MINERAL TRIOXIDE AGGREGATE VERSUS CALCIUM HYDROXIDE IN INDIRECT PULP TREATMENT OF PERMANENT TEETH: A SYSTEMATIC REVIEW.

Marwa Aly¹, Dalia Moheb¹, Osama Elshahawy¹, Ahmed Abd-elsamad² and Mervat Rashed¹.

1. Pediatric Dentistry and Dental public health, Faculty of Oral and Dental Medicine, Cairo University –Egypt.
2. Oral Radiology, Faculty of Oral and Dental Medicine, Cairo University –Egypt.

Background:
The conventional procedure for indirect pulp treatment comprises the application of a bacteriostatic/bactericidal agent, such as calcium hydroxide, over the remaining dentin caries to encourage remineralization and pulp protection (Falster et al., 2002). However, several weaknesses were documented with the use of calcium hydroxide material as: the presence of tunnels in dentin barrier, excessive dentin formation obliterating the pulp chamber, absence of adhesion and solubility in oral fluids (Accorinte et al., 2008). New materials have evolved recently as alternatives to CH because of its fore mentioned disadvantages. MTA became a widespread alternative for CH (Camilleri 2008).

This systematic review aimed to compare the effectiveness of mineral trioxide aggregate (MTA) and calcium hydroxide (CH) in indirect pulp treatment of permanent teeth.

Abstract

Background: Different materials were used in the treatment of deeply decayed vital teeth. For many years, the gold standard for indirect pulp capping procedures was Calcium hydroxide. Nevertheless, the disadvantages reported with its use has led to its replacement with other materials such as mineral trioxide aggregate.

Objective: The purpose of this systematic review is to compare the effectiveness of mineral trioxide aggregate (MTA) and calcium hydroxide (CH) in indirect pulp treatment of permanent teeth.

Methods: Detailed search on PubMed, Web of science, Cochrane Library, Google and Ebsco databases was performed. Studies meeting the criteria for inclusion were accepted, and necessary information was independently extracted by 2 authors by means of a standardized form. Evaluation was done for the success rate and dentin bridge formation.

Results: The inclusion criteria were met in three studies that were processed for data extraction and qualitative assessment.

Conclusions: Due to presence of high risk of bias in the included studies, there is no conclusive evidence on the superiority of one material over the other.
Materials and Methods:

Identifying the review Question:
Firstly, a PICO structure (Patient, Intervention, Comparators, Outcome) was used for the development of the research question as follows:

Patient / Population: Permanent teeth with deep caries.
Intervention: Indirect pulp treatment using Mineral trioxide aggregate
Control/ Comparator: Indirect pulp treatment using Calcium hydroxide.
Outcome measures: success rate and dentin bridge formation.

Research Question:
In deeply decayed permanent teeth, will indirect pulp treatment using CH in comparison to indirect pulp treatment using MTA differ in terms of success rate and dentin bridge formation?

Search Strategy:
In the present study, PubMed, Web of science, the Cochrane Library, Google and Ebsco were used as the electronic databases. The following key words were used: indirect pulp capping, indirect pulp cap, indirect pulp therapy, indirect pulp treatment, MTA, mineral trioxide aggregate, calcium hydroxide and Ca(OH)2. Additional search methods included a manual review of the reference lists of relevant studies.

Figure 1. Flow diagram for the search results.

Inclusion Criteria:
1. Randomized controlled trials (RCTs),
2. Indirect pulp treatment on permanent teeth,
3. Studies comparing mineral trioxide aggregate and calcium hydroxide,
4. The success rate and or dentin bridge formation were recorded.

Data Extraction:
Studies that fulfilled the inclusion criteria were processed for data extraction. Two authors independently extracted the necessary information. The following information were extracted from each study: year of publication, country of origin, study design, informed consent obtained, ethical approval, funding, setting, aim of the study, participants age, numbers and gender, inclusion and exclusion criteria, details of material, methods, restoration, duration of follow up, principal and secondary outcome measures, methods of assessing outcome measures and studies results.

Methodological Quality Appraisal:
Assessment of the quality of included studies was performed using the Cochrane Collaboration’s tool for assessing risk of bias.

