# Direct Pulp Capping with Calcium Hydroxide or Mineral Trioxide Aggregate: A Meta-analysis

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## Abstract

**Introduction:** The purpose of this study was to compare the effectiveness of mineral trioxide aggregate (MTA) and calcium hydroxide (CH) as pulp capping materials in humans by means of a meta-analysis. **Methods:** The PubMed, Cochrane Library, Embase, and Web of Knowledge databases were used in the literature search from their establishment date until December 7, 2014. Studies that met the inclusion criteria were accepted, and necessary information was extracted by 2 authors independently using a standardized form. The success rate, inflammatory response, and dentin bridge formation were evaluated. **Results:** Thirteen studies met the inclusion criteria. There was no significant heterogeneity between studies, so a fixed-effects model was used. The MTA treatment groups showed a significantly higher success rate compared with CH-capped groups (randomized controlled trials: odds ratio [OR] = 2.26; 95% confidence interval [CI] = 1.33–3.85; $P = .003$; retrospective nonrandomized trials: OR = 2.88; 95% CI, 1.86–4.44; $P < .00001$). MTA was superior to CH in terms of the absence of an inflammatory response as well as dentin bridge formation, with the OR being 4.56 (95% CI, 2.65–7.83) and 3.56 (95% CI, 1.89–6.70), respectively. **Conclusions:** MTA has a higher success rate and results in less pulpal inflammatory response and more predictable hard dentin bridge formation than CH. MTA appears to be a suitable replacement of CH used for direct pulp capping. *(J Endod 2015;41:1412–1417)*

## Key Words

Calcium hydroxide, direct pulp capping, meta-analysis, mineral trioxide aggregate

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Direct pulp capping (DPC) is performed when a healthy pulp has been inadvertently exposed from traumatic injury or by iatrogenic means (1). During DPC, a medicament is placed directly over the exposed site and thus can stimulate the healing process. If successful, it will preclude the need for further treatments (2) (eg, root canal therapy). The most frequently used material for DPC in clinical treatment is calcium hydroxide (CH), which was introduced to the dental profession in 1921 and has been considered the "gold standard" of direct pulp capping materials for several decades (3, 4).

CH has outstanding antibacterial properties, which can minimize or eliminate bacterial penetration and subsequent irritation of pulpal tissue (5). The clinical success rate can be tracked for years by using this agent. However, CH exhibits some obvious disadvantages including pulp surface inflammation and necrosis after pulp capping; the presence of tunnel defects in the dentin bridge, which fails to provide a hermetic seal to the underlying pulp against recurring infection because of microleakage; high solubility in oral fluids; lack of adhesion; and degradation over time (2, 6–9).

As a result of the aforementioned disadvantages, a number of new materials have been tested during the last 2 decades as alternatives to CH. Recently, mineral trioxide aggregate (MTA) has become a popular alternative for CH, which is composed of calcium oxide in the form of tricalcium silicate, dicalcium silicate, tricalcium aluminate, and bismuth oxide for radiopacity (10). Histologic studies and *in vitro* trials report favorable results regarding the chemical and physical properties, antibacterial activity, biocompatibility, and sealing properties of MTA (11–13).

There appear to be differences in pulpal tissue reaction to MTA compared with CH in direct pulp capping. Dentin bridge formation with MTA seems to be more homogenous (fewer tunnel defects) and more localized than that formed with CH (14–17). Histologic evaluations of exposed pulp tissue from animals capped with MTA have shown the formation of a thicker dentinal bridge with a lower inflammatory response, hyperemia, and pulpal necrosis compared with CH (18, 19). Thus, MTA might be a good material of choice for dental pulp capping procedures. Despite its many advantages, MTA has some drawbacks such as discoloration potential, difficult handling characteristics, long setting time, and the difficulty of its removal after curing (20). A search of the literature showed the absence of a meta-analysis comparing the effectiveness of MTA and CH as pulp capping materials in humans.

The aim of the present meta-analysis was to compare the effectiveness of MTA and CH on direct pulp capping in humans in terms of success rate, inflammatory response, and dentin bridge formation, which can provide the basis for clinical application.

