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Biodentine or Mineral Trioxide Aggregate as Direct Pulp Capping Material in Mature Permanent Teeth with Carious Exposure? A Systematic Review and Meta-analysis

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Clinical Relevance

Mineral trioxide aggregate (MTA) and Biodentine demonstrated high success rates when used as direct pulp capping (DPC) agents in mature permanent teeth with carious exposure. This meta-analysis conducted from clinical studies reveals that both the materials have comparable clinical outcomes.

SUMMARY

Objective: To evaluate the success rate of direct pulp capping (DPC) with Biodentine in mature permanent teeth with carious vital pulp exposure compared to that of DPC with mineral trioxide aggregate (MTA) by means of a systematic review and meta-analysis.

Data Sources: The two authors searched independently the literature published through July 31, 2020, in five electronic databases (PubMed, the Cochrane Central Register of Controlled Trials, Web of Science Core Collection, the Wiley Online Library, and the SCOPUS database).

Study Selection: The research protocol was previously registered in the PROSPERO database (CRD42020192511). Clinical studies that met the inclusion criteria were chosen and independently screened by the authors.

Data Extraction: A custom-designed spreadsheet was used to extract the data. The quality of each study was evaluated by means of the revised Cochrane risk of bias (ROB) tool or the ROB of nonrandomized studies of interventions tool.

Data Synthesis: Three randomized controlled trials and one retrospective study met the inclusion criteria. Only one study had a high risk of bias. The included studies reported data on a total of 95 participants with an age range of 8-51 years. No significant difference was observed in the overall treatment outcome when comparing Biodentine with MTA (Risk

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ratio=1.00, 95% confidence interval [0.93-1.07], p=1.00).

Conclusions: Biodentine had comparable clinical and radiographic success to that of MTA when used as a DPC agent in mature permanent teeth with carious vital pulp exposure. Additional high-quality studies are needed.

INTRODUCTION

Dental caries is a chronic, infectious, transmissible disease affecting the primary and permanent teeth.[1] Clinically, carious lesions have a variant appearance, ranging from microscopic incipient demineralization to cavitated lesions.[2] Therefore, different treatments can be proposed, ranging from nonrestorative treatment in the early stages to complex restorative treatment for large carious defects.[3,4] During treatment, efforts should be directed toward tooth preservation as much as possible.[5]

Vital pulp therapy (VPT) aims to preserve the dental pulp by placing a biocompatible capping material over the thin layer of remaining dentin (indirect pulp capping), small pulp exposure [direct pulp capping (DPC)], partially removed coronal pulp (partial pulpotomy), or fully removed coronal pulp (full pulpotomy). In primary teeth, pulp capping following carious pulp exposure is not recommended by the American Academy of Pediatric Dentistry.[6] Furthermore, the results of published trails comparing different dental materials as pulp capping agents in primary teeth were inconclusive.[7] In permanent teeth, VPT has a good success rate if the pulp is not irreversibly inflamed, the hemorrhage is well controlled, and a good seal with a biocompatible capping material is obtained.[8] Recent evidence has shown successful outcomes of VPT, even when performed on cases with irreversible pulpitis.[9]

Direct pulp capping (DPC) has a long history of clinical use after carious or traumatic pulp exposure. For several decades, calcium hydroxide [$Ca(OH)_2$] was the material of choice for DPC.[10] However, $Ca(OH)_2$ results in incomplete dentinal bridge formation with tunnel defects.[11] Since the introduction of mineral trioxide aggregate (MTA) in the early 1990s, it immediately attracted interest as a pulp capping agent. MTA can form a thick dentin bridge that is continuous with the adjacent dentin.[12] Mente and others[13] reported that the success rate of DPC with $Ca(OH)_2$ is 59% and that with MTA is 80.5%. However, MTA has several drawbacks, including the ability to discolor the tooth structure, difficulties in handling, and an extended setting time.[14] Biodentine (Septodont Ltd, Saint Maur des Fausse's, France) is a newer calcium silicate cement that was developed to overcome the drawbacks of older cements, such as MTA.[15] When used as a pulp capping material, Biodentine causes the formation of a continuous dentin bridge that is similar to the one formed by MTA.[16] Multiple studies have reported that VPT using Biodentine is a successful treatment option for mature permanent teeth.[17-22]

