A comparative Clinical and Radiographic Study of Collagen based Pulpotomy Versus Biodentine Pulpotomy in Children with cariously exposed Vital Primary Molars A Randomized clinical trial

Protocol submitted to The Faculty of Dentistry, Cairo University
for partial fulfillment of the requirements for the Master'sDegreein Pediatric Dentistry

By:

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Code:

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Protocol checklist

Section and topic	Item no.	Checked item	Reported on page No.	Reviewer's check
I. Administrative information	1	Title	4	
	2	Protocol registration	4	
	3	Protocol version	4	
	4	Funding	4	
	5	Roles and responsibilities	4	
II. Introduction				
A) Background and Rationale	6 a	Research question	5	
		Statement of the problem	5	
		Rationale for carrying out the trial	5&6	
	6 b	Review of literature	6	
B) Objectives	7	Aim of the study	7	
		Hypothesis	7	
C) Trial design	8	Trial design	8	
III. Methods				
A) Participants, interventions & outcomes	9	Study setting	8	
	10	Eligibility criteria	8	
	11	Interventions	9&10	
	12	Outcomes	10	
	13	Participant timeline	10&11	
	14	Sample size	11	
	15	Recruitment	11	
B) Assignment of interventions	16	**Allocation**	11	
	16 a	Random sequence generation (Randomization)	11	
	16 b	Allocation concealment mechanism	11	
	16 c	Implementation	11&12	
	17	Blinding (masking)	12	
C) Data collection, management, and analysis	18	Data collection methods	12	
	19	Data management	12	
	20	Statistical methods	12	
D) Monitoring	21	Data monitoring	12	
	22	Harms	12	
	23	Auditing	13	
IV. Ethics and dissemination	24	Research ethics approval	13	
	25	Protocol amendments	13	
	26	Informed Consent	13	
	27	Confidentiality	13	

	28	Declaration of interests	13	
	29	Access to data	13	
	30	Ancillary and post-trial care	14	
	31	Dissemination policy	14	
V. Appendices	32	Informed consent materials	14&15	
	33	Biological specimens		
VI. References			17	

Evidence based committee (Reviewers)		
Name	**Signature**	**Date**
1.		
2.		
Research plan committee		
Name	**Signature**	**Date**
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2.		

I.Administrative information:

1. Title:

A comparative Clinical and Radiographic Study Of Collagen based Pulpotomy Versus Biodentine Pulpotomy in Children with Cariously exposed Vital Primary Molars.
A Randomized Clinical Trial.

2. Protocol Registration:

Protocol will be registered on clinicaltrials.org

3. Protocol version: 1

4. Funding:

The proposed clinical trial is self-funded.

5. Roles and responsibilities:

Nihal Alaa Eldin Bayoumi: Department of Pediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Cairo University.

- Performs the clinical trial.
- Ensures participants' adherence throughout the trial.
- Collects the baseline data, results, interpretation and conclusions.
- Provide proper ancillary and post-trial care for all participants.
- Write the thesis.

Main supervisor & scientific advisor:

Prof.Dr. Eman El Masry: Professor of Pediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Cairo University.

- Monitors the whole process from the beginning of the trial and data collection.
- Assesses the final results and data collected from the study.
- Revises the thesis.

Co-supervisor:

Dr. Passant Nagi: Lecturer of Pediatric Dentistry and Dental Public HealthDepartment, Faculty of Dentistry, Cairo University.

- Helps developing the protocol.
-Generates a random sequence to enroll the participants and undergoes proper allocation concealment, implementation, and access to the final data.
-Monitors the process of data collection and checks if there are any harms to the participants.
- Revises and helps in writing the thesis.

II. Introduction:

A) Background and rationale:

6.a. Research question:

In a child with cariously exposed vital primary molars, would it be better to use Collagen based pulpotomy or Biodentine based pulpotomy in terms of clinical and radiographic success of the pulpotomy procedure?