## Materials and Methods

### Search Strategy

In the present study, PubMed, the Cochrane Library, Embase, and the Web of Knowledge were used as the electronic databases (last search updated on December 7, 2014). The following key words were used for an initial search conducted on PubMed: (mineral trioxide aggregate) AND (calcium hydroxide) AND (direct pulp capping) with the application of the following limit: English language. The same key words and search limit were used on the Cochrane Library, Embase, and the Web of Knowledge. Additional search methods included a manual review of the reference lists of relevant studies.

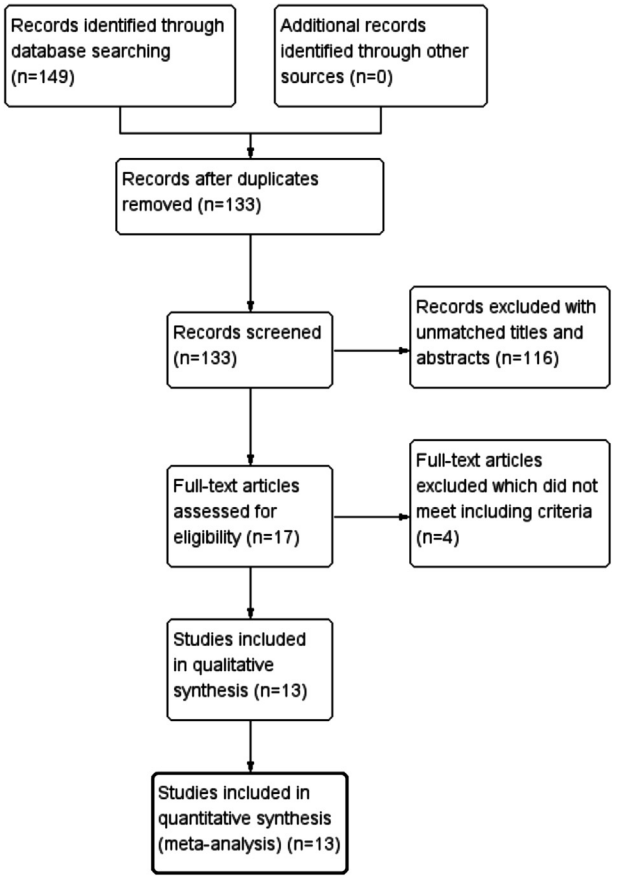



**Figure 1.** A flow diagram of the included studies.

## Inclusion and Exclusion Criteria

Articles were included in the meta-analysis if they met all the following criteria:

1. The design type of studies were randomized controlled trials (RCTs) or retrospective nonrandomized trials (RNTs).
2. The direct pulp capping treatment was performed in human permanent teeth *in vivo*.
3. The studies compared MTA versus CH.
4. The success rate, inflammatory response, and dentin bridge formation were recorded.

Exclusion criteria were as follows:

1. Studies were performed *in vitro*.
2. Experimental studies were performed in animals or in human primary teeth.
3. The absence of a comparison of the 2 materials.

Abstracts, conference reports, and studies with insufficient information were also excluded.

## Data Extraction

Studies that fulfilled the inclusion criteria were processed for data extraction. Two authors independently extracted the necessary information using a standardized form. Discrepancies were resolved by discussion and consensus. The following information was extracted from each study: name of the first author, year of publication, country of origin, study design, the number of teeth, teeth type, success rate, inflammatory response, and dentin bridge formation. If studies involved multiple groups, only the control and experimental groups associated with this study were extracted.

## Methodological Quality Appraisal

Assessment of the quality of included studies is essential for a proper understanding of meta-analytic results. Thus, the quality assessment of individual RCT studies was performed using the Cochrane Collaboration's tool for assessing risk of bias. The quality of each RNT study was assessed according to the methodological index for nonrandomized studies.

## Statistical Analysis

Different study categories were analyzed separately. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to compare the treatment results between MTA and CH. The standard chi-square test and $I^2$ statistic were used to test for heterogeneity among studies; $P < .1$ or $I^2 > 50\%$ suggested the presence of heterogeneity. If heterogeneity existed between studies, a random-effects model was used; otherwise, a fixed-effects model was used. Finally, publication bias was assessed by performing funnel plots qualitatively. All analyses were performed using Revman 5.0 statistical software (The Cochrane Collaboration, Oxford, UK).

