A Preliminary Report of a Randomized Controlled Clinical Trial Comparing Ferric Sulfate With Zinc Oxide Eugenol and Non-eugenol Based Materials for Pulpotomy in Primary Molar Teeth

Balal, S[1] , Dhar, V. [2] , Carrico, C. [3] , Jayaraman, J. [4]

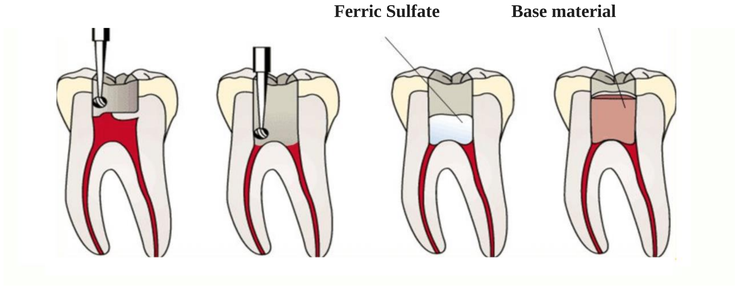
[1] Pediatric Dentistry Resident, Virginia Commonwealth University, Richmond, VA. [2] Department of Orthodontics and Pediatric Dentistry, School of Dentistry, University of Maryland, Baltimore, Maryland . [3] Department of Dental Public Health and Policy, Virginia Commonwealth University, Richmond, Virginia. [4] Department of Pediatric Dentistry, School of Dentistry, Virginia Commonwealth University, Richmond, Virginia.

Abstract

- **Objective:** This randomized controlled clinical trial aimed to evaluate the effect of eugenol and non-eugenol- based Zinc Oxide Eugenol (ZOE) cements on primary tooth pulpotomies where Ferric Sulfate (FS) is used as a medicament.
- **Methods:** Children aged 3-7 years with dental caries in their primary molars that have clinical and radiographic diagnosis of reversible pulpitis and undergoing dental treatment under Oral Conscious Sedation (OCS) or General Anesthesia (GA) were recruited. Children were randomly assigned to receive either FS and ZOE or FS and non-eugenol base material. The outcomes were failure rates based on clinical or radiographic evidence of pulp degeneration, pathologic mobility, swelling or fistula, spontaneous pain, tenderness to percussion or palpation, internal root resorption, inter radicular or periapical radiolucency. The patient are followed up at 6 months, 12 months and 18 months.
- **Results:** A total of 61 patients were recruited and 19 were treated per protocol. 33 ultimately received an alternative treatment in lieu of pulpotomy (i.e. extraction or indirect pulp cap). Of the 19 patients treated per protocol, 7 have returned for their follow-up. 2 received Pulpotomy with FS+IRM (29%) and the remaining 5 received Pulpotomy with FS+ CAVIT (71%).
- **Conclusion:** At 6 months, in primary molars pulpotomy, non-eugenol-based ZOE placed over ferric sulphate shows similar success to using eugenol-based zinc oxide as a base material.

Introduction

- Dental caries is the most common chronic disease in children.[1] Untreated caries can lead to several complications including affect in vitality, infections, and premature tooth loss.[1] Vital Pulp Therapy (VPT) for primary deciduous teeth aims to maintain the pulp vitality and the tooth's function.
- There are several factors that potentially can affect the success of VPT pulpotomy, including adequate blood supply, severity of inflammation, obtaining hemostasis, disinfection of exposure site, the pulp covering agents, the definitive restoration and their antibacterial and biocompatibility properties. [2]
- The most frequently used medicament in pulpotomy vital therapy is mineral trioxide aggregate (MTA), formacresol (FC), ferric sulphate (FS), calcium hydroxide (CH), Biodentine (BD) and laser.[2]
- Due to its high success rate, FC is described as the 'gold standard' for pulpotomy procedures.[3] However, FC is a controversial medicament, because of its major component Formaldehyde, which been classified by the international Agency for Research on Cancer (IARC) as a possible human carcinogen in 2004 . In the dental setting, there is very low exposure of formaldehyde, and it should not exhibit any carcinogenic actions.[4] Despite these findings dentists in Europe still have some concerns and alternatively prefer other medicaments such as Ferric Sulfate (FS). [5]
- MTA is a widely used pulpotomy medicament due to its excellent sealing ability, hard tissue formation and biocompatibility. [6] However, MTA is expensive, and is not the material of choice in some parts of the world.
- FS is a hemostatic agent, non-aldehyde chemical that is commonly used for pulpotomies in primary teeth. This agent forms a protective metal protein clot over the vital pulp tissue. The evidence suggested that both FC and FS showed similar clinical success rates. However, FC achieved a 10% higher radiographic success rate over FS at 24 months' time interval. Internal resorption in the most common cause of failure in FS. This has been attributed to the release of free eugenol from the zinc eugenolate mixture of the base material over the pulp tissue . Zinc oxide-eugenol (ZOE) paste is the most common base material during pulpotomies of primary molars.
- Cavit is another base material that contains zinc-oxide without eugenol. This has been used a temporary restorative material with excellent sealing capability. [8] Therefore, using FS for pulpotomy VPT with Cavit, could potentially results in better radiographic success. However, the evidence is lacking. Therefore, this preliminary report will discuss the result of a pilot study of a randomized controlled clinical trial that aims to evaluate and compare the effect of eugenol and non-eugenol-based ZOE on the clinical and radiographic success rate of primary molar pulpotomies with FS as the medicament of choice.