In a recent meta-analysis comparing Biodentine with MTA on DPC success rate to permanent teeth, it was reported that there is no statistically significant difference between MTA and Biodentine.[23] However, studies with immature permanent teeth were included in their analysis.[23] In a more recent meta-analysis, the influence of different pulp capping materials on DPC success rates was evaluated.[24] It was concluded that MTA had better success than $Ca(OH)_2$, and there was no difference in success rates between MTA and Biodentine. The present study focused on comparisons between MTA and Biodentine, when used for DPC in mature permanent teeth. Therefore, the aim of this systematic review and meta-analysis was to evaluate the success rate of DPC in mature permanent teeth with carious pulp exposure using Biodentine compared to MTA.

METHODS

The current systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analyses Protocols (PRISMA-P) guidelines.[25] The protocol was registered on PROSPERO (Registration Number: CRD42020192511).

Developing the research questions

The PICO approach (**P**opulation, **I**ntervention, **C**omparison, and **O**utcome) was used for formulating the following research question: *In a mature permanent tooth with carious exposure and vital pulp, what is the success rate of using Biodentine as a DPC agent in comparison to MTA?*

Search methodology

An electronic search of PubMed, Cochrane Central Register of Controlled Trials, Web of Science Core Collection, Wiley Online Library, and SCOPUS databases was conducted using the following search terms: permanent dentition, mature teeth, dental caries, dental pulp capping, vital pulp therapy (VPT), DPC, tricalcium silicate, MTA, Biodentine,

Table 1: *Search Strategy through PubMed*

Number	Search Strategy	Results
1	Dental caries	58,865
2	Permanent dentition OR "mature teeth"	6223
3	Dental pulp capping OR "vital pulp therapy (VPT)" OR "direct pulp capping (DPC)"	2728
4	Tricalcium silicate OR mineral trioxide aggregate OR "MTA" OR Biodentine	10604
5	Treatment outcome OR "success rate" OR prognosis OR survival rate	2,264,290
6	#1 and #2 and #3 and #4 and #5	10

success rate, prognosis, treatment outcome, and survival rate. Table 1 displays an example of the electronic search strategy that was conducted through PubMed. The last search was performed on July 3, 2020.

Eligibility criteria

Initially, titles and abstracts of the papers were evaluated to remove articles that were out of the scope of this review. In case of any doubt, the full text of the article was read. After the evaluation of all abstracts, full-text articles of the selected papers were obtained for further assessment. The reference lists of the selected articles or relevant reviews were searched for any potential articles to be included. Articles were included if they fulfilled all of the following criteria:

1. Original clinical studies of DPC performed on fully formed human permanent teeth with carious exposure.
2. Biodentine was used as a pulp capping material.
3. MTA was included for comparison.
4. At least 6 months of follow-up.
5. The outcome was defined in terms of a clinical and radiographic examination.
6. Published in the English language.

Studies failing to meet any of these criteria were excluded. The two authors independently identified the relevant articles and, in cases of disagreement, a consensus was reached through discussion.

Data extraction

A custom-designed spreadsheet was used independently by two reviewers to extract the following data from included articles: name of the first author, publication year, country, study design, pulpal diagnosis, age of patients, total sample size, tooth type, number and specialty of the operators, isolation method, use of magnification, method used for bleeding control and disinfection, time needed to control bleeding, placement of the final restoration, follow up, success rate in the MTA group, success rate of Biodentine, and any evidence of tooth discoloration. Any missing information was obtained by contacting the authors.

Assessment of risk bias

The quality of the randomized clinical trials (RCTs) was assessed using the revised Cochrane risk of bias (ROB) tool.[26] The following domains were evaluated: randomization process, deviation from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results. The categories for ROB judgments of randomized trials are of low risk of some concerns and a high risk of bias.

