other endodontic materials on the market. (2) Materials and methods: The study was prepared according to PRISMA guidelines using databases such as: Medline, Pubmed, Cochrane. In vivo studies performed within the last ten years were included. (3) Results: The research initially collected 762 scientific articles of which 28 were excluded as duplicates and 701 following analysis of abstracts and titles, according to the exclusion criteria of the present study. 33 full-text papers were examined, 25 of which were excluded according to the eligibility criteria. Therefore, only 8 studies were included for qualitative analysis and data mining. (4) Conclusion: Bioactive cements can be considered first choice materials in endopedodontics due to their chemical-biological characteristics and long-term prognosis. However, in the treatment of the necrotic permanent tooth with an immature apex, pulp regeneration procedures show significantly superior results compared to apexification techniques, especially in terms of root length and thickness.

Keywords: Bioceramic sealers, MTA, Biodentine, Pulpotomy, deciduous dentition, permanent dentition, Apexogenesis, Apexification, pulp Revascularization.

Introduction

Permanent and deciduous dentitions are often subject to carious lesions or traumas of different degrees that in some cases require endodontic therapy (1,2). Research has produced increasingly biocompatible endodontic materials such as bioactive endodontic cements (3). In fact, biocompatibility and bioactivity are fundamental characteristics for the treatment of vital tooth (4) as they provide support for proper cellular activity by optimising tissue regeneration without any harmful side effects, either local or systemic (5,6). These materials are bioinert, have antibacterial properties and release calcium ions over time, promoting the formation of the dentine bridge and the osteogenic differentiation of mesenchymal stem cells (7,8). In vitro studies have shown that tricalcium silicates (MTA, Biodentine) generate an apatite layer by promoting the adhesion of new odontoblasts (9,10,11). Scientific evidence shows that these materials, in addition to being well tolerated by periapical tissues, they have an effective root canal seal as they are characterized by a basic pH (12,5). However, they show some disadvantages such

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as low compressive strength (12), the longer reaction time (more than 3 h) and the possible discoloration of dental hard tissues (13). The new bioactive cements have better mechanical properties, due to their alumina-rich composition, zirconia, calcium silicate, bioglass and glass-ceramic(14). The aim of the present study is to analyse, through a systematic review of the literature, the efficacy of bioactive cements in endo-paediatric dentistry, comparing them with other endodontic materials on the market.

Materials and methods

The systematic review was performed following the PRISMA guidelines. Studies were selected based on the following eligibility criteria:

Inclusion Criteria:

Studies carried out in the last 10 years

In vivo studies

Randomized clinical trials concerning the comparison between bioactive and traditional cements

Studies including analysis of vital deciduous teeth

Studies that include permanent vital teeth (with immature apex)

Studies that include permanent necrotic teeth (with immature apex)

Exclusion Criteria:

- Studies carried out for more than 10 years
- Animal studies
- Editorial opinions
- Case reports
- In vitro studies
- Studies on the systemic effects of bioactive cements
- Studies with a surgical therapeutic approach

- Genetics studies
- Studies that include necrotic deciduous teeth
- Studies that include permanent teeth with mature apex

The identification of the studies was carried out from February to April 2023 using the main search engines such as Pubmed, Medline and Cochrane. The following filters were used: randomized clinical trials (RCTs), studies performed in the last ten years, studies in English or Italian. Keywords such as: Bioceramic sealers, MTA, Biodentine, Pulpotomy, deciduous dentition, permanent dentition, Apexogenesis, Apexification, pulp Revascularization. The study process was divided into two phases: an initial analysis of the abstracts that could potentially meet the inclusion requirements, and then a qualitative analysis of the papers that met the eligibility criteria of the present research. The parameters collected from each study were: the treated teeth, the materials used, the follow-up, the type of treatment, the pre-treatment and post-treatment conditions