**TABLE 1.** The Characteristics of the Included Studies

| Author | Year | Country | Study design | No. of teeth | Teeth type | Age range (y) | No. of MTA | No. of CH | Minors score |
|---|---|---|---|---|---|---|---|---|---|
| Accorinte (21) | 2008 | Brazil | RCT | 40 | Premolars | 15–30 | 20 | 20 | — |
| Accorinte (22) | 2008 | Brazil | RCT | 40 | Premolars | 15–30 | 20 | 20 | — |
| Aeinehchi (23) | 2003 | Iran | RCT | 14 | Third molars | 20–25 | 8 | 6 | — |
| Cho (24) | 2013 | Korea | RNT | 175 | Patients | — | 70 | 105 | 17 |
| Eskandarizadeh (25) | 2011 | Iran | RCT | 90 | Premolars | 14–21 | 60 | 30 | — |
| Hilton (26) | 2013 | US | RCT | 358 | Patients | >7 | 183 | 175 | — |
| Iwamoto (27) | 2006 | US | RCT | 45 | Third molars | 18–60 | 22 | 23 | — |
| Mente (28) | 2010 | Germany | RNT | 122 | Patients | 8–78 | 69 | 53 | 19 |
| Mente (29) | 2014 | Germany | RNT | 229 | Patients | 7–78 | 170 | 59 | 21 |
| Min (30) | 2008 | Korea | RCT | 19 | Third molars | 21–50 | 9 | 10 | — |
| Nair (31) | 2008 | Switzerland | RCT | 33 | Third molars | 18–30 | 20 | 13 | — |
| Parolia (32) | 2010 | India | RCT | 24 | Premolars | 15–25 | 12 | 12 | — |
| Swarup (33) | 2014 | India | RCT | 20 | Premolars | 11–15 | 10 | 10 | — |

CH, calcium hydroxide; MTA, mineral trioxide aggregate; RCT, randomized controlled trials; RNT, retrospective nonrandomized trials.

**TABLE 2.** Data Summary of the Included Studies

| Studies | No. of teeth MTA/CH | Success rate MTA/CH | Absent inflammatory response MTA/CH | Dentin bridge formation MTA/CH |
|---|---|---|---|---|
| Accorinte (21) | 20/20 | -/- | 17/16 | 19/15 |
| Accorinte (22) | 20/20 | -/- | 18/16 | 18/20 |
| Aeinehchi (23) | 8/6 | -/- | 4/0 | 7/4 |
| Cho (24) | 70/105 | 63/75 | -/- | -/- |
| Eskandarizadeh (25) | 60/30 | -/- | 32/6 | 59/24 |
| Hilton (26) | 183/175 | 158/130 | -/- | -/- |
| Iwamoto (27) | 23/24 | 23/22 | 17/14 | 20/18 |
| Mente (28) | 69/53 | 54/32 | -/- | -/- |
| Mente (29) | 170/59 | 137/35 | -/- | -/- |
| Min (30) | 9/10 | -/- | 2/1 | 9/6 |
| Nair (31) | 20/13 | -/- | 18/5 | 11/6 |
| Parolia (32) | 12/12 | -/- | 10/3 | 10/7 |
| Swarup (33) | 10/10 | -/- | 7/0 | 10/4 |

-/-, not mentioned; CH, calcium hydroxide; MTA, mineral trioxide aggregate.

# Results

## Characteristics of Included Studies

From 149 potentially relevant studies, 13 eligible studies (21–34) (10 RCTs and 3 RNTs) that compared the effectiveness of MTA and CH were recruited and applied to the final meta-analyses (Fig. 1). A total of 673 cases and 536 controls were included in this research. Human premolars were used as specimens in 5 studies and third molars in 4 studies, and the research objects of the remaining 4 studies were patients who had received direct pulp capping treatment with MTA or CH. Of these studies, 5 reported the success rate. Nine studies investigated the inflammatory response of the exposed pulp to the 2 different materials and dentin bridge formation. The corresponding characteristics of the identified studies are presented in Tables 1 and 2.