6.a. Statement of the problem:

Pulpotomy of vital primary molars is indicated when caries removal results in pulp exposure. Treatment approaches consist of devitalization using formocresol, preservation using ferric sulfate and regeneration of the remaining pulp tissue using mineral trioxide aggregate and recently Biodentine have been utilized. The ideal pulpotomy medicament would be biocompatible and bactericidal, in addition, to promoting the healing of the root pulp and be compatible with the physiological process of root resorption. (1)

Searching for more pulpotomy agents, Collagen, a protein that's present abundantly in humans, is an important component of connective tissues and performs multiple functions including wound healing.

Enamel and dentin contain Collagen as one of the components in their organic ground matrix.

Collagen has been used widely in dentistry in periodontal and implant therapy as scaffold for preventing the migration of epithelia cells and encouraging wound repopulation by cells with high regenerative potential. (2)

The Collagen available for dental implication is already sterilized and also reinforced with antibiotic particles to efficiently aid in regeneration and repair without any contaminations. The collagen particles can be sterilized by various methods like irradiation, dry heat, and ethylene oxide, among which irradiation is the most frequently used method as it does not affect the structural stability. (3)

6.a. Rationale for carrying out the trial:

There is insufficient evidence on the outcome of pulpotomies in carious exposed young permanent molars with newer biomaterials.

Searching for new and alternative pulpotomy materials with higher clinical efficacy and minimum secondary (adverse) effects.

Dental caries has a higher prevalence rate in children, especially in mixed dentition period due to their diet pattern change or lack in maintaining proper oral hygiene. In the case of dental caries with pulpal involvement, preserving the natural tooth by pulp therapy until its time of exfoliation is a vital aim in pediatric dental management, as they are said to be the best space maintainers. Among different pulp therapy strategies, vital pulpotomy is the topic of interest in this study.

By definition, a pulpotomy is defined as partial removal of the pulp (coronal potion) and leaving radicular pulp intact, after establishing effective hemostasis, restoration with biocompatible materials.(4)

Benefits for the practitioner:

- providing new and alternative treatment options.
- Less technique sensitive.
- Easier application of the material during pulpotomy that eliminates hand mixing (auto-mix).
- Improved chairside delivery owing to its better consistency and adequate working time.

Benefits for the patient:

- A faster and easier process leading to a more efficient dental procedure which could develop better outcomes in terms of success.
- A more comfortable dental procedure to improve patient as well as parent satisfaction.

Benefits for community:

- Using alternative material that can be more cost effective, affordable treatment for children thus saving more primary teeth.
- To boost overall oral health.

6.b. Review of literature:

Pulpotomy is considered the gold standard procedure for treating cariously exposed pulps in asymptomatic primary teeth. Which is based on the healing ability of the radicular pulp tissue following amputation of the infected coronal pulp. (5)

Mineral trioxide aggregate (MTA) has been recommended as the gold standard for vital pulp therapy; however, it has some disadvantages, such as long setting time, poor handling properties, high cost, and the potential for tooth discoloration. Biodentine (Septodont, Saint-Maur-des-Fossés, France), one of the new-generation, bioactive endodontic cements, has been claimed to have improved properties over MTA.
Biodentine presents high biocompatibility with the dental pulp, it has high antibacterial effects and antifungal activity, has a shorter setting time than MTA as a result of the calcium chloride in the liquid component of Biodentine. It also has higher flexural strength, compressive strength and modulus of elasticity than MTA.
Consequently, Biodentine can be used as a pulp dressing as well as a base material. (6)

Quest is on for newer pulpal medicaments that are biocompatible and capable of healing the dental pulp by producing reparative dentin and/or dentinal bridge in response to various stimuli and surgical exposure.
Collagen has a proven rate of success in the field of dentistry as guided tissue regeneration, root conditioning, hemostatic, and wound dressing agent. It has inherent properties like low immune response and toxicity, ability to promote cellular growth and attachment, homeostasis, and added advantage of antibiotic incorporation. (7)

7. Objectives:

Aim of the study

To assess clinical and radiographic success after collagen based pulpotomy versus Biodentine pulpotomy in children with cariously exposed vital primary molars.

