Comparison of Mineral Trioxide Aggregate and Diluted Formocresol in Pulpotomized Human Primary Molars: 42-month Follow-up and Survival Analysis

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Abstract

Purpose—The purpose of this study was to test the hypothesis that there is no significant difference in the clinical and radiographic outcomes of diluted formocresol (DFC) compared to gray mineral trioxide aggregate (GMTA) pulpotomy in human primary molars.

Methods—A total of 152 children with 252 primary molars met selection criteria. Of those, 119 and 133 teeth were randomly assigned to the GMTA and DFC groups, respectively. Periapical radiographs, taken pre- and/or postoperatively and at each 6-month follow-up, were digitized and evaluated by three blinded and calibrated examiners.

Results—Over a 42-month period, a total of 865 clinical and radiographic evaluations were conducted. There was no significant difference in clinical success, with the cumulative proportion of GMTA-treated teeth surviving at 0.98 vs DFC-treated teeth at 0.95 (P>.05). Radiographic success, however, was significantly greater for GMTA vs DFC, with the cumulative proportion of GMTA-treated teeth surviving at 0.90 vs DFC-treated teeth at 0.47 (P<.001). Overall, DFC-treated teeth were 5.1 times more likely to fail than GMTA-treated teeth. Radiographic pathologies were observed more frequently in the DFC-treated teeth (P<.05).

Conclusion—Gray mineral trioxide aggregate can be considered an acceptable replacement for diluted formocresol when used as a medicament for primary molar pulpotomies.

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Pulpotomy is the most widely applied clinical procedure for treatment of primary teeth with inflammation of the coronal pulp due to caries. The many methods and materials that are currently used to carry out primary tooth pulpotomy emphasize the limitation that there is not yet a single medicament or technique that is biocompatible and can be used consistently to achieve success clinically and radiographically.

Formocresol (FC) is the widely accepted medicament for primary teeth pulpotomy. While there is much debate regarding its potential adverse effects, formocresol at full strength or diluted to one fifth has shown clinical success rates ranging from 55 percent to 98 percent and is the most universally taught pulpotomy agent. Despite clinical success, the pulpal responses following FC pulpotomies demonstrate a wide-spectrum of tissue reactions, which may range from no change to vital tissue without inflammation. Some of the observed reactions include, but are not limited to: variable dentin resorption and/or hard tissue deposition; chronic inflammation with internal resorption and variable hard tissue deposition; or necrosis without internal resorption. Searches for suitable alternatives as pulpal medicaments have been ongoing for more than three decades, with aims to identify a biocompatible medicament that preserves the function of a pulpally involved primary tooth in a growing patient.

The application of gray mineral trioxide aggregate (GMTA), primarily in endodontic procedures, provides the initial evidence that GMTA may be a biocompatible medicament for pulp therapy, specifically because of properties similar to that of the calcium hydroxide. GMTA was used experimentally for a number of years before being approved for human usage by the FDA in 1998. In the presence of moisture, mineral trioxide aggregate (MTA) becomes a colloidal gel with a pH of 12.5; it sets via hydration, with a setting time of four hours and compressive strength of 70 MPA, which is comparable to intermediate restorative material (IRM). It has been shown to have antimicrobial properties similar to that of zinc oxide-eugenol (ZOE) and the ability to stimulate cytokine release from bone cells and odontoblasts. MTA facilitates bone regeneration and overgrowth of cementum when used as a root-end filling material, and its sealing ability is better than amalgam, ZOE, or Super EBA. Because of MTA’s biocompatibility and excellent sealing ability, investigations into the use of MTA as a medicament in the pulpotomies of primary teeth have shown promising results.

An investigation was initiated in 2006 to test the efficacy of GMTA vs DFC as a medicament for pulpotomies, with the specific hypothesis that there is no significant difference in clinical and radiographic outcomes among primary molars treated with either DFC or GMTA over a 42-month period. With an understanding of the strengths and weaknesses of existing literature, the purpose of this paper was to conduct a long-term study of a collaborative, multicenter, multioperator, prospective, randomized, controlled clinical trial with appropriate experimental design, adequate sample size, blinded evaluation with proper calibration/training, and survival analysis and histologic evaluations. The
findings of the preliminary study and 2-year follow-up were previously reported. This manuscript details the 42-month outcomes, survival analysis, and histologic evaluation of the treated teeth.