Results

The research initially collected 762 scientific papers, of which 28 were excluded as duplicates. A total of 734 studies were considered, of which 701 were excluded, following the analysis of abstracts and titles according to the exclusion criteria of the present study. A total of 33 full-text papers were examined, 25 of which were excluded according to the eligibility criteria. Therefore, only 8 studies were included for qualitative analysis and data extraction (Fig.1). For the qualitative comparative analysis, the following were taken into account:

- Vital deciduous teeth
- Vital permanent teeth with immature apex

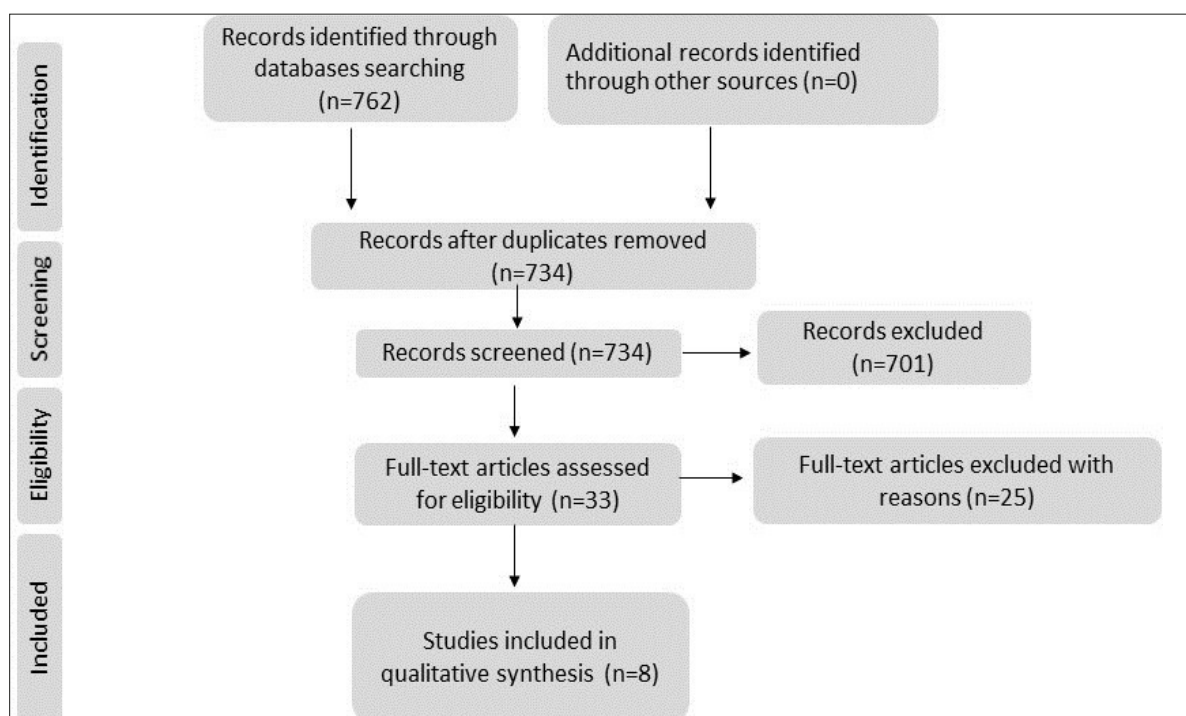


Figure 1. Flow Chart Prisma

• Necrotic permanent teeth with immature apex
 Studies that appeared to be relevant to the question of the present study but would have deviated from the goal of the research were excluded, such as articles that included the comparison of teeth with mature and immature apex or that did not guarantee the use of the rubber dam during clinical procedures as they compared the success rate with or without the use of the dam. In addition, all articles that used materials or methods that were difficult to reproduce and standardize were excluded (Table 1). The collected data were entered schematically according to a clinical order: deciduous vital dentition, permanent vital dentition with immature apex and finally permanent necrotic dentition with

immature apex.