## Results of Methodological Quality Assessment

The quality of 3 RNT studies was assessed according to the methodological index for nonrandomized studies with a total score of 17, 19, and 21, respectively (Table 1). Ten RCT studies were assessed using the Cochrane Collaboration's tool for assessing risk of bias. The judgments about each risk of bias item for each RCT study are shown in Figure 2. Although all studies mentioned randomization, 4 RCTs failed to describe methods for random sequence generation. Seven studies did not adequately describe allocation concealment. Blinding participants and personnel was impossible because the handling characteristics of the materials were dissimilar, but the outcome assessments of 7 studies were objective. Hence, we considered detection bias as low risk. A description of withdrawals and dropouts was given in every study. No reporting or other bias was found in these RCT studies.

## Meta-analysis

**Success Rate.** Five studies involving 931 teeth compared the success rate between MTA and CH. A meta-analysis was conducted separately according to study design. According to the chi-square statistic and $I^2$, the results showed no heterogeneity (RCT: $\chi^2_1 = 0.30$, $P = .59$, $I^2 = 0\%$; RNT: $\chi^2_2 = 0.48$, $P = .79$, $I^2 = 0\%$). Therefore, a fixed-effects model was used for the meta-analysis. In the fixed-effects models, the MTA treatment groups showed a significantly higher