Results:

Results Characteristics of Included Studies:
From 62 potentially relevant studies, only 3 studies were eligible (Leye Benoist et al. 2012, Petrou et al. 2014 and Sultana et al. 2016). Two studies reported the success rate (Leye Benoist et al. 2012 and Petrou et al. 2014). The success rate was higher for MTA compared to CH in both studies as follows: (MTA 94.5 %, CH 86.9 %, p =0.72) and (89.6% with MTA, and 73% with CH, P = 0.63). Also, two studies (Leye Benoist et al. 2012 and Sultana et al. 2016) reported the dentin bridge formation. Leye Benoist et al. 2012 showed that at 6 months, there was an increase of 0.235 mm with MTA and of 0.221 mm with CH. No statistically significant difference was found in the dentine thickness between the two groups. While, Sultana et al. 2016 showed that at 12 months' observation period, 24 teeth (96%) of MTA and 19 teeth (76%) of CH with reparative dentin formation.
**Results of Methodological Quality Assessment:**

The three studies were assessed using the Cochrane Collaboration’s tool for assessing risk of bias. Table 4, shows the findings for each risk of bias in each study. All studies revealed randomization, but they failed to define means for random sequence generation and did not sufficiently define allocation concealment. Blinding of the participants and personnel was mentioned in only one study that MTA and CH could be distinguished by the operator and so a double-blind clinical trial was not possible. Regarding the assessments of the outcomes in two studies, there was blinding of the assessor and detection bias was considered low risk. A description of withdrawals and dropouts was given in two studies. Other sources of bias were not found in the three studies.
Table 1: The Characteristics of the Included Studies.

| Reference          | Country of origin | Year of publication | Study design                                                                 | Informed consent obtained? | Ethical approval | Funding | Setting | Aim of study                                                                 |
|--------------------|-------------------|---------------------|------------------------------------------------------------------------------|-----------------------------|------------------|---------|---------|--------------------------------------------------------------------------------|
| Petrou et al. 2014 | Germany           | 2014                | prospective in vivo clinical trial with three parallel treatment arms        | yes                         | The study was approved by the ethical committee at University of Greifswald/Germany | Not mentioned | The dental clinic of Greifswald University and in a private practice. | To compare the clinical and microbiological outcomes of mineral trioxide aggregate (MTA), medical Portland cement, and calcium hydroxide on the dentin–pulp complex of permanent and primary teeth treated with two-step IPT. |
| Leye Benoist et al. 2012 | Senegal          | 2012                | single-blind clinical trial                                                  | yes                         | The study had been approved by the ethics commission of the institution. | The study was not financed by any company or manufacturer and has no commercial aim. | The faculty clinic of the Department of Dentistry, Université Cheikh Anta Diop, Dakar, Senegal. | To assess the effectiveness of mineral trioxide aggregate (MTA) used as an indirect pulp-capping material in human molar and premolar teeth. |
| Sultana et al. 2016 | Bangladesh        | 2016                | prospective comparative study.                                              | yes                         | The proposed study protocol was approved by the Ethical Review Committee, BSMMU | Not mentioned | The Department of Conservative Dentistry and Endodontics, Faculty of Dentistry, BSMMU | To assess the clinical and radiological outcomes of MTA and calcium hydroxide as indirect pulp capping agents in deep carious lesions of permanent teeth. |

Table 2: Data Extraction of the Included Studies (participants and intervention).

| Reference       | Participants | Interventions |
|-----------------|--------------|---------------|
| Petrou et al.   | Eighty-six  | (a) Aqueous suspension of Glass ionomer 6 m |
|                 | 17.2 year    | Three groups  |
|                 | 51           | (a) deep caries lesion with absence of Parti al |
### Table: 2014 Leye Benois et al.

| Year | Type | Number | Age | Gender | Description | Treatment | Study Conclusion | Other Details |
|------|------|--------|-----|--------|-------------|-----------|-----------------|--------------|
| 2014 | teeth | 60 | 16–34 | Male - 26, Female - 34 | Active deep carious lesion on either the occlusal or proximal surface with reversible pulp inflammation. Teeth with periodontal lesions, internal or external root resorptions, and patients with systemic medical conditions, were excluded from the study. | Two groups: (a) calcium hydroxide (b) MTA | MTA (ProRoot; Dentsply/Tulsa Dental, Tulsa, OK, USA) and calcium hydroxide material (Dycal_Ivory, Dentsply Caulk, Dentsply, L.D. Caulk, Milford, DE, USA) | One visit Glass ionomer cement placed during the 6-month evaluation period. The final restoration was either amalgam or composite |

### Table: Leye Benois et al. 2012

| Year | Type | Number | Age | Gender | Description | Treatment | Study Conclusion | Other Details |
|------|------|--------|-----|--------|-------------|-----------|-----------------|--------------|
| 2012 | teeth | 60 paired permanent teeth (30 in each group) | 16–34 years | Male - 34, Female - 26 | Radioluencies at the periapical regions (b) Absence of pulp exposure, fistula, swelling of periodontal tissues, abnormal tooth mobility, and history of spontaneous pain; (c) Healthy appearance of adjacent gingiva; (d) Normal tooth color; (e) Positive vitality. Whereas non-restorable teeth or without functional use were excluded from the study. | Calcium hydroxide | Caries removal on 2 visit s, 6 mont hs interval |