The quality of observational studies was assessed using the ROB for nonrandomized studies interventions tool,[27] which covers seven domains: bias due to confounding, bias in the selection of the participants, bias in the classification of interventions, bias due to a deviation from the intended interventions, bias due to missing data, bias in the measurement of outcomes, and bias in the selection of the reported results. The categories for overall ROB judgments in such studies are a low risk, a moderate risk, a serious risk, and a critical risk of bias.

The ROB of each study was evaluated independently by the two reviewers. Any discrepancy in the quality assessment was resolved by discussion.

Data analysis

The statistical analysis was conducted using MedCalc software (version 19.1.1, Ostend, Belgium; http://www.medcalc.org). Meta-analysis with the random-effects method was used. The heterogeneity was investigated using the I^2 statistic. The estimated relative risk (RR) and confidence interval (CI) for the outcome measures were computed. A p-value of <0.05 was considered statistically significant. The confidence intervals (CIs) are given at the 95% level. Results were presented in a table and forest plots. Publication bias was not evaluated due to few numbers of included studies.[28]

Results

Study Selection

The literature search and selection processes are illustrated in Figure 1. After removal of duplicates,

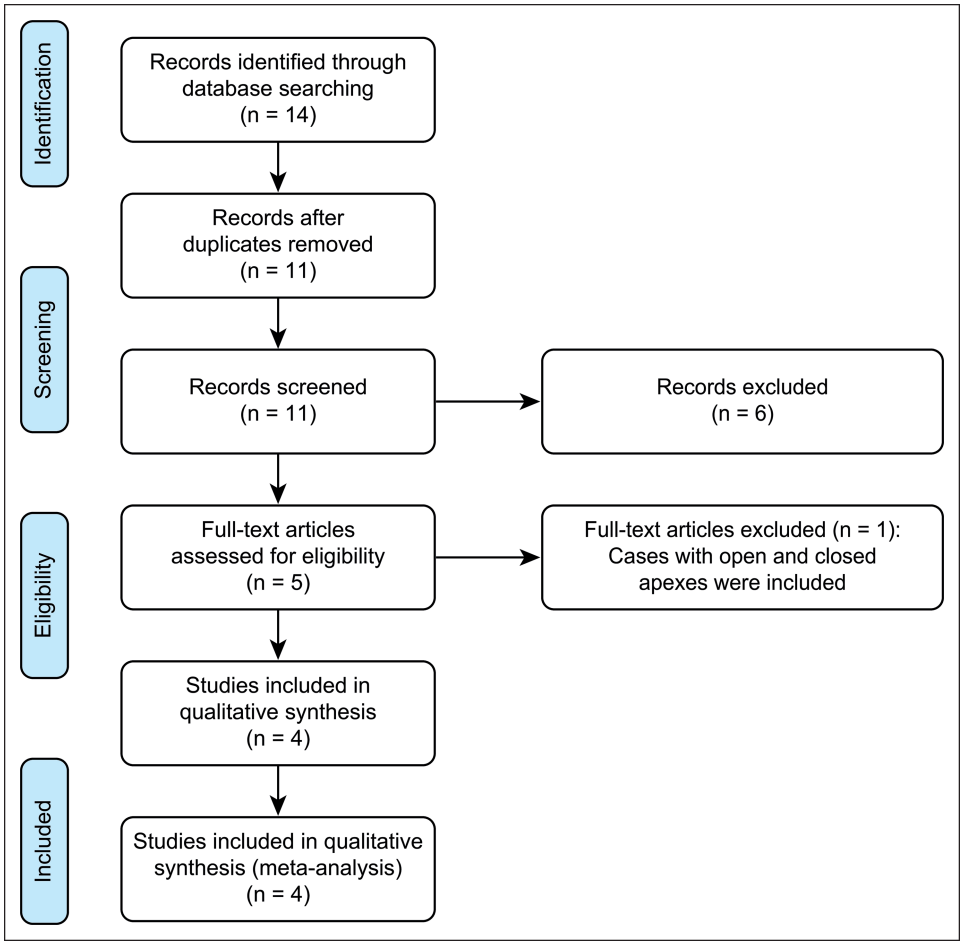

Figure 1. *A flow diagram summarizing the systematic review process for article selection according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.*

the initial search yielded 11 articles that met the initial search criteria. At this stage, the titles and abstracts were screened, and five articles were identified for full-text reviewing. Among these studies, one was excluded,[18] because DPC was performed in molars with open and closed apexes, and the results regarding the success rate in the closed apex group alone was not shown. Finally, four studies were included for this systematic review and meta-analysis.