Hypothesis:

Null hypothesis: No added benefits will be gained from the collagen based pulpotomy clinically and radiographically.

PICO approach:

P: Population: Children 4-7 years with carious vital primary molars.
I: Intervention: Sterile medicated Collagen particles.
C: Control: Biodentine.
O: **Outcome:**

Outcome		Method of measurement	Unit
1ry outcome: Clinical success	**1- Absence of internal root resorption**	Periapical X-ray (parallel technique)	Binary
2ry outcome:	**1- Absence of pain**	Questioning the patient	Binary
	2- Absence of swelling	Visually by intraoral and extraoral examination	Binary
	3- Time elapsed till final restoration performed	Stopwatch	Continuous outcome measured in minutes

(S) Study design: Randomized controlled.

(T) Time of follow up:6 months.

8. Trial design:

Randomized controlled trial (R.C.T).

III. Methods

A) Participants, interventions & outcomes:

9. Study settings:

This study will be carried out on patients attending the out-patient clinic in Pediatric Dentistry and Dental Public Health Department-faculty of Dentistry, Cairo University, Egypt.
The procedure will be carried out by postgraduate student Nihal Bayoumi, B.D.S(2014)-Pharos University in Alexandria (PUA) and without an assistant.

10. Eligibility criteria:

Inclusion criteria:

- Children:

1- Aged 4 to 7, in good general health and medically free.
2- Cooperative patients who will comply to follow ups.
3- Parents provided with written informed consent.

- Teeth:

1- Bilaterally Carious vital primary molars with reversible pulpitis.
2- Restorable teeth with no more than 1/3 of root resorption.

Exclusion criteria:

- Children:

1- Children with medical, physical, or mental conditions.
2- Unable to attend follow up visits.

- Teeth:

1- Primary molars with any congenital anomalies.
2- Previously accessed teeth.
3- At operative procedure, haemorrhage control is unachievable after pulpotomy.

11. Interventions

The principal investigator will carry out all treatment procedures, using the split mouth technique, meaning that both groups (I & II) will be in the same patient.

For both interventions:

1.Informed consent from participating parents.

2.Baseline records photographs, percussion test, periapical radiograph, and personal data collection (Appendix 1: Diagnostic chart).

3.Allocation (concealed by withdrawing a sealed opaque envelope containing eight times folded paper containing the type of dressing material that will be used then writing patient name and ID on it and will be opened after performing the access cavity).

4. Diagnostic chart with personal, medical, and dental history will be filled (Appendix 1: Diagnostic chart).

5. Clinical examination will be performed to assess the clinical inclusion criteria. (Pulpal and periapical diagnosis is established after clinical examination).

6. Preoperative and Postoperative photographs will be taken.

7. The radiographic examination will be performed by taking periapical x-ray using (parallel technique) through machine to assess the inclusion criteria. The preoperative radiograph will serve as a reference for the follow-up radiographs. Standardization of the technique to avoid any distortion in the vertical dimension and to provide reproducible images using x-ray holding device.

8. Preoperative and postoperative radiograph will be taken by parallel technique using XCP film holder (Super Bite, Hawe Neos DentalSA, Switzerland).

9. Administration of inferior alveolar nerve block (Septodont, Scandonest® 2% L Mepivacaine HCl. 2% and Levonordefrin 1:20,000 Injection, U.S.P.) at the side of the affected tooth.

10. Application of rubber dam for isolation, then a standardized pulpotomy procedure will be performed using a large sterile round end bur in a high-speed handpiece with copious irrigation, a sharp spoon excavator will remove pulpal tissues to the orifice level. Hemostasis will be achieved by the application of a wet cotton pellet to achieve complete hemostasis.

11. Children will then be allocated into either one of the groups alternatively depending on the pulpotomy medicament used as follows:

Group I (Experimental group) collagen based pulpotomy.

Group II (Control group) Biodentine pulpotomy.