The materials mentioned in this systematic review are bioactive cements including: calcium hydroxide (CH) belonging to the category of cements from traditional regeneration (analyzing two different viscosities), Biodentine (BD), Theracal, Mineral Trioxide Aggregate (MTA) and traditional mummifying agents such as Formocresol (FC) and Pulpotec, no longer used in Italy. The study includes an endo-periodontal regeneration material such as Emdogain, composed of enamel protein matrix mainly formed by amelogenins, secreted by the Hertwig sheath during root development in order to induce cement formation and stimulate the proliferation of periodontal ligament cells (Table 2). Biological materials can be traced back

Table 1. Excluded studies

Author, Year	Reason for exclusion
Aminabadi et al [2016]	Sample limited to necrotic deciduous teeth
Tirone et al et al [2018]	Study limited to the surgical therapeutic approach only
Hashem et al [2015]	Sample limited to permanent teeth with mature apex
Lima et al [2020]	Sample limited to observation of aesthetics prognosis
kusum et al [2015]	Not scientifically relevant materials
Hilton et al [2013]	Procedure not applied uniformly
Asawaworarit et al [2016]	In vitro studies
Arikan et al [2016]	Sample limited to necrotic deciduous teeth
Dimitraki et al [2019]	Methods that are difficult to reproduce and standardize
Wassel et al [2022]	Method that is not very reproducible and standardizable
Alnassar et al [2022]	Sample limited to necrotic deciduous teeth Sample limited to necrotic deciduous teeth
Bjorndal et al [2019]	Sample limited to permanent teeth with mature apex
Sharaan et al [2022]	Sample limited to permanent teeth with mature apex
Asgary et al [2021]	Sample limited to permanent teeth with mature apex
Ferreira et al [2020]	Sample limited to permanent teeth with mature apex
Ravi Kalgan et al [2019]	Animal Studies
Zahra Jamali et al [2018]	Methods that are difficult to reproduce and standardize
Reem Siraj Alsulaimeni et al [2016]	Sample limited to permanent teeth with mature apex
Brinda Godhi et al [2016]	In vitro studies
Yeliz Guven et al [2017]	Poor chamber cleansing during the clinical procedure
Abuelniel et al [2021]	Not relevant results
Burak et al [2021]	Methods that are difficult to reproduce and standardize
Ragab et al [2019]	Methods that are difficult to reproduce and standardize
Celik et al [2016]	Methods that are difficult to reproduce and standardize
Hassanpour et al [2022]	Not relevant results