Characteristics of the Included Studies

The characteristics of the four included clinical studies are presented in Table 2. Three of the selected studies were RCT,[19-21] and one was a retrospective study.[29] The countries of origin of studies were: India,[19,29] Thailand,[21] and Jordan.[20] The selected studies included a total of 95 participants with an age ranging from 8-51 years. Two studies included molar teeth only,[19,29] and the other two included anterior and posterior teeth.[20,21] All teeth had a positive response to sensitivity pulp tests. Linu and others excluded teeth with a lingering response to pulp tests.[29] On the other hand, Parinyaprom and others included cases with early periapical involvement, with a widened PDL space or condensing osteitis.[21] Furthermore, one study reported the specialty of the operator,[21] while the other three studies did not report this data.

In all included studies, the treatment procedures were performed under rubber dam isolation with no specific mention of using magnification aids. To achieve hemostasis after pulp exposure, a cotton pellet soaked in sodium hypochlorite (NaOCl) was used. Two studies used a high concentration of NaOCl,[20, 29] while the other two used a lower concentration.[19,21] The reported time for bleeding control before the placement of the capping agent varied from 3 to 10 minutes. In one study, the treatment was finalized in a single visit,[21] while, in the other studies, the final restoration was placed after 1-3 weeks. There was a wide variability in the follow-up periods across the studies, ranging from 6 months to 3 years. However, all studies had a minimum follow-up period of 6 months. Treatment outcomes in all studies were based on clinical

Table 2: *Characteristics of the Studies Included in the Review*

Study	Country	Design	Age (Years)	Type of Teeth Included	Number of Operators	Operator Specialty	Isolation Method	NaOCl Concentration (%)	Time to Control Bleeding	Final Restoration	Time for Final Restoration	Follow-up (Months)
Hegde and others (2017)	India	RCT	18-40	M	1	NS	RD	3%	NS	Composite	3 week	6
Linu and others (2017)	India	RS	15-30	M	NS	NS	RD	5%	10 minutes	Composite	MTA: 1 w BD: 2 week	6, 12, 18
Parinyaprom and others (2018)	Thailand	RCT	8-18	I, M	8	PG	RD	2.5%	Within 10 minutes	Composite, amalgam, or SSC	Immediate	Range (6-54)
Awawdeh and others (2018)	Jordan	RCT	16-51	I, P, M	NS	NS	RD	5%	3-6 minutes	Composite or amalgam	1 week	6, 12, 18, 24, 36

RCT, randomized clinical trials; RS, retrospective study; I, incisors; P, premolars; M, molars; NS, not specified; PG, Postgraduate residents; RD, rubber dam; NaOCl, sodium hypochlorite; min, minutes; w, week; MTA, mineral trioxide aggregate; BD, Biodentine; SSC, stainless steel crown; NS, not specified.

examinations and radiographic appearance. Additionally, evidence of tooth discoloration was reported in all studies. The study conducted by Parinyaprom and others[21] was the only study that did not radiographically evaluate the formation of a dentin bridge underneath the capping material.

Results of the Individual Studies

Hegde and others[19] included 24 teeth in their study (MTA=12, Biodentine=12). Three teeth failed within the first 3 weeks (2 with Biodentine and 1 with MTA). At the 6-month follow-up, the success rate for MTA was 91.7%, and the success rate for Biodentine was 83.3%. At the 1-year follow-up, two teeth from the MTA group and two teeth from the Biodentine group showed dentin bridge formation. The authors reported the presence of tooth discoloration in the majority of teeth capped with MTA.