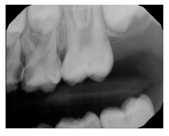
Methods

- **Trial Design:** Preliminary report of a randomized control trial.
- **Inclusion criteria:** Children aged 3 to 7 years old. At least one tooth with reversible pulpitis, whose parents sought for treatment at the Children's Hospital of Richmond at VCU. Tooth is restorable with Stainless Steel Crown (SSC). Patient receiving treatment under General Anesthesia (GA) or Oral Conscious Sedation (OCS). Only teeth having no more than one third of their roots undergoing physiologic resorption were included.
- **Exclusion Criteria:** Clinical or radiographic evidence of pulp degeneration: Deterioration/damage of the normal pulp tissue, Excessive bleeding from the pulp, pathologic mobility, swelling or fistula, history of spontaneous pain, tenderness to percussion or palpation, internal root resorption, external root resorption, periapical radiolucency.
- **Sample calculation:** The analysis suggests that you would need between 150 and 175 subjects to achieve 80% power. This gave a minimal sample size of 87 teeth.
- **Interventions:** All potential patients seeking pediatric dental treatment will have an initial consultation appointment in the Pediatric Dentistry department by a resident. All restorations and children's treatment needs were performed by trained dentists at VCU under GA or OCS. All teeth were randomly allocated between the groups (1)Ferric sulphate pulpotomy with a zinc oxide-eugenol cement (IRM) , (2) Ferric sulphate pulpotomy with non-zinc oxide eugenol cement (CAVIT) as base materials. All teeth treated with the study's intervention received rubber dam isolation and SSCs.
- **Evaluation of procedure:** The patients will be evaluated at the time intervals of 6 months, 12 months, 18 months, and 24 months. The patients were blinded to the used base material.
- Two examiners completed a blinded examination of the follow-up x-rays and evaluated the teeth in terms of the following: Internal resorption, external resorption, furcation involvement, periapical radiolucency, adequate crown coverage and adequate compaction of material. The two examiners looked at their difference and produced consciences regarding the follow up x-rays.
- **Statistical Analysis:** Agreement between two independent raters for the radiographic assessment was determined with Kappa statistic and descriptive statistics of the rate of disagreement. Fisher's exact test was used to determine if the radiographic findings differed between the two treatment groups. SAS EG v.8.2 (SAS Institute, Cary, NC) was used for all analyses.

Figure 1. Scoring criteria of the radiographs for reliability testing

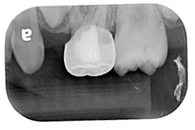
Tooth #J

Pre - tx



	PDL Space Widening	Internal Resorption	External Resorption	Furcation involvement	Periapical Radiolucency
YES					
NO	x	x	x	x	x

Post - tx



	PDL Space Widening	Internal Resorption	External Resorption	Furcation involvement	Periapical Radiolucency	Adequate compaction of material	Adequate Crown Coverage
YES						x	x
NO	x	x	x	x	x		

Results

- A total of 61 patients were recruited and 19 were treated per protocol. Of the remaining 42, 4 are awaiting their scheduled treatment date, 33 ultimately received an alternative treatment in lieu of pulpotomy (i.e. extraction or indirect pulp cap), 16 patients received indirect pulp cap, 3 were lost to follow-up, and 2 received alternative medicaments with pulpotomy procedure.
- Of the 19 patients treated per protocol, 7 have returned for their follow-up. 2 received Pulpotomy with FS+IRM (29%) and the remaining 5 received Pulpotomy with FS+ CAVIT (71%).
- Two independent raters evaluated the pre-operative and post-operative radiographs. Neither rater indicated any of the findings for the pre-operative images (Figure 1). Kappa statistics ranged from 28% to 59%. Disagreements were discussed until a consensus was reached. The agreed upon determinations were used for subsequent analyses.
- There were no negative findings among the cases treated with IRM. For cases treated with CAVIT, 20% presented with each of the following: PDL space widening, internal resorption, furcation involvement, and periapical radiolucency. Two cases demonstrated external resorption (40%) (Figure 2).

