Clinical and Radiographic Evaluation of MTA versus Biodentine as Pulpotomy Agents in Immature First Permanent Molars: A Randomized Clinical Trial

Protocol submitted to the Faculty of Dentistry, Cairo University
by

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18 Jan 2017

I. Administrative information:

1. Title:

Clinical and Radiographic Evaluation of MTA versus Biodentine as Pulpotomy Agents in Immature First Permanent Molars: A Randomized Clinical Trial

2. Protocol Registration:

To be registered on Clinicaltrial.gov

3. Protocol version:

Final version.

4. Funding:

This trial is self-funded.

5. Roles and responsibilities:

1. **Dr. Gihan Abuelniel (Abuelniel G.M)** Associate Professor of Pediatric Dentistry, Cairo University. Responsible for the clinical part of study, and Data monitoring.
2. **Professor Monty Duggal (Duggal M.S)** Professor of Pediatric Dentistry, National University of Singapore, responsible for the writing revision and proof reading.
3. **Dr. Nihal Kabel (Kabel N.R)** Associate Professor of Pediatric Dentistry, Misr University for sciences and technology. Responsible for the clinical evaluation of the cases at the evaluation intervals

II. Introduction

6-background and rationale:

Description of research question:

P: children with cariously exposed immature mandibular first permanent molars

I: Pulpotomy using Biodentine

C: MTA pulpotomy

O:

	Outcome	Tool/Device	Unit
Primary Outcome	spontaneous pain, sensitivity to percussion⁄ palpation)	Pain questionnaire	Binary
	Swelling or sinus tract	Visual examination by the third author	Binary
	Mobility	Back of the mirror	Binary
Secondary outcome	Stage of root development	Standardized periapical	3 stages
	Crown: Root ratio	Standardized periapical	2:1 ≥2:1
	Apex	Standardized periapical	Blunder apex, partially open, constricted
	Presence of radiolucency	Standardized periapical	Binary

S: Randomized clinical trial
T: 18 months (Baseline,6, 12 and 18 months)

Research question: is Biodentine used as pulpotomy material in cariously exposed immature mandibular first permanent molars more successful clinically and radiographically than MTA pulpotomy?

Justification for undertaking the trial:

Dental caries and its tremendous effects are considered one of the greatest challenges to the integrity of the developing dentition. Although the debates exist regarding the success rate of vital pulp therapy in cariously-exposed pulps, the technique is recommended to be performed on immature teeth [1,2].

Carious exposures in young permanent molars may cause irreversible damage to the pulp tissue and arrest root development, which can jeopardize the long-term tooth retention [3]. Hence, the main objective of treating carious-exposed immature teeth is to

maintain pulp vitality and enhance continuation of root development and apical closure. This approach is called apexogenesis. [4]

Vital pulp therapies should provide a biologically conductive environment for the pulp tissue to regenerate and prevent future bacterial contamination by using an appropriate pulp-capping agent. [3] The pulp capping material should possess biocompatibility, bactericidal effect, ensure a biologic seal, and induce hard tissue formation. [3,5]

A new era of regenerative endodontics recommended Mineral trioxide aggregate (MTA), to be considered the new gold standard for vital pulp therapies, that provides long-term seal, acceptable biocompatibility [6], and dentinal bridge formation as reported by various animal and human studies. [7,8] When the role of Calcium hydroxide (CH), that has been the most commonly used material for vital pulp therapy for many decades, was diminished, [9] claims raised against its use. The claims were attributed to several disadvantages including the exitance of tunnel defects in induced dentinal bridges, poor adherence to dentine, and lack of long-term seal. [10]

MTA is a powder that consists of fine hydrophilic particles that set in the presence of moisture. The setting time of MTA in moisture is less than 4h. MTA consists of tricalcium silicate, tricalcium aluminate, tricalcium oxide and silicate oxide. [11] MTA was considered a remarkable biocompatible material with various clinical applications that include surgical and non-surgical applications such as pulp capping [12], furcation and Perforation repairs [13], apexification and root end fillings [11,14]. Although the high clinical success of MTA material, there were always Issues prevented the clinicians to use it for many cases. The main reasons were related to very long setting time and difficult manipulation. [15]

Biodentine new bioactive calcium silicate-based cement has been recently launched in the dental market as a 'dentin substitute'. This new biologically active material facilitates its penetration through opened dentinal tubules to crystallize interlocking with dentin and provide mechanical properties. Biodentine has been developed using MTA based cement technology and hence; added improved properties such as physical qualities and handling, and its wide range of recommended applications in endodontic repair and pulp capping. [16]

Radiographic imaging of the dentoalveolar complex has been assessed using conventional periapical radiography, the benchmark for intraoral radiographic imaging for decades. Their known limitations of image magnification, distortion, superimposition and overlap of anatomy always led to unclear and misrepresentation of structures. Although the advent of digital intraoral radiography didn't improve these limitations, it provided a more active image manipulation than the film-based radiographs and reduced patient exposure

substantially. [17, 18]

7 - Objectives and hypothesis:

The objective of this prospective randomized clinical trial is to compare the clinical / radiographic outcomes of MTA and Biodentine as pulpotomy biomaterials used in apexogenesis treatment of symptomatic / asymptomatic vital immature mandibular permanent first molars with carious pulp exposure.