Linu and others[29] assessed the outcome of DPC in 26 teeth (MTA=13, Biodentine=13). The success rate in the MTA group was 84.6% (11/13), and it was 92.3% (12/13) in the Biodentine group. None of these cases failed after 1 month. Radiographically, a visible dentin bridge and diffuse calcifications of the pulp chamber were observed for both the groups (69.2% and 7.7% in the MTA group vs. 61.5% and 23.1% in the Biodentine group). Furthermore, 69.2% of cases treated with MTA showed coronal discoloration, whereas no discoloration was noticed in teeth treated with Biodentine.

Parinyaprom and others[21] compared the outcome of DPC using MTA or Biodentine. Teeth with open and closed apices were included. The authors were contacted to provide additional data for teeth in the closed apices group. The sample size was 28 teeth (MTA=15, Biodentine=13). No failed cases were reported for all observed follow-up times. Furthermore, discoloration was observed in the MTA group only.

Awawdeh and others[20] studied the outcomes of DPC and pulpotomy using MTA and Biodentine. The authors were contacted to provide detailed information about the DPC group. Seventeen teeth were treated (MTA=6, Biodentine=11). At the 1-year follow-up, a tooth from the Biodentine group was excluded, because the coronal restoration was broken, and the pulp was exposed. During the 24-month follow up, all included teeth were considered successful. Radiographically, there was no evidence of a dentin bridge or calcifications. The authors reported the presence of coronal discoloration in all teeth treated with MTA, whereas no discoloration was observed in teeth treated with Biodentine. At the 36-month follow-up, the success rate in the MTA group was 100% (6/6), and it was 88.89% (8/9) in the Biodentine group.

Quality Assessment of the Risk of Bias

Figure 2 shows the quality assessment of the included studies. Among the selected RCTs, only one study presented a low ROB.[20] The study by Parinyaprom and others[21] triggered some concerns, because the clinical evaluation and the decision of the final outcome were performed by unblinded operators. Hegde and others[19] had a high ROB, because they did not report the demographic and baseline clinical characteristics for each group, such as patient age or the type of the treated teeth. Furthermore, no analysis was performed to evaluate the distribution of the partici-