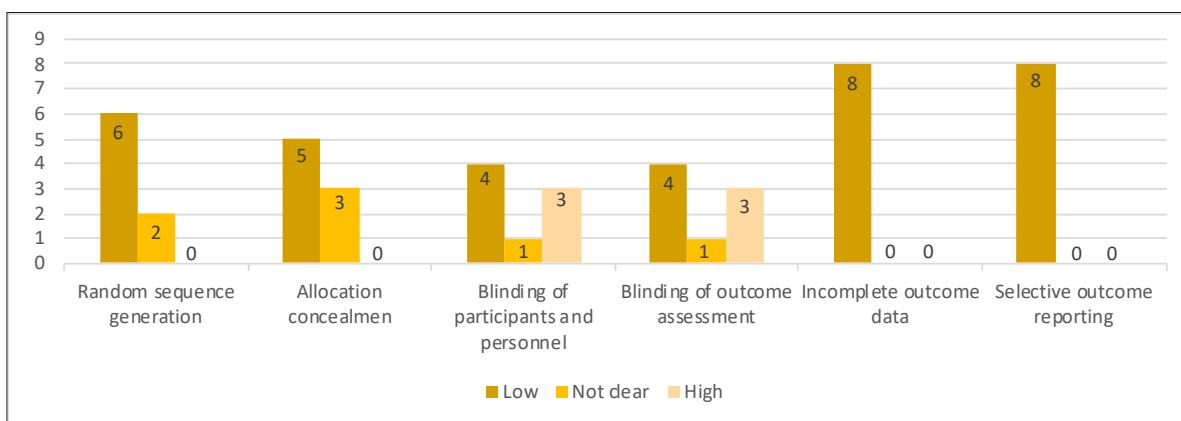
Table 2 Treated materials

Material	Composition	Category
Biodentine	Tricalcium silicate, zirconium oxide, calcium oxide, calcium carbonate. (powder+liquid)	Bioactive regeneration material
MTA	Tricalcium silicate, aluminate tricalcium, bismuth oxide and calcium sulphate. (powder+liquid)	Bioactive regeneration material
Theracal	Calcium silicate modified with Light-curing resin. (putty)	Bioactive regeneration material

To be continued

continued

Emdogain	Enamel Matrix Derivative (amelogenins) (putty)	Endo/periodontal regeneration
Formocresolo	Formaldehyde and Creosote.	Traditional Mummifying
Pulpotec	Iodoform, formaldehyde, dexamethasone.	Traditional Mummifying
Dycal CH ()	Calcium hydroxide: -Pasta+pasta (Dycal)-Powder + saline vs powder + glycerol.	Traditional regeneration
Biological	-Apical cells of the vital pulp - Stem cells -Growth factors	Endodontic regeneration (Revascularization)



Graph 1 Risk of bias

to the presence of viable pulp apical cells, stem cells and growth factors (platelets, tissue, vascular). Graph 1 shows a partial or total lack of triple or double-blind in some studies, which may change the conclusive

results. An assessment of the risk of bias was also carried out using the ROBIS method, resulting in a “low” degree (Table 3). However, the percentage of error may depend on the complex procedure performed in all clinical

Table 3: Risk of Bias

Authors/year	Random sequence generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Outcome Reporting
Ahuja et al. 2020	Low	Unclear	High	Alto	Low	Low
Sunitha et al. 2017	Unclear	Low	High	Incerto	Low	Low
Meligy et al. 2019	Low	Low	Low	Low	Low	Low
Silva et al. 2018	Low	Low	Low	Low	Low	Low
Rahman et al. 2021	Low	Low	Low	Low	Low	Low
Uyar et al. 2021	Low	Low	Low	Low	Low	Low
Bonte et al. 2015	Low	Low	Unclear	High	Low	Low
Caleza- Jimenez et al. 2022	Low	Unclear	High	High	Low	Low

trials and the different operators whose level of clinical experience with each materials used is not known.

Ahuja et al. have shown that in pulpotomy treatments, in deciduous dentition, it is possible to highlight a high success of Biodentine (100% clinical, 95% radiographic at 9 months) compared to MTA (95% clinical, 60% radiographic at 9 months) and Formocresol (70% clinical, 25% radiographic at 9 months) (15). The Trioxide Mineral Aggregate has achieved high results in deciduous dentition, with pulpotomy treatments, when compared with materials such as Formocresol, Pulpotec and Emdogain. Sunitha et al. state that Emdogain as an endoperiodontal regeneration material, compared to traditional pulp mummifying materials (Formocresol and Pulpotec) and bioactive materials such as MTA, obtains inferior clinical and radiographic results (83.3% and 72% respectively) as can be observed in the summary table (Table 4) (15,16).

Meligy et al. confirm the clinical success of Biodentine at 12 months (100%) compared to Formocresol (98.1% at 12 months) (17). Silva et al., however, compare MTA to calcium hydroxide with different viscosities (diluted with physiological solution or with glycerol), in cases of pulpotomy, finding greater stability and a success of 73% at 12 months for the higher viscosity calcium hydroxide. The physiological solution, decreases this percentage, reaching 33% at 12 months, with a higher percentage of internal reabsorptions. The addition of glycerol, however, leads to a limited failure of 18% at 12 months. Finally, MTA achieves 100% success at follow up (18). Rahman et al. analyzed the use of Biodentine, Theracal and calcium hydroxide on vital permanent teeth, finding a success of 94.44% for Biodentine, 100% for Theracal and 77.77% for calcium hydroxide (in paste-paste formulation) (19).

