Clinical and Radiographic Evaluation of Pulpotomy Technique for Preserving Vitality of Traumatized Anterior Permanent Immature Teeth: A Randomized Clinical Trial

Protocol submitted to the Faculty of Dentistry, Cairo University

by

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I. Administrative information:

1. Title:

Clinical and Radiographic Evaluation of Pulpotomy Technique for Preserving Vitality of Traumatized Anterior Permanent Immature Teeth: 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 vital traumatized exposed immature maxillary permanent incisors

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	4 stages
	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 vital traumatized exposed immature maxillary permanent central incisors more successful clinically and radiographically than MTA pulpotomy?

Justification for undertaking the trial:

The occurrence of dental trauma in permanent teeth is a common event worldwide [1]. Children and adolescents are most frequently affected, and two-thirds of all dental trauma are found among these populations [1,2]. with the anterior permanent teeth being the most affected [1, 4-6].

Traumatic injuries affecting teeth may result in pulpal and periapical disease. Complicated crown fractures which involve the enamel, dentin and pulp occur in 0.9 - 13% of all dental injuries [2,3]. Vital pulp therapy (VPT) is the treatment of choice for traumatized immature teeth with pulp exposure [5,6]. VPT aims for continuation of root development, which leads to apical closure and strengthening of the root structure [7]. If the pulp vitality of a traumatized immature tooth is lost,

endodontic treatment will constitute a real challenge. It is difficult to obtain an appropriate apical seal in these teeth by using the conventional obturation methods. Furthermore, thin root canal walls make the teeth susceptible to future fractures [8].

Primary objective of pulp therapy is to maintain the integrity and health of the teeth and their supporting tissues and to preserve vitality of the tooth pulp, especially in young permanent teeth with immature roots, where the pulp is integral to continue apexogenesis. Long term retention of a permanent tooth requires a root with a favorable crown/ root ratio and dentinal walls that are thick enough to withstand normal function. therefore, pulp preservation is a primary goal for treatment of the young permanent dentition. [9]

In modern dentistry, vital pulp therapy (VPT), whenever feasible, should be considered as an effective reasonable alternative to endodontic treatment [10]. In clinical practice, VPT includes stepwise excavation, pulp capping (direct and indirect) and pulpotomy (miniature, partial and complete), based on the amount of preserved coronal pulp [11]. The main goal of these conservative methods is to maintain the normal pulp or remove contaminated pulpal tissue in order to promote the repair process [9-11]. Therefore, immature teeth eventually gain additional benefit from VPT, considering their weak structural nature [11].

Vital pulp therapy has been increasingly considered as a minimally invasive approach for the management of teeth with inflamed pulps compared to the conventional approach of root canal treatment [12,13]. Among the factors that contributed to this choice are (1) the high frequency of technically inadequate root fillings and associated apical periodontitis despite new technologies in root canal preparation and filling , (2) the numerous advantages of VPT in terms of preserving tooth structure ,maintaining possible proprioceptive defensive mechanisms of the remaining pulp, and reducing the propensity of tooth fracture, (3) comparable success rates of VPT compared to RCT over five years of follow-up [6,7] .

Traditionally Ca $(OH)_2$ has been used for VPT for many years [14]. Recently MTA has replaced Ca $(OH)_2$ due to its ability to form an apatite-like layer, its

biocompatibility and its lack of cytotoxicity [15]. MTA due to its, biocompatibility and its ability to form cementum attachment has not only been used as a root-end filling material but also has been used as in pulpotomy, apexification, direct pulp capping and as a perforation repair material but has some drawbacks like handling property, high cost, long setting time and discoloration [14].

A magical capsule to overcome the limitations of MTA raised in the dental field called (Biodentine) [15]. It is considered a calcium silicate cement that was introduced as a 'dentine replacement' material, comparable to MTA in terms of biocompatibility and induction of a calcific barrier [16]. It possessed additional improvement of several properties such as mixing, handling, shorter initial setting time (12 min, with reports from 6.5–45 min) and less coronal discoloration [13].

Limited clinical data were available on the use of Biodentine in VPT; recently only three clinical trials compared Biodentine to MTA as pulp capping materials for cariously exposed teeth with high success rate approaching 100% at 1-year follow-up in young patients. [16] In a case report, Biodentine was successful in pulpotomy of traumatized permanent incisors at 48 months of follow-up [17,18].

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. [19, 20]

7 - Objectives and hypothesis:

The objective of this prospective randomized clinical trial is to compare the clinical and radiographic outcomes of MTA and Biodentine as vital pulp therapy materials (pulpotomy) preserving the vitality of traumatized immature anterior permanent teeth.

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

- The patient age range 7.5-9 years.
- Noncontributory medical history
- Unilateral/ and or bilateral central incisors tooth with complicated trauma (exposure size ≥ 1mm)
- The tooth should give positive response to cold testing
- Clinical diagnosis of reversible pulpitis without periapical rarefaction
- The tooth is restorable, mobility was within normal limits
- No signs of pulpal necrosis including sinus tract or swelling

Exclusion criteria

- Teeth with mature roots
- Signs and symptoms of irreversible pulpitis
- Non-restorable teeth
- Negative response to cold testing, the presence of sinus tract or swelling
- No pulp exposure
- Bleeding could not be controlled after full pulpotomy in 6 minutes

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. 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 before final restoration of composite resin (Clearfil™, Kuraray, New York, USA) will be done.
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 white mineral trioxide aggregate (MTA) ProRoot® MTA (Dentsply/ Johnson City, TN, USA) will be used as the reference material for comparison 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 deep onto the radicular pulp. A self-cure glass ionomer (GC; GC Corporation, Tokyo, Japan) will be placed over the pulpotomy agent before final restoration of composite resin (Clearfil™, Kuraray, New York, USA) will be done.

Postoperative care:
Instructions to avoid lip biting in addition to oral hygiene measures.

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

Criteria for discontinuing or modifying intervention:

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

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	4 stages
	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, 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 9 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 and presence of radiolucency			√	√	√

14- Sample size calculation:

Sample size is calculated based upon the results of Alqaderi et al (2014) [21] 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 will be performed using IBM® SPSS® Sample Power® Release 3.0.1.

15- Recruitment:

All patients attending the outpatient clinic in pediatric dentistry department complaining from traumatized immature permanent maxillary central incisors will be screened and enrolled in the study if they meet the eligibility criteria.

16- Allocation:

Sequence generation:

Access cavity in traumatized central incisors 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 access preparation so that the operator knows which pulpotomy agent will be used. 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 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. Quantitative data will be presented as mean and standard deviation values. Chi-square test and Fisher's Exact test will be used for comparisons regarding qualitative data. Student's t-test will be used to compare between mean age values in 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 of each participating child who is willing to participate in the 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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