8-Trial Design:

Randomized clinical trial (RCT), parallel groups with 1:1 allocation ratio, Triple blinded (patient, clinical and radiographic assessor of the results and statistician)

III- Methods:

9-Study settings:

This study will be carried out on patients attending the outpatient clinic in Pediatric Dentistry department, Faculty of Dentistry, Cairo University, Egypt. the procedures will be carried out by Dr. Gihan Abuelniel Associate Professor of Pediatric Dentistry in Pediatric Dentistry clinic. expected time duration from 2017 to 2018.

10- Eligibility criteria:

Inclusion criteria:

- Medically free children.
- Bilaterally Symptomatic / asymptomatic vital immature mandibular first permanent molars (with clinical carious exposure of the pulp and presence of bleeding upon exposure)
- Patients with an age range from 7-8 years.
- Absence of sinus tract, soft tissue swelling.

The exclusion criteria:

- Molars were excluded if non-restorable.
- excessive mobility (more than 1 mm horizontally).
- Radiographic evidence of peri- and /or inter-radicular lesions, internal/ external root resorption, pulp/ canal calcifications.

IV- Intervention:

Diagnosis:

1. Full history data will be collected, including personal, medical and previous dental data
2. Clinical examination using mirror and probe to assess the inclusion criteria.
3. Radiographic examination using preoperative digital periapical radiograph to assess the inclusion criteria.
4. Preoperative photograph will be taken.

Operative procedure:

Experimental group:

1. Injection of local anesthesia and rubber dam isolation.
2. caries and roof of the pulp chamber will be removed by a fissure diamond bur (Diatech, Heerbrug, Switzerland) and high-speed handpiece with coolant.
3. The pulps will be amputated to the orifice level using a long-shank diamond round bur.
4. Haemostasis will be achieved by gentle placement of a saline-moistened cotton pellet over amputated pulps for 5–10 min.
5. Calcium silicate-based Biodentine™ (Septodont Ltd., Saint Maur des Fausse´s, France) will be mixed according to the manufacturer's instructions, radicular pulp will be covered by the material using a wet cotton pellet.
6. A self-cure glass ionomer (GC; GC Corporation, Tokyo, Japan) will be placed over the pulpotomy agent as a final restoration.
7. Immediate post-operative radiograph and photograph will be taken.

Control group:

The same procedures will be carried out as the experimental group, but the pulp stumps will be covered with fast-setting mineral trioxide aggregate (MTA) ENDOCEM MTA (Maruchi, Wonju, Korea) and will be prepared according to the manufacturer's instructions. A 3-mm-thick layer of MTA will be placed over the amputated pulps and will be gently adapted to the dentinal walls using a wet cotton pellet. A self-cure glass ionomer (GC; GC Corporation, Tokyo, Japan) will be placed over the pulpotomy agent as a final restoration.

Postoperative care:

Instructions to avoid lip and cheek biting in addition to oral hygiene measures.

Follow up:

Assess the outcomes clinically and radiographically at (baseline, 6, 12 and 18 months).

<u>Criteria for discontinuing or modifying intervention:</u>

In case of an unsuccessful outcome after pulpotomy, the molars will be managed by other pulp therapy techniques or extraction.

Strategies to improve adherence to intervention:

Explanation to the parents about the importance of follow up visits in addition to treatment of other dental problems.

Concomitant care:

None needed.

12- Outcomes:

	Outcome	Tool/Device	Unit
Primary Outcome	spontaneous pain, sensitivity to percussion/ palpation)	Pain questionnaire	Binary
	Swelling or sinus tract	Visual examination by the third author	Binary
	Mobility	Back of the mirror	Binary
Secondary outcome	Stage of root development	Standardized periapical	3 stages
	Crown: Root ratio	Standardized periapical	2:1 ≥2:1
	Apex	Standardized periapical	Blunder apex, partially open, constricted
	Presence of radiolucency	Standardized periapical	Binary

Primary outcome:

Clinical assessment of the findings in the table will be conducted at follow up intervals (baseline, 6, 12 and 18 months)

Secondary outcome:

Radiographic assessment of stage of root development, crown: root ratio, apical closure and presence of radiolucency will be conducted through digital periapical radiographs by parallel

technique using film holders. The assessments will be carried out at follow up intervals (baseline, 6, 12 and 18 months)

13- Participants timeline:

	Study period				
	Enrolment	Allocation	Post allocation		Close out
Time point	For 7 months	0	6 months	12 months	18 months
Enrolment:					
Eligibility screen	√				
Informed consent	√				
History taking	√				
Clinical examination	√				
Preoperative radiograph	√				
Allocation		√			
Interventions:					
Access preparation		√			
Placement of Biodentine (experimental group)		√			
Placement of MTA (Control group)		√			
Final restoration		√			
Assessment					
Periapical radiograph as baseline reference			√	√	√

Clinical examination to assess pain, swelling, fistula, tooth mobility			√	√	√
Periapical radiograph to assess stage of root development, crown: root ratio, apical closure and presence of radiolucency			√	√	√

14- Sample size calculation:

Sample size is calculated based upon the results of Alqaderi et al (2014) [15] who reported clinical success rate (primary outcome) for MTA = 90%. Since no relevant literature reported the clinical success rate of Biodentine in permanent teeth of pediatric patients, the success rate was assumed to be 50%. Using alpha level = 0.05 and β level = 0.20 (80% Power); the minimum estimated sample size will be 20 subjects per group for a total of 40 subjects. To compensate for a drop-out rate of 15%, the number is increased to 23 subjects per group for a total of 46 subjects.