Uyar et al. analyzed the apicogenesis process, demonstrating a success rate of 72.2% after 12 months following treatment with calcium hydroxide compared to 94.4% for MTA and Biodentine. However, the Authors underline the importance of the apical blood supply as a fundamental variable for a correct apical closure (20). Bonte et al. found better results for MTA in case of apexification, following six and twelve month follow up, with a success of 64.7% and 82.4% respectively, with a statistically significant difference compared to the success rates obtained with calcium hydroxide (21). However, comparing apexification performed with MTA with pulp regeneration using apical stem cells, it is possible to observe better results in root development (12.76% at 6 months) in the second case (22) (Table 4).

Discussion

This systematic review of the literature has allowed us to analyze very current issues in clinical practice and above all at the center of the debate in the endodontic field. In deciduous dentition, bioactive cements such as Mineral Trioxide Aggregate (MTA) and Biodentine are considered first choice materials in case of Pulpotomy (15). Emdogain, known as an endo-periodontal regeneration material, achieves lower success rates when compared with bioactive materials or with materials no longer used today (in Italy) such as Pulpotec and Formocresol (16). The use of calcium hydroxide with increased viscosity (with the addition of glycerol) showed greater clinical and radiographic

success at 12 months compared to that with lower viscosity. The results obtained are however inferior to the use of MTA (18). In permanent dentition, bioceramic cements such as Biodentine are considered first choice materials in indirect pulp treatment by promoting the secretion of growth factors deriving from pulp cells, increasing the stimulation of odontoblasts and faster cell differentiation which generates the formation of reaction dentin (tertiary dentin). The study by Uyar et al. analyzes the apicogenesis process and demonstrates how at the follow-up after 12 months there is an 87% success and a 13% failure. In particular, calcium hydroxide has a success of 72.2% and a failure of 27.8%, while MTA and Biodentine have a success of 94.4% and a failure of 5.6%. The Authors underline that the failures occurred in teeth in which the apical seal is almost complete, demonstrating that the apical blood supply for pulp regeneration is the fundamental variable that determines the correct apical closure (20). Furthermore, it has been demonstrated that in case of apexification the use of bioactive materials decreases the risk of root fractures (21). However, comparing the clinical result of apexification with MTA with that of pulp regeneration we observe different results in the anatomical development of the forming apex. In fact, MTA can certainly guarantee a high level of root growth but requires longer time and root development reaches smaller thicknesses with consequent fragility. On the contrary, pulp regeneration promotes physiological root growth with better results in terms of root length and thickness, thanks to four possible biological processes. The first derives from the presence in the apical region of vital cells of the pulp which can proliferate and differentiate into odontoblasts, the second relating to the presence of stem cells in the periodontal ligament which stimulate the growth of the root apex, the third considers the presence of stem cells apical level which seems to have the ability to survive infectious phenomena by preserving the proliferative and differentiation capacity of new dentin tissue, while the fourth process is attributable to the formation of a blood clot which contains platelet, tissue and vascular growth factors capable of stimulating the proliferation and differentiation of odontoblasts (22).

Conclusion

Bioactive cements can be useful in cases of root canal perforation or in the presence of vital deciduous teeth with traumatic, iatrogenic or carious pulp exposure. In fact, in the deciduous tooth, bioactive materials show a greater success rate than calcium hydroxide. However, the use of tricalcium cements remains limited mainly for economic reasons, which do not allow their frequent use in both public and private contexts. Furthermore, bioactive cements are indicated in the treatment of vital or necrotic permanent teeth with immature apices, in case of internal and external resorptions and for retrograde endodontic surgery. However, in the treatment of the necrotic permanent tooth with immature apex, pulp regeneration protocols obtain better results than apexification procedures in terms of root length and thickness. In conclusion, bioactive cements can be considered first choice materials in endodontics due to their chemical-biological characteristics, especially for the long-term prognosis.