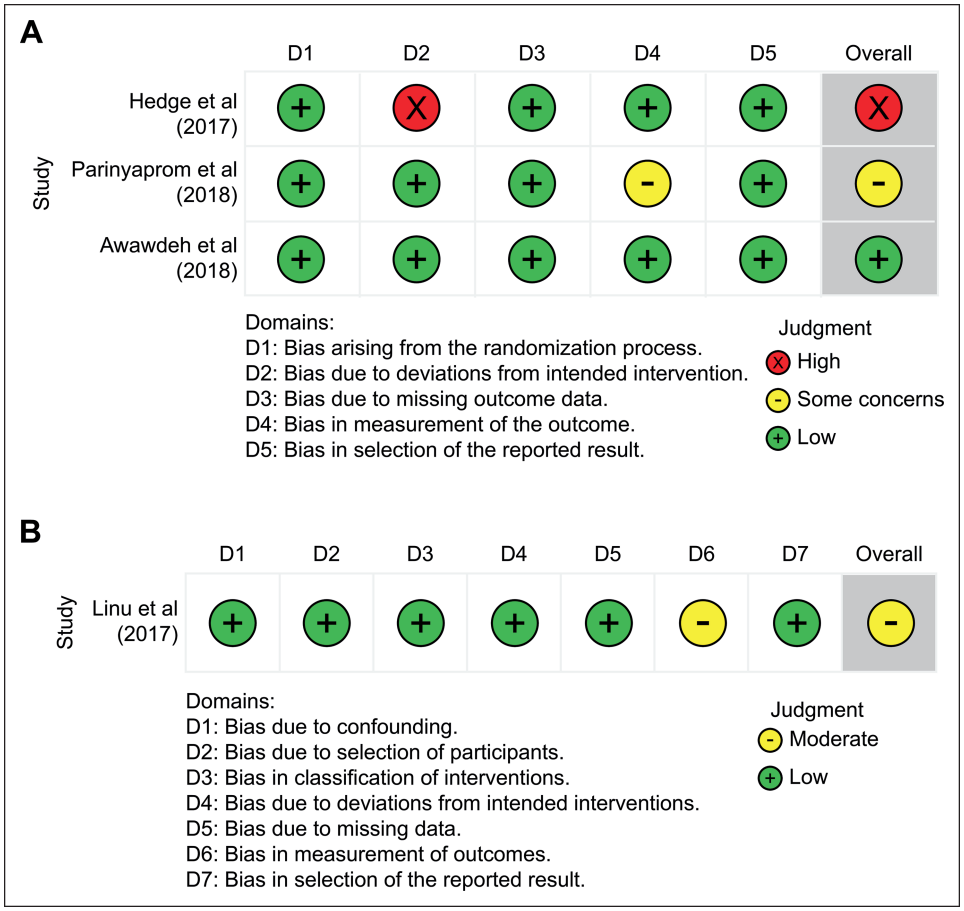

Figure 2. *Quality assessment results using (A) the revised Cochrane risk of bias (ROB) tool for randomized clinical trials (RCT) and (B) the ROB for nonrandomized studies of interventions tool for observational studies.*

pants between the two groups regarding the baseline variables.

The ROB in nonrandomized studies of interventions tool[27] was used to assess the quality of study done by Linu and others,[29] which presented a moderate ROB, because no information was provided regarding the operator who assessed the treatment outcome (Figure 2B).

Meta-Analysis

Meta-analysis was performed, considering the success rate of MTA and Biodentine, when used as a DPC agent. As shown in Figure 3, there was no significant difference in the overall success rate between MTA and Biodentine (RR=1.00, CI [0.93-1.07], heterogeneity: I^2=0.000%, p=1.00). Due to the limited number of studies that included follow-up period of ≥12 months, the subgroup analysis was feasible for 6 months only. The results showed that there was no significant difference in the success of treatment between MTA and Biodentine at 6 months (RR=1.00, CI [0.90-1.11], heterogeneity: I^2=0.000%, p=0.86) (Figure 4).

Discussion

Traditionally, carious exposed pulps in mature teeth were managed with complete root canal treatment. However, several recent studies have demonstrated the successful management of such cases using the VPT approach with different calcium silicate-based cements.[20,21,30] MTA and Biodentine are examples of calcium silicate cements that have similar reported success rates when used as pulp capping agents.[20,21,30] However, conducting a meta-analysis to determine the differences in the success rates of these materials is important for clinicians to select the best possible pulp capping agent based on the best scientific evidence available. Therefore, this study was focused on comparing the outcome of Biodentine to MTA when used as a DPC agent in mature permanent teeth and carious exposure by using a systematic review with meta-analysis.

The findings of the present review are based on the results from four clinical studies. The overall quality of the included studies was found to have some concerns[20,21]—to be at a moderate[29] or high