### Table: Sultan a et al. 2016

| Year | Type | Number | Age | Gender | Description | Treatment | Study Conclusion | Other Details |
|------|------|--------|-----|--------|-------------|-----------|-----------------|--------------|
| 2016 | teeth | 50 permanent teeth from 43 patients | 16–30 years | | Permanent teeth having a deep carious lesion closer to but not involving the pulp, having reversible pulp status based on the clinical sign, symptom, and radiograph and could be restorable. | Two groups: (a) calcium hydroxide powder (Deepti Dental Product, India) mixed with normal saline (b) MTA | Calcium hydroxide powder (Deepti Dental Product, India) mixed with normal saline MTA (Proroot, Dentsply, Tulsa Dental, USA) powder mixed with sterile water in a 3:1 ratio. | One visit The base of the cavity was filled with FujiIX glass ionomer cement and restored by composite restoration (Giomer) |
Table 3: Data Extraction of the Included Studies (outcomes and results)

| Reference | Principal and secondary outcome measures | Methods of assessing outcome measures | Results |
|-----------|------------------------------------------|--------------------------------------|---------|
| Petrou et al. 2014 | The success rate -Clinical (color, humidity, and consistency of dentin) -Microbiological (Lactobacilli/Mutans Strep. counts) | -The color of the dentin either: light yellow, yellow, light brown, dark brown, or black. -The consistency of the dentin either: very soft, soft medium hard or hard -The existence of humidity(wet/dry) | The success rate (MTA 94.5 %, Portland cement 90.5 %, CH 86.9 %, χ2-test p =0.72). |
| Leye Benoist et al. 2012 | The success rate and the thickness of the newly formed dentine | -Maintenance of pulp vitality with a normal response to thermal and electrical tests without signs of spontaneous pain. -Dentine bridge formation and no furcation radiolucency, periodontal ligament space widening, internal or external root resorptions. | At 3 months, the clinical success rates of MTA and calcium hydroxide were 93% and 73%, respectively (P = 0.02). At 6 months, the success rate was 89.6% with MTA, and remained steady at 73% with calcium hydroxide (P = 0.63). The mean initial residual dentine thickness was 0.23 mm, and increased by 0.121 mm with MTA and by 0.136 mm with calcium hydroxide at 3 months. At 6 months, there was an increase of 0.235 mm with MTA and of 0.221 mm with calcium hydroxide. |
| Sultana et al. 2016 | Postoperative pain, the vitality of the pulp and formation of reparative dentin | Pain assessment was performed according to VAS (Visual Analogue Scale) system. Pulp vitality was assessed by vitality test. Reparative dentin formation was assessed by means of intraoral periapical radiograph (IOAP). Reparative dentin formation was observed (present/absent) from the radiograph. | In all observation periods, MTA showed more capable of reducing pain and maintain pulp vitality which was statistically significant than that of calcium hydroxide. At 12 months observation period, 24 teeth (96%) of MTA and 19 teeth (76%) of calcium hydroxide showed reparative dentin (formation). |

Table 4: Assessment of the quality of included studies

| Reference | Random sequence generation* | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment. | Incomplete outcome data | Selective reporting |
|-----------|----------------------------|------------------------|----------------------------------------|---------------------------------|------------------------|-------------------|
| Leye Benoist et al. 2012 | High risk                  | High risk              | Participants: unclear Operator: unclear Rad. Assessor: low risk | Clinical assessor: unclear         | Low risk              | Unclear           |
| Petrou et al. 2014 | Unclear                    | Unclear                | Unclear                                | Unclear                          | High risk             | High risk         |
| Sultana et al. 2016 | Unclear                    | Unclear                | Unclear                                | Low risk                         | Unclear              | Unclear           |

**Interpretation:**
The available studies showed a higher success rate for MTA compared to CH. Also, more dentin bridge formation was shown with MTA. Regarding the quality of the investigated studies (Table 4), a high risk of bias was found.
Conclusions:
Due to presence of high risk of bias in the included studies, there is no conclusive evidence on the superiority of one material over the other.

Further, high quality and long span clinical trials for indirect pulp treatment materials are still required to assess the most effective material owing to the high risk of bias and the short-term follow-up in the available studies.

References:
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