Table 4. Systematic review data collection

Author	Materials compared	Dentition	Follow-up	Type of treatment	Pre-operative status	Post-operative status	Conclusion
Ahuja et al [2020]	Biodentine vs MTA vs Formocresol	Deciduous	3-6-9 months	Pulpotomy	Absence of painful symptoms, Absence of abscess lesions	At 9 months BD: 100% success clinical, 95% radiographic MTA: 95% success clinical, 60% radiographic. FC: 70% success clinical, 25% radiographic	Biodentine and MTA have been more successful than Formocresol
Sunitha et al [2017]	Formocresol, Pulpotec vs MTA, Emdogain	Deciduous	6-12-18-24 months	Pulpotomy	Presence of a carious lesion with the presence of large pulp exposure during the elimination of the carious tissue. Absence of symptoms and detectable abscess lesions	At 24 months FC and Pulpotec: Clinical success at 94.4%, radiographic: 88.8% and 83.3% respectively EMD: 83.3% success. and radiographic 72%. MTA: 100% clinical success and radiographic 94.4%	MTA demonstrated a higher success rate (94.4%) followed by Pulpotec (83.3%) and EMD (72%).
Meligy et al [2019]	Biodentine vs Formocresol	Deciduous	3-6-12 months	Pulpotomy	Absence of pain, mobility and abscess lesions.	At 12 months: Biodentine: 100% success Formocresol: 98.1% success	Biodentine and Formocresol can have similar results.
Silva et al [2018]	CH glycerol (PEG) >viscose Physiological CH (saline) <viscose vs MTA	Deciduous	3-6-12 months	Pulpotomy	Absence of signs of pulp degeneration, internal root resorption, periapical lesions and no more than a third of physiological root resorption.	At 12 months: CH+PEG: Failure in 18% due to internal resorption. Success in 73% CH+saline: failure in 67% due to internal resorption, success in 33% MTA: 100% success	CH+PEG (glycerol) achieves high clinical success. It generates fewer failures due to reabsorption than CH+saline. CH+saline (physiological) causes numerous failures due to internal reabsorption and low clinical success rate.

To be continued

Rahman et al [2021]	Biodentine vs Theracal vs Dycal	Permanent	3-6-12-18-24 months	Indirect pulp treatment	Carious lesion extended to dentin, teeth with immature apices, sensitivity to thermal stimulus	At 24 months: Biodentine: 94.44% success rate Theracal: 100% success Dycal (pasta + pasta): 77.77% success rate	Calcium hydroxide has a low success rate. Bioactive materials are considered first choice for indirect pulp treatment
Uyar et al [2021]	CH vs MTA, Biodentine	Permanent	1-3-6-12 months	Parcial pulpotomy	Vital teeth with immature apex, absence of symptoms, pulp exposure < 2mm that occurs during the removal of the carious lesion	At 12 months Specifically: CH: success 72.2%, failure 27.8%. MTA: success 94.4%, failure 5.6%. Biodentine: success 94.4%, failure 5.6%.	The failures all occurred in teeth that were at the ninth stage of Nolla (when they started treatment), a phase in which the apical seal is almost at the end. This emphasizes that the apical blood supply for pulp healing is the variable that basically determines the correct apical closure
Bonte et al [2015]	MTA vs CH	Permanent	6-12 months	Apexification	Necrotic teeth, periapical lesion present, immature apex	12 months: CH: 50% MTA: 82.4%	Apexification with MTA is more successful than calcium hydroxide to limit the risk of root fracture
Caleza-Jimenez et al [2022]	MTA vs Patient's Intrinsic Biological Material	Permanent	3-6-12-24 months	Apexification/ Revascularization	Necrotic teeth with radiographic examination showing immature apex with apical lesion	Root size increase at 6 months: Revascularization: 12.76% MTA apexification: 0.29%	Root size increase at 6 months: Revascularization: 12.76% MTA apexification: 0.29%

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