**Methods**

The study protocol and consent forms were reviewed and approved by the School of Medicine, University of Michigan, Ann Arbor, Mich., and the Institutional Review Board for Human Subject Research of Mott Children’s Health Center, Hurley Medical Hospital, Flint, Mich. The study population included patients who presented to the Children’s Clinic at the School of Dentistry, University of Michigan (UMOPD) and Mott Children’s Health Center (MCHC) between March 1, 2007 and February 29, 2008, having at least one carious primary molar requiring pulpotomy that met specific inclusion and exclusion criteria. A sample size of 250 teeth was determined as a minimum sample size to show validity and 80 percent power, assuming 20 percent attrition.

A total of 33 operators, including first-, second-, and third-year pediatric dental residents, and faculty from UMOPD and MCHC took part in the study. To ensure consistency, each operator and dental assistant, prior to performing treatment on study subjects, completed a training and calibration session conducted by three primary investigators in 2007, 2008, and 2009.

Randomization of the pulpal medicament was achieved by an envelope draw for both study sites, separately. A tally sheet was created for each treatment site and was consulted to determine which medicament was to be used on the first treated tooth in a newly enrolled patient. Preoperative and, in some cases, immediate postoperative periapical radiograph (with parental permission) of the enrolled teeth were obtained. Upon local anesthesia using two percent lidocaine with 1:100,000 epinephrine, a rubber dam and clamp were placed and occlusal reduction and caries removal with a round bur were achieved. The pulp chamber was accessed with a no. 330 bur in a high-speed handpiece, and the coronal pulp tissue was removed with large, slow-speed round bur (nos. 6 or 8) and/or a sharp spoon excavator. After verification of complete removal of the pulp tissue down to the canal orifices, control of moisture and pulp hemorrhage was achieved using direct pressure with sterile cotton pellets. If hemostasis was not achieved within five minutes, the tooth was treated by pulpectomy or extraction and excluded from the study.

When hemostasis was achieved, the control group was treated with a 5-minute application of a cotton pellet dampened with a 1:5 dilution of FC (20 percent Buckley’s diluted formocresol, Sultan Healthcare, Englewood, N.J., USA) and pressed into a sterile gauze to remove excess. The experimental group was treated with a minimum layer of 3 mm of ProRoot Gray Mineral Trioxide Aggregate (Tulsa Dentsply, Tulsa, Okla., USA) material, which also covered the pulpal floor over the furcation. A mixture of reinforced ZOE (IRM, Dentsply Caulk, Milford, Del., USA) was immediately placed in the chamber of both the experimental and control groups, and a preformed stainless steel crown (3M/ESPE, St. Paul, Minn., USA) was fitted, checked for occlusion, and cemented with glass ionomer cement (GC Fuji I, GC America Inc, Alsip, Ill., USA, or Rely-X, 3M/ESPE).
Subjects in the study were asked to return for 6-, 12-, 18-, 24-, 30-, 36-, and 42-month follow-up visits. Both clinical and radiographic signs were scored based on modified scales that were adapted from Zurn and Seale.

All periapical radiographs were digitized with specifications described in Sushynski et al. Evaluation tables were organized using spreadsheets (Microsoft Office Excel 2007, Microsoft Corp, Redmond, Wash., USA) that contained the following recall information: patient no.; tooth no.; tooth treated; evaluation pathoses; and hyperlinks to pre- and post-treatment radiographic images stored on a USB flash drive. Radiographic images could be viewed sequentially by recall month in the Explorer (Microsoft Corp, Redmond, Wash., USA) window by selecting multiple hyper-linked images and toggling between them.

Raters evaluated each follow-up radiograph for the presence of radiographic pathoses: unchanged or within normal limits (WNL) from treatment date; dentin bridge formation (DB); pulp canal obliteration (PCO); pathologic nonperforated (IRR) and perforated internal root resorption (IRR-P); external root resorption (ERR); and inter-radicular or periapical bone destruction (PRL). In the absence of other concurrent pathoses, periodontal ligament space widening was recorded but not considered a failure. Radiograph evaluations were retrospectively applied to missed recalls. Teeth that presented with failures were counted as a failure at the time of that recall. If a recall was missed, and the next recall showed a failure, the failure was considered to have occurred at a time point 6 months after the last successful observation.