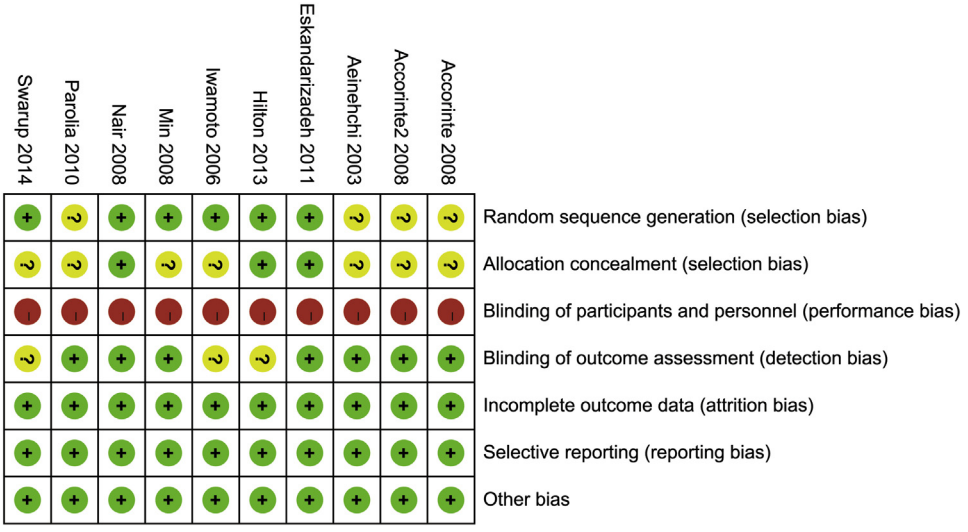
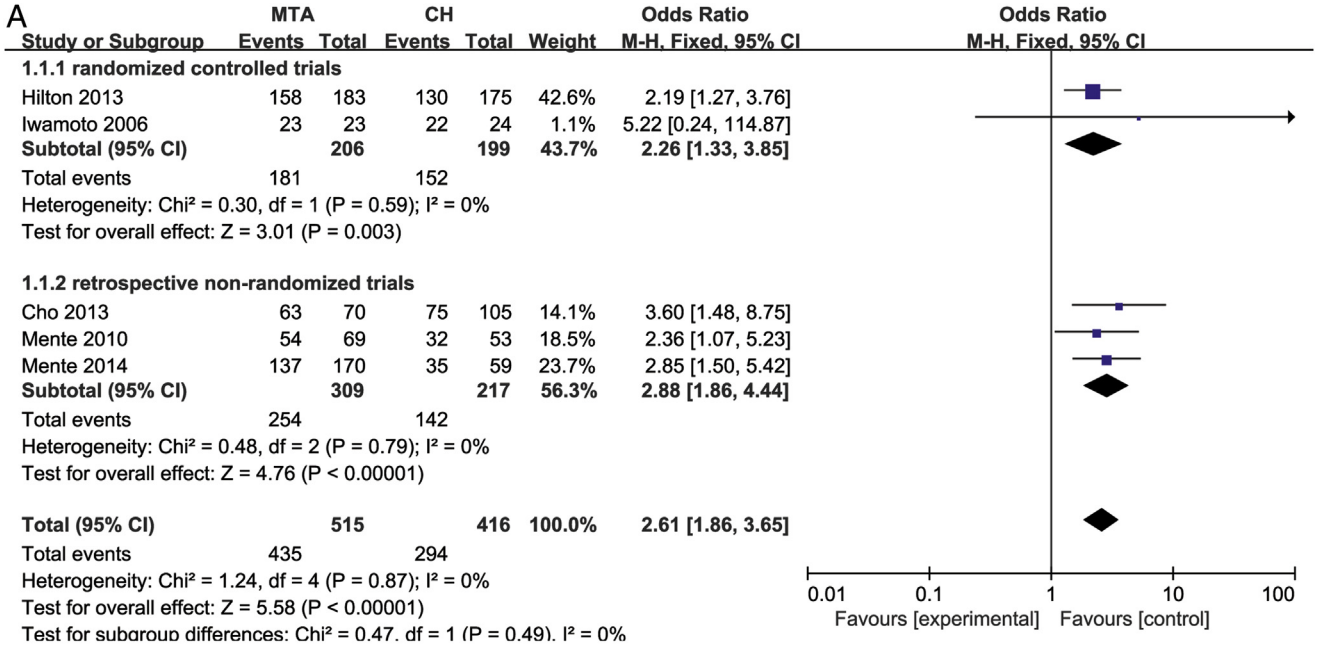
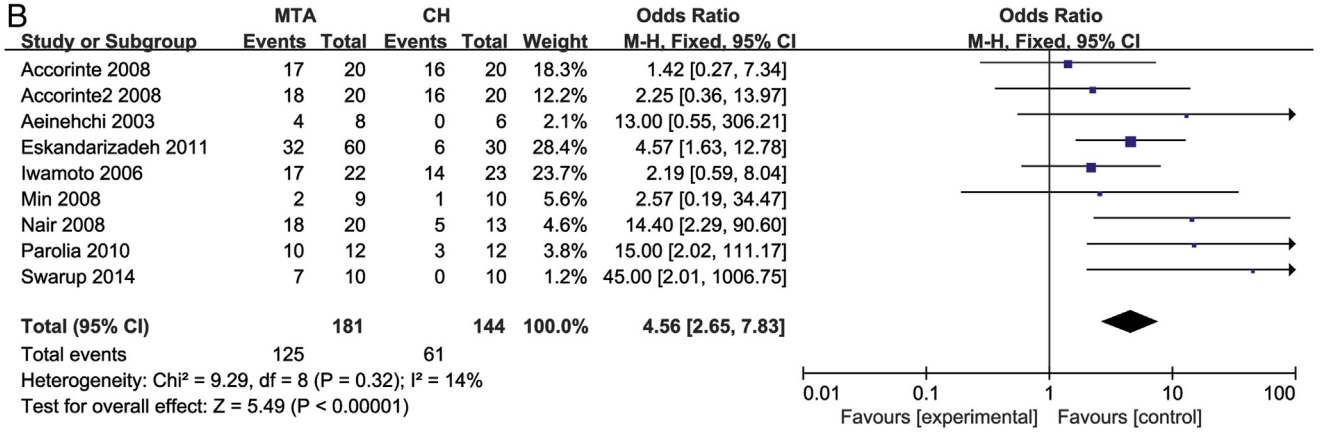