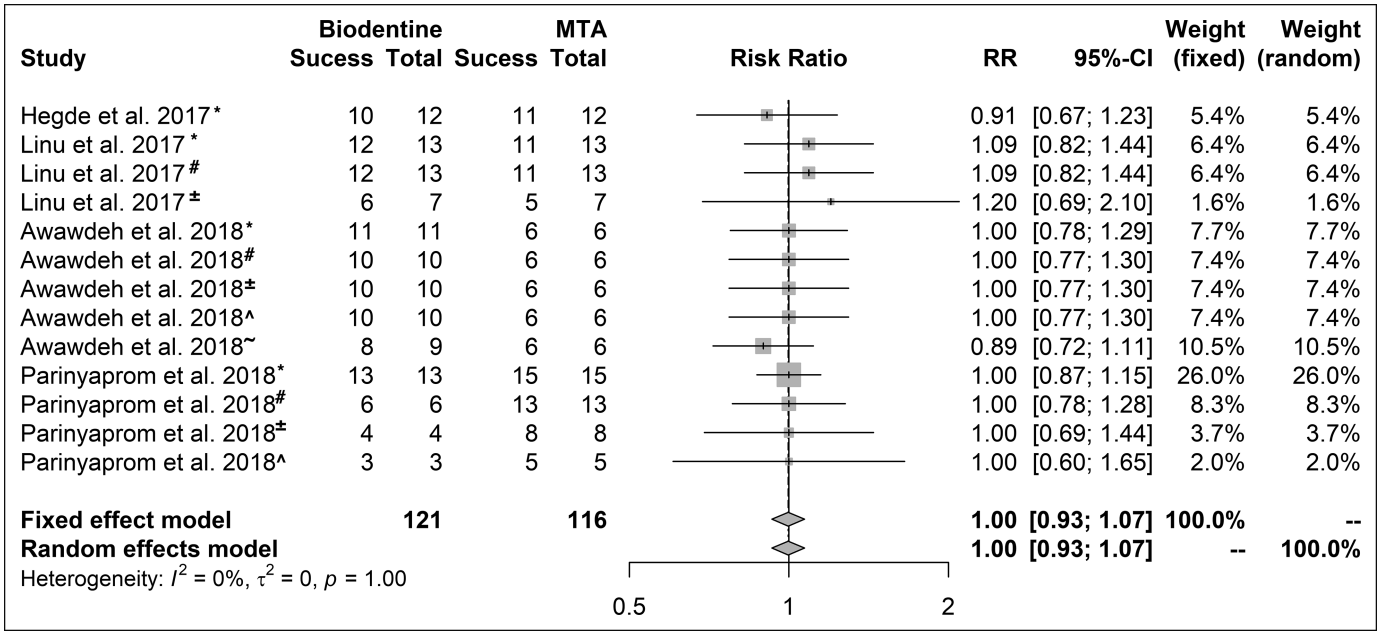

Figure 3. *Forest plot comparing the overall outcome of direct pulp capping (DPC) in cariously exposed pulp with Biodentine and mineral trioxide aggregate (MTA). (*) 6, (#), 12, (±) 18, (^) 24, and (~) 36 month.*

risk of bias.[19] Only one study mentioned that a blinded assessor evaluated the final outcome.[20] Considering the differences between MTA and Biodentine in appearance and handling characteristics, it is not possible to blind the operator. Therefore, performance bias seems to be unavoidable. Furthermore, the study of Hegde and others[19] did not show the baseline clinical characteristics or differences between the two groups. Thus, these results should be interpreted cautiously.

The results of the present systematic review and meta-analysis indicate that there is no difference in the success rate of MTA and Biodentine when used as DPC agents in mature teeth with carious pulp exposure in terms of clinical and radiographic assessments. The formation of a hard tissue barrier was not included in the present review as an indicator for the treatment success, because it is best evaluated by using histologic sections.[31] An ideal pulp capping material should be nontoxic, bioactive, and able to bond to the tooth structure.[32] MTA and Biodentine have comparable biocompatibility and bioactivity.[33] Furthermore, both materials have similar bond strength to dentin,[34] and they formed a mineralized tissue bridge after pulpotomy in an animal experiment.[35] In the study by Linu and others,[29] diffuse calcifications in the pulp chamber were observed in 7.7% (1/13) and 23.1% (3/13) of cases of MTA and Biodentine, respectively. Total canal obliteration was not observed in any of the