All radiographs were viewed by three blinded raters: two pediatric dentists who were full-time faculty members in the Department of Orthodontics and Pediatric Dentistry, and one endodontist who was a full-time faculty member in the Department of Cariology, Restorative Sciences, and Endodontics at the University of Michigan, Ann Arbor, Mich., USA. The practice experience of the three observers ranged from seven to 25 years, with a mean of 18 years. Before recall radiograph evaluation, the three raters were familiarized with standardized Microsoft Excel rating worksheets and trained in scoring. Intrarater and inter-rater reliability between the three raters, and with the consensus for each session, was calculated using Cohen’s unweighted kappa (κ) values. For teeth that did not receive a clear consensus in the initial independent scoring of the radiographic pathoses described in the previous paragraph, a final consensus session was held to discuss discrepancies in scoring among the three evaluators. A consensus of 3:0 was used to allocate a final rating to the tooth in these cases.

Data collected for each patient during the study included: chart number; gender; date of birth; treatment date; age at time of pulpotomy treatment; tooth number; material used; treatment operator; follow-up time in months; clinical findings of each recall visit; radiographic findings at each recall visit; location of treatment (dental clinic or operating room); and recall operator. Data were tabulated, entered into an Excel spreadsheet, and analyzed using the SPSS 19.0 software (SPSS Inc, Chicago, Ill., USA).

Preliminary analyses consisted of testing clinical success and failures for each variable using chi-square tests of independence as well as Fisher’s exact test. Radiographic success and
failures and overall success and failures were also tested with each variable using chi-square
and Fisher’s exact tests to compare the treatment response of DFC and GMTA.

A Kaplan-Meier analysis was performed for the 42-month study data to establish survival
probability and survival plots of teeth treated with GMTA and DFC. A discrete time failure
analysis, using a generalized linear model (logistic regression) with generalized estimating
equations, was fitted to the data to analyze predictor variables such as age, gender, arch,
tooth, and location of treatment. Descriptive statistics for all data sets were also analyzed.

With proper consent, exfoliated or extracted teeth enrolled in this study were collected and
immediately immersed in 10 percent formalin until processed for histologic evaluation.
Using a no. 330 bur in a high-speed handpiece, the stainless steel crown was removed from
each tooth sample and the remaining cement and IRM in the pulp chamber was carefully
removed under a dissecting microscope. The tooth sample was then immersed in four
percent ethylene-diamine-tetra-acetic acid for decalcification.

Upon completion of decalcification, which took up to four weeks, each tooth sample was
subjected to routine histologic processing, embedding, and sectioning at 6 μm thickness. The
mid-sections of each sample were collected onto glass slides, which were placed on a warm
plate overnight to allow flattening of the sections. The sections were then stained with
hematoxylin and eosin, mounted with glass coverslip and Permount (Fisher Scientific,
Pittsburgh, Pa., USA), evaluated under a microscope, and photographed using a digital
camera (Nikon Eclipse 600 and DXM1200, Nikon Inc., New York, N.Y., USA).

Results

A total of 168 children were enrolled in this study, with 81 females and 87 males
contributing 128 and 142 teeth, respectively. The mean age of the recruited subjects was
5.4±1.4 years old, with a range of 2.5 to 10 years old. A total of 270 teeth were initially
recruited; however, 18 teeth did not meet the inclusion criteria. Specifically, six teeth had
greater than one-third root resorption, 10 teeth were deemed to have furcation radiolucencies
apparent on the preoperative radiographs, and two teeth did not meet radiographic criteria.
The total number of recruited teeth that satisfied the inclusion criteria and were entered into
the study was 252 (in 152 children). Most treated teeth (81 percent) were treated in the clinic
vs the operating room (19 percent) setting.

Overall, mandibular molars (61 percent) were more frequently recruited than maxillary
molars (39 percent). The most frequently treated tooth was the mandibular second molar (32
percent), followed by the mandibular first molar (29 percent), maxillary first molar (20
percent), and maxillary second molar (19 percent). At six months, 222/252 (88 percent)
teeth entered into the study were available for evaluation, resulting in 12 percent lost at
follow-up. The recall rate decreased to 74 percent at 12 months, 62 percent at 18 months, 52
percent at 24 months, 38 percent at 30 months, 24 percent at 36 months, and only six percent
at 42 months. Teeth recalled after 42 months but before 48 months were included in the 42-
month recall group. Seven flowcharts summarized the clinic sites and the no. of teeth
recruited, treated, and recalled at each follow-up (see Figure 1).
The level of inter-rater agreement between each rater and the group consensus showed an increase between the initial training session and the final evaluation session, on average, with average kappa values increasing from 0.49 (moderate agreement) to 0.57 (moderate agreement). This increase, however, was not found to be significant ($P > .05$).