**Figure 2.** A methodological quality assessment of the RCT studies.



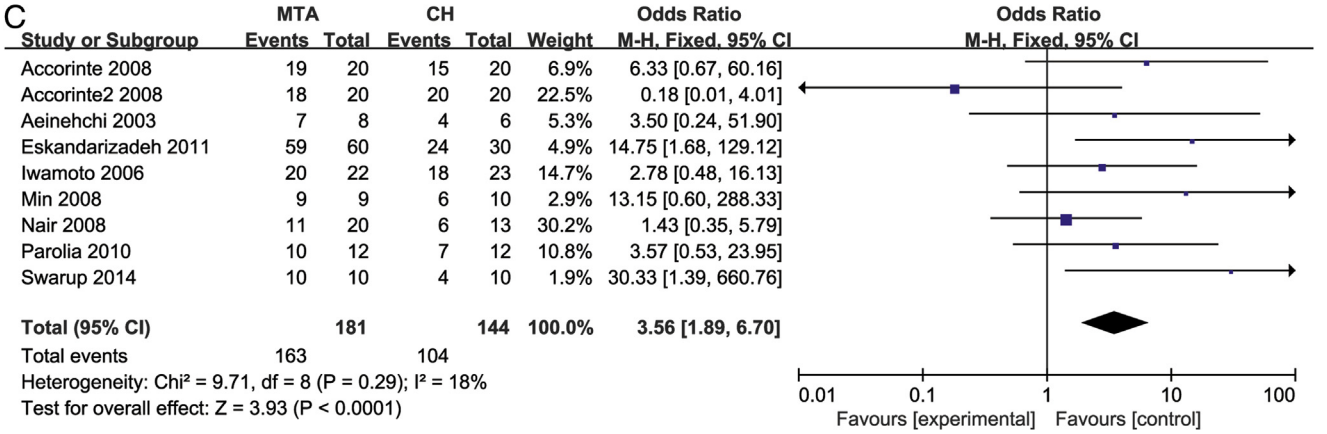




**Figure 3.** A Forest plot of the OR of (*A*) success, (*B*) inflammatory response, and (*C*) dentin bridge formation: MTA versus CH.

success rate compared with the CH-capped groups (RCT: OR = 2.26; 95% CI, 1.33–3.85; $P$ = .003; RNT: OR = 2.88; 95% CI, 1.86–4.44; $P$ < .00001) (Fig. 3*A*).

### Inflammatory Response

Nine studies of 325 teeth compared the inflammatory response between MTA and CH. There was no apparent statistical heterogeneity between these studies ($\chi^2_8$ = 9.29, $P$ = .32, $I^2$ = 14%), so we used a fixed-effects model for the meta-analysis. In the fixed-effects models, MTA specimens showed significantly less inflammation compared with CH samples (OR = 4.56; 95% CI, 2.65–7.83; $P$ < .00001) (Fig. 3*B*).

### Dentin Bridge Formation

Nine studies of 325 teeth compared dentin bridge formation between MTA and CH. There was no significant heterogeneity between studies ($\chi^2_8$ = 9.71, $P$ = .29, $I^2$ = 18%). The difference in the ability of the materials to produce a reparative dentin bridge was found to be statistically significant. MTA-capped groups showed a higher percentage of calcified dentin bridge formation than CH-capped groups (OR = 3.56; 95% CI, 1.89–6.70; $P$ < .0001) (Fig. 3*C*).

### Heterogeneity Analysis

Substantial heterogeneities were analyzed among studies. There was no significant heterogeneity between studies.

### Publication Bias Analysis

Publication bias exists because research with statistically significant results is more likely to be submitted and published than work with null or nonsignificant results. It may compromise the validity of conventional reviews as well as the quantitative overview techniques of the meta-analysis, which often rely on published data. We included only published clinical trials in our meta-analysis and searched only 4 electronic databases with a language restriction, which could have increased the risk of publication bias. Although the funnel plots displayed good symmetry, it had an isolated point at the right bottom, and we could not draw a firm conclusion that publication bias did not exist. The most direct way to circumvent publication bias is to obtain data on all studies, published and unpublished. A better solution is to establish registration of clinical studies, which provides a sampling frame for meta-analysis (35, 36).