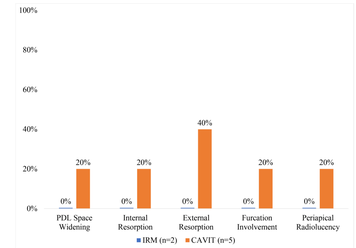


Figure 2. Radiographic success of restorative materials based on changes in the root morphology

- All of the cases treated with IRM demonstrated adequate compaction of materials and crown coverage (100%). For cases treated with CAVIT, only 60% were deemed to have adequate compaction of material (n=3 of 5) and 80% adequate crown coverage (n=4 of 5) (Figure 3).
- When comparing the two methods, the results of the Fisher's exact test were p-value>0.999 for all comparisons due to the low sample size.

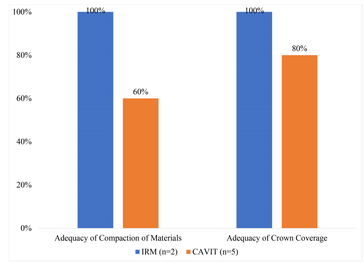


Figure 3. Radiographic success of restorative materials based on coronal restoration

Conclusions

- This pulmonary report shows agreement to the null hypothesis; indicating that in primary molar pulpotomy, non-eugenol-based ZOE placed over FS do not show higher success rate compared to eugenol-based zinc oxide as a base material. However, these results are not finalized, and they are due to the low sample size.
- The trend is going towards more conservative treatment, which is support by evidence. Therefore, deep caries on primary teeth are being treated more with indirect pulp. Out of the 33 patient who received alternative treatment to pulpotomy, almost half (48%) were treated with indirect pulp cap.
- More radiographic failure is observed with lack of adequate compaction of material and crown coverage.
- Kappa analysis indicated a moderate level of agreement between the two examiners, future research is suggested to include more examiners to assess agreement more accurately.
- Due to the high usage of FS around the word, the continuity of this randomized control trial is essential to get more data supporting the effect of using different base material on the success of FS pulpotomy procedure.

References

1.Coll JA, Seale NS, Vargas K, Marghalani AA, Al Shamali S, Graham L. Primary Tooth Vital Pulp Therapy: A Systematic Review and Meta-analysis. *Pediatr Dent.* 2017;39(1):16-123.

2.Fei AL, Udin RD, Johnson R. A clinical study of ferric sulfate as a pulpotomy agent in primary teeth. *Pediatr Dent.* 1991;13(6):327-332.

3. Fuks AB. Current concepts in vital primary pulp therapy. Eur J Paediatr Dent. 2002 Sep;3(3):115-20.

4.International Agency for Research on Cancer, World Health Organization. *IARC Classifies Formaldehyde as Carcinogenic to Humans.*; 2004.

5. Duggal M, Gizani S, Albadri S, Krämer N, Stratigaki E, Tong HJ, Seremidi K, Kloukos D, BaniHani A, Santamaría RM, Hu S, Maden M, Amend S, Boutsiouki C, Bekes K, Lygidakis N, Frankenberger R, Monteiro J, Anttonnen V, Leith R, Sobczak M, Rajasekharan S, Parekh S. Best clinical practice guidance for treating deep carious lesions in primary teeth: an EAPD policy document. Eur Arch Paediatr Dent. 2022 Oct;23(5):659-666. doi: 10.1007/s40368-022-00718-6. Epub 2022 Oct 11. PMID: 36219336; PMCID: PMC9637614.

6.Al-Haj Ali SN, Al-Jundi SH, Ditto DJ. In vitro toxicity of formocresol, ferric sulphate, and grey MTA on human periodontal ligament fibroblasts. *Eur Arch Paediatr Dent Off J Eur Acad Paediatr Dent.* 2015;16(1):51-55. doi:10.1007/s40368-014-0147-7 (8)

7.Milnes AR. Is formocresol obsolete? A fresh look at the evidence concerning safety issues. *Pediatr Dent.* 2008;30(3):237-246.

8.Sivakumar JS, Suresh Kumar BN, Shyamala PV. Role of provisional restorations in endodontic therapy. *J Pharm Bioallied Sci.* 2013;5(Suppl 1):S120-124. doi:10.4103/0975-7406.113311

Thank you to Dr. Jayaraman Jayakumar, Dr. Caroline Carrico and Dr. Vineet Dhar for all their help and guidance during this project.