Clinical findings

A combined total of 865 clinical evaluations were made at six to 42 months (Table 1). The average clinical scores were higher for the DFC group (1.06) than the GMTA group (1.03), indicating more clinical changes over the period of evaluation. These changes were not significant ($P > .05$). One tooth in the GMTA group was judged to be a clinical failure (99 percent success rate), and four teeth in the DFC group were judged to have failed (99 percent success rate). There was no significant difference found between these two groups ($P < .05$). A total of 865 radiographic evaluations were also made (Table 1). In the DFC group, 49 percent of the teeth scored a 2 and 32 percent of those teeth involved IRR. In the GMTA group, 47 percent of the teeth scored a 2 and only seven percent involved IRR. The average radiographic scores, excluding teeth scored for exfoliation, were higher for the DFC group (1.8) than the GMTA group (1.6), indicating more radiographic changes over the period of evaluation. Radiographic success in the GMTA group (95 percent) was judged to be higher than in the DFC group (79 percent) over the combined 6- to 42-month period. This difference was found to be significant ($P \leq .001$).

The definition of survival time for this study was as follows: time from pulpotomy treatment to the time when a failure (either clinical or radiographic) was recorded. The minimum recall time interval was six months, and the maximum recall interval was 42 months, with intervals categorized by units of six months to account for expected recall date. Teeth that were considered a failure at recall were excluded from the analysis at future time points. Teeth that had missed a recall and then displayed a failure at a future recall were considered to have failed six months after the last successful observation. A Kaplan-Meier analysis was performed to establish survival probability and survival curves. A discrete time failure analysis using a generalized linear model (logistic regression) with generalized estimating equations was fitted to the data in order to analyze predictor variables such as age, gender, arch, tooth, type, and locale of treatment.

The 222 teeth of 140 children—68 females (49 percent) and 72 males (51 percent)—that were recalled at six-month intervals during this study were followed for the survival analysis. A total of 865 observations were made, however, when cases with returning radiographic failures were accounted for; a total of 777 observations over the study period were included in the final calculation. Once a failure was recorded for a tooth, that tooth was considered failed and was no longer included in the analysis at future time points. The mean follow-up time for the data set was 23.2 months, with a range of 5.7 to 45.8 months.

The clinical failures that occurred over the evaluation period included five total failures from the original 222 teeth entered into the study (two percent). Of the five clinical failures that occurred, four of the failures were observed in teeth treated with DFC, while one failure was observed in a GMTA-treated tooth. Of those clinical failures that occurred, there was only one clinical failure that was not also considered a radiologic failure.
**Radiographic findings**

The radiologic failures that occurred over the evaluation period included 42 total failures from the original 222 teeth recalled during the study period (19 percent). Of the radiographic failures that occurred, 34 (81 percent) were observed in teeth treated with DFC, while eight (19 percent) were observed in a GMTA-treated tooth.

A total of 45 observations were made for either clinical or radiographic failure. Of these, 36 (80 percent) were in DFC-treated teeth, while nine (20 percent) were in an MTA-treated teeth. Of the 222 teeth that were recalled, failure was noted in 43 teeth, resulting in a 19 percent failure rate overall. There were 40 radiographic failures that were not considered clinical failures. It should be noted that, because two teeth received radiographic failures as well as clinical failures at the same time point, the overall number of failure events observed (n=45) is higher than the overall number of failed teeth (n=43). For the purpose of this analysis, 43 teeth experienced a failure either at the earliest indication clinically or radiographically or at six months after the last successful observation.

When combining radiographic outcomes over the evaluation period, there was a significant effect of material on survival \((P \leq 0.001)\). Teeth treated with DFC were less likely to survive than teeth treated with GMTA (Figures 2 and 3). The total number of terminal events or failures was 34 for the DFC group and eight for the GMTA group. The greatest number of failures occurred within the first six months for both groups, with 15 in the DFC group and five in the GMTA group. At six months, teeth in the DFC-treated group had a cumulative proportion survival rate of 0.82 vs 0.95 for GMTA-treated teeth. At 12, 18, 24, 30, and 36 months, the cumulative proportion survival rate for the DFC-treated teeth was 0.76, 0.75, 0.64, 0.59, and 0.59, respectively, vs 0.93, 0.93, 0.93, 0.90, and 0.90, respectively, for GMTA-treated teeth. At the end of the study interval, the cumulative proportion survival rate for the DFC group was 0.47 vs 0.90 for the GMTA group. The cumulative proportion surviving at each time point, it should be noted, is lower than any independent success rate at a given time point, as it takes into account the proportion of teeth surviving at each of the previous time intervals.