Group I (Experimental group) collagen based Pulpotomy:

1. Collagen based pulpotomy will be applied (sterile medicated collagen particles, Biofil-AB ,Eucare Pharmaceuticals Pvt. Ltd, Chennai, India)according to the manufacturer's instructions and gently placed over the pulp stumps to a thickness of 2 mm.

Group II (Control group) Biodentine pulpotomy:

1.Biodentine (Septodont, Saint-Maur-des-Fossés, France)will be applied according to the manufacturer's instructions and placed over the radicular pulp with the help of a suitable sterile amalgam carrier.

Gentle condensation of the mix will be done in the pulp chamber with a moistened cotton pellet.

12. For both groups;
The rest of the pulp chamber will be filled with glass ionomer cement.
Tooth will then be restored with stainless steel crown (3M ESPE, St Paul, MN, U.S.A.).

12. Outcomes:

Primary outcome:

Absence of periapical radiolucency and internal/ external root resorption (Binary outcome detected with periapical x-ray by Parallel technique using XCP film holder (Super Bite, Hawe Neos DentalSA, Switzerland).

Secondary outcome:

1- Survival rate (absence of any complication or complementary treatment) in terms of:

1-Absence of spontaneous pain. (Binary outcome measured with direct questioning to the patient).
2-Absence of swelling. (Binary outcome measured visually by intraoral/extraoral examination).

2- Time elapsed till final restoration performed.

13. Participant timeline:

Patients will be diagnosed to determine whether they are eligible for the inclusion criteria of this study or not. Eligible patients will then start their treatment on the same visit.

		STUDY PERIOD				
		Enrolment	Allocation	Treatment visit	Post-treatment	Close-out
TIMEPOINT		-t1	0	0	T1 (3m)	T2 (6m)
ENROLMENT:						
Eligibility screen and patient selection		X				
Informed consent from participating pts		X				
Allocation (concealed in closed white envelop)		X				
INTERVENTIONS:						
The pulpotomy procedure (gaining access to the pulp)			X			
Allocation of the patient to one of the treatments groups (open the closed white envelope)			X			
Application of pulp dressing material (collagen and Biodentine)				X		
Final restoration				X		
ASSESSMENTS:						
baseline variables	1- photographs	X		X	X	X
	2- percussion test	X		X	X	X

	3- preoperative periapical radiograph	X				
	4- personal data	X				
outcome variables	Calculation of time-elapsed till final restoration			X		
	Questioning the patient about the absence of spontaneous pain	X			X	X
	Visual examination of patient to check the absence of sinus or Swelling	X			X	X
	Periapical radiograph to check the absence of periapical radiolucency, internal/ external root resorption	X		X	X	X

14. Sample size:

Sample size will be calculated.

15. Recruitment:

Patients attending the out-patient clinic in the pediatric dentistry department- Cairo University, having bilateral carious lower molars will be carefully assessed for eligibility to participate in our study by one of the main investigators Nihal Bayoumi, then a full explanation of the nature of our experiment and the importance of maintaining this primary tooth and restoring it for proper functions and the drawbacks of extracting it. Full mouth treatment will be offered for them.

B) Assignment of interventions:

16. Allocation:

16a. Random sequence generation (Randomization):

Teeth that will be included in the current trial will be randomly assigned one of the experimental groups using closed white envelopes (simple randomization 1:1 ratio).

a) Sequence generation:

By shuffling the envelops then selecting envelop for each patient upon their enrolment.

b) Allocation Concealment:

Using 8-time folded paper on which dressing material was written contained in the closed white envelope.

c) Implementation:

When a patient agrees to participate in the trial, an envelope will be drawn by one of the residents present at the clinic and name, telephone number and patient's ID will be written on it. Those selected envelops will be opened at treatment visit after performing pulpotomy to choose which material should be used.

Randomization and allocation concealment will be performed by the co-supervisor to avoid selection bias.

17. Blinding:

The blinding is not possible (unfortunately) due to the nature of the trial.
Trial participants, outcome assessors and statistician will be blinded.