Sample size calculation was performed using IBM® SPSS® Sample Power® Release 3.0.1.

15- Recruitment:

All patients attending the outpatient clinic in pediatric dentistry department complaining from carious mandibular first permanent molars will be screened and enrolled in the study if they meet the eligibility criteria.

16- Allocation:

Sequence generation:

Access cavity prepared molars will be assigned into experimental or control group using simple randomization 1:1 by the help of the computer software(random.org).

Allocation concealment mechanism:

Numbered opaque sealed envelopes.

Implementation:
The child will choose an envelope randomly and open it after caries removal so that the operator knows which pulpotomy agent will be used only after finishing the access cavity. Sequence generation will be done by the third author and the patient assignment will be done by the operator.

17- Blinding:

Patients and their parents, the assessor and the statistician will be blinded.

18- Data collection methods:

Primary outcome:

Clinical assessment of the following findings:

1. postoperative pain: through asking the child and the parent if there is pain either continuous or intermittent
2. Swelling: through visual examination by the assessor either intraorally or extra-orally.
3. Sinus or fistula through visual examination of the gingiva by the assessor.
4. Tooth mobility: By the back of the mirror checked by the assessor to detect mobility in any direction

This assessment will be conducted every follow-up visit throughout the study period at baseline, 6, 12 and 18 months.

Secondary outcome

Radiographic assessment to detect stage of root development, crown: root ratio, apical closure and presence of radiolucency through standardized periapical radiograph by parallel technique using film holder. This assessment will be conducted every follow-up visit throughout the study period at baseline, 6, 12 and 18 months.
Postoperative records will be performed by the assessor to avoid individual variability and to promote data quality.

19- Data management:

Explanation to the parents about the importance of the follow-up visits in addition to treatment of other dental problems are plans to promotes participants retention and complete the follow-up. Also, phone calls before the dates before the next follow-up visit will be scheduled.
All findings will be documented in the examination sheet then transferred electronically to computer in secured lace sequentially.

20- statistical methods:

All data will be collected, checked, revised, tabulated and entered into the computer. Qualitative data will be presented as frequencies and percentages. Since the study is a split-

mouth design; Wilcoxon signed-rank test will be used to compare between the two groups. Friedman's test will be used to study the changes by time within each group. Kaplan-Meier survival curve will be constructed to calculate the mean survival estimates of the two groups. Comparison between survival times will be performed using Log rank test.

The significance level will be set at $P \leq 0.05$. Statistical analysis will be performed with IBM® SPSS® Statistics Version 20 for Windows.

21-Monitoring:

The study data and results will be monitored regularly by the assessor who will have full access to these data.

22- Harms:

No reported adverse effects for both testing pulpotomy agents. Any adverse events appear during the trial will be recorded, documented and treated.

23-Auditing:

Auditing of the study design will be done by the evidence-based committee, Faculty of Dentistry -Cairo University.

V- Ethics and dissemination:

24-Research ethics approval:

This protocol and the template informed consent form will be reviewed by the Ethics Committee of Scientific Research - Faculty of Oral and Dental Medicine - Cairo University.

25-Protocol amendments:

Any modification to the protocol which may have an impact on the conduction of the study, potential benefit of the patient or my affect patient safety including, the changes of study objectives, study design, sample size or significant administrative aspects will require a formal amendment to the protocol.

26-Consent and Assent:

Researcher will discuss the trial with legal guardian of each participating child. They will be able to have an informed discussion with the researcher after explaining the procedure in simple words. Verbal assent will be taken orally from the participating child while written consent will be taken from the legal guardian f each participating child who is willing to participate in the

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® IBM Corporation, NY, USA.

® SPSS, Inc., an IBM Company.

trial. All consent forms will be translated into Arabic.

27-confidentiality:

All study related information will be stored securely. All participants information will be stored in locked file cabinets in an area with limited access. Process and administrative forms will be identified by a coded ID (identification number) only to maintain participants confidentiality. All records that contain names or other personal identifiers will be store separately from study records identified by code number

28-Declration of interests:

Non-financial.

29- Access to data:

All principal investigators will be given access to the data sets. All data sets will be password protected. To ensure confidentiality, data dispersed to study team members will be blinded of any identifying participants information.

30-Ancillary and post-trial care:

Full mouth treatment will be offered to all participating children in addition to postoperative care and preventive measures though regular follow up visits after the end trial.

31- Dissemination policy:

-Study results and articles will be published in related journal.

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