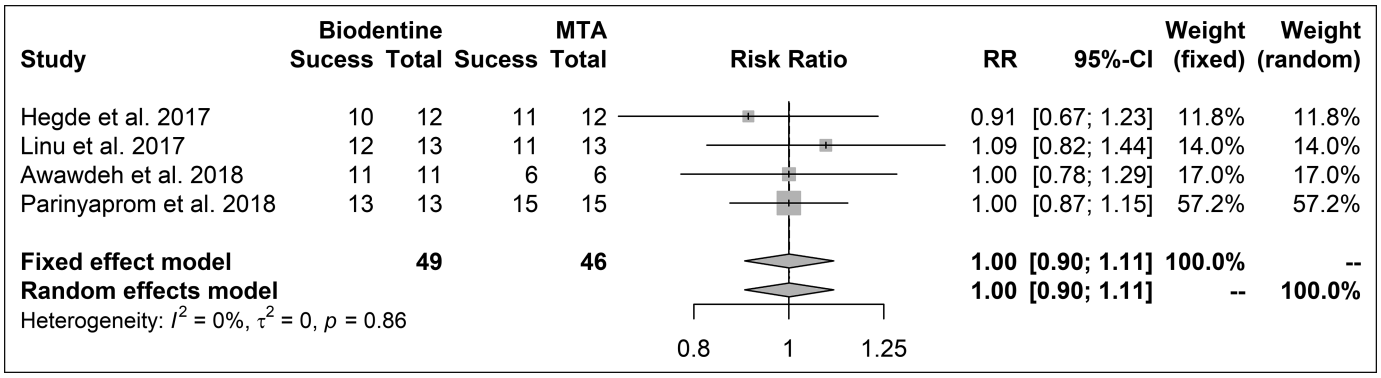

Figure 4. *Forest plot comparing the outcome of direct pulp capping (*DPC*) in cariously exposed pulp with Biodentine and mineral trioxide aggregate (MTA) at 6 month.*

included studies. The available literature suggests that the risk of developing an obliteration is higher after complete pulpotomy.[36] However, long-term follow-up is required for the evaluation of its incidence after DPC. It is important to note that the findings of this review are consistent with a recent meta-analysis of pooled data from three studies.[24] Furthermore, it is consistent with a previous meta-analysis on success rates of DPC in mature and immature teeth.[23]

All clinical studies included in this review reported the presence of tooth discoloration in the majority of the cases after the use of MTA, while no discoloration was noted when Biodentine was used.[19-21,29] This finding is consistent with various *in vitro* studies.[37,38] The discoloration associated with MTA may be explained by the presence of bismuth oxide as a radiopacifier within the powder. NaOCl was used in all included studies for bleeding control and disinfection before the placement of the capping agent. When bismuth oxide comes into contact with NaOCl, a dark-brown to black discoloration occurs.[39] Furthermore, bismuth oxide interacts with dentin collagen and forms a black discoloration.[40] The lack of bismuth oxide in Biodentine may explain its superior color stability compared to MTA.[38] This is of clinical significance, especially for teeth with aesthetic considerations. Considering the other advantages of Biodentine over MTA, including its shorter setting time,[41] better handling characteristics, and lower cost, together with the findings of this systematic review and meta-analysis, Biodentine can be used more confidently for DPC to avoid future patient dissatisfaction.

Factors other than the type of capping material play an important role in the success of the VPT, including control of the pulpal bleeding before placement of the capping agent.[42] Different methods have been proposed to control pulpal hemorrhage, including the use of saline, NaOCl, or hydrogen peroxide.[42,43] In all of the included studies, the bleeding was controlled using NaOCl[20] or a cotton pellet soaked with NaOCl at concentrations ranging from 2.5% to 5%.[19,21,29] In addition to its hemorrhage control,[43] NaOCl has excellent antimicrobial properties,[44] which can assist in the disinfection of the perforated area. The adverse effect of microorganisms on pulpal tissue is well known.[45] Therefore, in these studies, pulp capping procedures were performed under rubber dam isolation to avoid the introduction of microorganisms into the perforated site. In addition to the use of a rubber dam, the final restoration was placed within 3 weeks. The significant effect of having a permanent restoration on the favorable outcome of VPT has been reported previously.[46]

The major limitation of this review was that the results of the meta-analysis are limited in terms of the number of cases due to the few available clinical studies that directly compared the outcomes of these two materials in mature permanent teeth. Therefore, additional high-quality RCT with long-term follow-up are required. Another limitation of this review is that the search strategy was restricted to the English language. On the other hand, this review has elements of strength. It has answered a focused clinical question, and the study selection and evaluation process were performed according to standard protocols.

CONCLUSIONS

Within the limitations of this systematic review and meta-analysis, only a limited number of clinical trials comparing MTA and Biodentine as DPC materials is available in the existing literature. Overall, MTA and Biodentine showed comparable clinical and radiographic success rates as DPC agents in mature permanent teeth with carious exposure.

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgements

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