C)Data collection, management, and analysis:

18. Data collection methods

Baseline data collection

Plans for assessment and collection of outcomes will be at 3 and 6 months clinically (using visual examination, palpation, and percussion test with back of the mirror) and 0 and 6 months radiographically (using periapical radiograph) and will be done by two blinded assessors independently, and differences will be solved by consensus. To promote data quality, duplicate measurements by the same examiner (intra-examiner agreement) and training of assessors (inter-examiner agreement) will be done.

19. Data management:

Data will be recorded on a diagnostic chart for each patient separately and will be stored with follow up periapical radiographs.

20. Statistical methods:

Clinical and radiographic outcomes will be submitted for statistical analysis by the Statistical Package for Social Science (SPSS) program windows version 13. Results will be calculated using risk reduction (R.R.).

D) Data monitoring:

21. Monitoring

The study work results will be monitored regularly by the supervisors who will have full access to these interim results make the final decision to terminate the trial.

22. Harms

- **Bur breakage:** the bur will be replaced by a new one and treatment will be proceeded.
- **Perforation of pulpal wall or floor:** The tooth condition and size of perforation will be assessed whether the treatment will be to repair the perforation and treatment will be proceeded (the tooth will be removed from the trial) or the tooth will be extracted, and space maintainer will be performed
- **No reported hypersensitivity from both tested materials.**
- **Failure of pulpotomy procedure**: retreatment of the tooth through partial pulpectomy and tooth will be removed from the trial.

23. Auditing

The study supervisors will regularly assess the trial process and documents. They will be involved in participant enrolment, consent, eligibility and allocation to study groups, adherence to trial interventions and policies to protect participants, including reporting of complications and their treatments.
Clinical procedures will be performed under their supervision.

IV. Ethics and dissemination

24. Research ethics approval:

This protocol, the template and specific informed consent forms (local language and English versions) will be reviewed, approved, and agreed upon by the (Research Ethics Committee) will review all the nature of interventions and will have the right to modify the study methods.

25. Protocol amendments:

The Ethics Committee will be notified of any administrative changes or modifications of the protocol. Any required changes during the trial period for the patient's own interest that might affect the conduct of the study, including changes of the study objectives, study design, patient population, sample sizes, intervention procedures will require a formal amendment to the protocol. Such amendment will be agreed upon by the Council of the Department of Pediatric Dentistry, Faculty of Dentistry, Cairo University.

26. Informed consent:

The investigator will discuss the trial with the legal guardian of each participating child:

- Verbal permission will be taken orally from participating child.
- Written informed consent will be taken from the legal guardian of each participating child willing to participate in the trial. The consent form will be written in Arabic.

27. Confidentiality:

All data, information, participant's personal information, family history, social and medical history will be stored in the files assigned to each patient with limited access to a minimum number of individuals necessary for quality control, audit, and analysis.

28. Declaration of interest:

This study is a part of a master's degree in Pediatric Dentistry, Faculty of Dentistry, Cairo University. No financial conflict of interests is confirmed. The study is self-funded by the principal investigator.

29. Access to data:

The investigator will be given access to data sets. All data sets will be password protected. To ensure confidentiality, data dispersed to project team members will be blinded of any identifying participant information.

30. post-trial care:

The investigator will offer full mouth treatment, post-operative care, and preventive measures to all participants.

31. Dissemination policy:

The Thesis defense will be done as the study is a part of the requirements for a master's degree in Pediatric Dentistry. Also, the results of the study will be published in Journals.

V. Appendices

Appendix 1: Chart filled for each patient in this trial:

Patient name:
Patient ID:
Tested material:
Age:
sex:
Address:
Telephone:
Chief complain of the patient:
Pretreatment medications:
Participating tooth:
Date of material application:

Follow up		1ry outcomes assessment clinical assessment (survival rate)		2ry outcomes assessment Radiographic assessment			Final assessment "success orfailure"
Time after	Date	1- Spontaneous pain	2- Swelling	3- Internal root resorption	4 - External root resorption	5- Periapical radiolucency	
3m	/ /20						
6m	/ /20						

VI. References:

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