## Discussion

MTA is a biocompatible material that has wide clinical applications such as surgical root-end filling, root and furcation perforation repair, apical barrier formation for teeth with open apexes, apexification, pulp capping and pulpotomy of primary and permanent teeth, and obturation of retained primary teeth (12). MTA has been used as a pulp capping agent in humans only during the past 12 years (23). As for CH, it has been considered the "gold standard" of direct pulp capping materials for several decades (3, 4). To compare the effectiveness of MTA and CH on direct pulp capping in humans, 13 studies were conducted since the year 2003. Of these studies, 5 reported the success rate. Nine investigated the inflammatory response and dentin bridge formation of the exposed pulp to the 2 different materials.

By recruiting all relevant studies, we conducted the current meta-analysis and found that the success rate of MTA was superior to that of CH. Regarding the definition of success, the treatment was regarded as successful when none of the following signs or symptoms was present: spontaneous pain, tenderness of percussion, swelling, fistulation, pathological mobility, furcation radiolucency, periodontal ligament space widening, or internal or external root resorption. However, the clinical criterion is inadequate for an evaluation of the long-term prognosis for teeth treated by pulp capping. Pulpal degeneration and necrosis can occur without any clinical signs or symptoms. Clinical success shows only gross pathological changes, which give hazy results. It is impossible to clinically diagnose teeth in which healing is complicated by inflammation (37). Therefore, we also incorporated comparative histologic analysis of the results of direct pulp capping with MTA or CH.

This meta-analysis shows the superiority of MTA in comparison with CH in terms of the absence of an inflammatory response as well as dentin bridge formation. In clinical practice, clinicians usually use thermal or electric pulp testing methods to confirm the presence of vital pulp tissue. In studies included in this meta-analysis, the inflammatory response was determined by the histologic method because the research objects were premolars or third molars that were scheduled to be extracted.

The foundation of restorative dentistry rests on the principle of the preservation of a healthy and functional pulp-dentin complex. Direct pulp capping is designed to treat reversible pulpal injuries by healing the exposed pulp and stimulating the formation of the dentin bridge, thereby restoring the structure and function of pulp tissue (32). Stanley (38) stated that in the absence of a dentin bridge, wounded pulp tissue is much closer to the surface and can therefore be invaded more easily by subsequent attacks of oral bacteria and their by-products if the events should occur. Unattached pulp tissue, in the absence of a bridge, eventually undergoes degeneration, atrophy, and shrinkage away from the dentin. Therefore, it appears that a dentin bridge is the best solution for final healing and long-term success. The predictable formation of a quality dentin bridge subjacent to MTA is likely to be a combination of multiple factors involving its excellent sealing ability, which is a critical factor for the success of the direct pulp capping procedure (39–41). MTA also stimulates the production of certain cytokines in human osteoblasts, allows good adherence of the cells to the material, and may provide an active role in dentin bridge formation (42–44).

However, some limitations that affected the final degree of reliability of the meta-analysis were shown, and these should not be neglected. First, none of the studies included in the present meta-analysis reported rationale for the sample size. A small sample size could decrease statistical reliability and lack adequate evidence. Second, we included 3 retrospective studies that come with inherent shortcomings. Of the remaining 10 RCT studies, 4 studies failed to adequately describe their randomization method, and only 3 studies stressed concealment during allocation. Inadequate allocation concealment leads to exaggerated estimates of treatment effect, on average, but with scope for bias in either direction (45). Third, double blinding of the treatment provided was impossible in each included study because the handling characteristics of the materials were dissimilar, but outcome evaluator blinding was possible. Seven studies reported blinding in their outcome assessment. Fourth, the dropout rate should be less than 5% of the total sample size to ensure the reliability and validity of a study. Dropout may be caused by a number of reasons, such as loss of contact, refusal to participate in the recall examination, and so on. Therefore, more RCTs with a proper sample size and a comprehensive design are needed to further confirm our findings.

## Conclusions

Based on the available information, the results of this meta-analysis allow the conclusion that MTA has a higher success rate and results in less pulpal inflammatory response and more predictable

hard dentin bridge formation than CH. The conclusion proves that MTA is a suitable material for direct pulp capping procedures and argues against the continuing recommendation of CH as the gold standard for such treatments.

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*The authors deny any conflicts of interest related to this study.*

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