**Histologic findings**

Eighteen teeth were collected for histologic processing over the course of the study. A majority of the teeth collected, 11 out of 18, did not contain sufficient pulpal tissues for a meaningful assessment. Histologic responses that were noted in five out of 11 teeth treated with DFC included: abscess; chronic inflammation; amorphous connective tissue repair; tertiary dentin formation; dentin bridging; and internal resorption (Figure 4). Histologic findings that were noted in two out of seven teeth treated with MTA included: dentin bridging; pulp canal obliteration; signs of inflammation, including blood vessel dilation and red blood cell aggregation; tertiary dentin formation; and normal pulpal tissue (Figure 5).

**Discussion**

This study’s results did not support the null hypothesis that there is no significant difference in clinical or radiographic outcomes between GMTA- and DFC-treated primary molars.
following a pulpotomy procedure. The study included two sites, multiple operators, and blinded yet calibrated evaluators with a large sample size randomly assigned into the control or experimental group with long-term follow-ups. There was an attempt to eliminate confounding factors, such as misdiagnosis of inflammation in the radicular pulp at the time of treatment\(^{25}\) and pulpal contamination via microleakage,\(^{26}\) by randomization and restoration of treated teeth with a stainless steel crown immediately following pulpotomy.\(^{10–12,27}\) The training/calibration sessions were conducted to standardize treatment delivery among all care providers and to ensure a moderate to good level of agreement within each rater and among raters. Histologic evaluation of treated teeth was conducted on attainable samples to assess pulpal responses following GMTA and DFC pulpotomy.

The reported clinical success rates ranged from 85 percent to 100 percent for FC and 93 percent to 100 percent for MTA after 24 months.\(^{15–17,19}\) In the present study, the 42-month radiographic success rate of MTA-treated teeth (95 percent) is similar to other studies performed over shorter intervals with reported success rates of 93 percent to 100 percent.\(^{10–14,16,18,27,28}\) While the 42-month success rate of the DFC-treated teeth (78 percent) is comparable to the reported 77 percent to 100 percent after 12 months observation.\(^{11,14,15,17,23,27–35}\) The collective finding of this study and other reports supports that GMTA had significantly better radiographic success rates than DFC.\(^{11,12,14,17,19,27,30,31,34,35}\) The similar success rates in the current study compared with previous reports validate this study and suggest that GMTA produces more positive radiographic outcomes than DFC.

In this study, dentin bridge formation was observed radiographically in 16 percent (79/501) of GMTA-treated teeth and less than one percent (2/457) of DFC-treated teeth. This difference was statistically significant (\(P<.001\)). Thus, dentin bridge formation occurs more frequently in teeth treated with GMTA than teeth treated with DFC. This, combined with the higher radiographic success rates found for GMTA-treated teeth, might indicate that dentin bridge formation, although different from normal tissue, is a favorable process that potentially promotes maintenance of healthy radicular tissue. Internal root resorption is a common radiographic finding in pulpotomized teeth, with studies showing increased frequencies of IRR in teeth that have been treated with DFC (1–15 percent)\(^{23,36,37}\) vs GMTA (0–6 percent).\(^{14,26,27,38}\) Recently, Ansari et al. reported IRR in 10 percent of teeth treated with DFC and zero percent in primary teeth treated with GMTA over 24 months. Similarly, a study by Erdem et al. reported IRR in five percent of DFC-treated primary teeth and zero percent of GMTA-treated teeth over 24 months.\(^{19}\) In this study, there was a significant difference observed for IRR between the two medicaments, as IRR was observed in 14 percent (66/457) of teeth in the DFC group and three percent (14/501) of teeth treated with GMTA (\(P<.001\)). These coincide with the ranges previously reported in the literature.

The influence of variables, such as time of recall, age, gender, and location (operating room vs clinic), analyzed with logistic regression, showed that there was no significant effect of time of recall, age, gender, or location on radiographic failure when controlling for material used over six to 42 months (\(P>.05\)). There were, however, some general trends noted for these variables. Overall, teeth were less likely to fail as time of recall increased. This
indicates that a pulpotomized tooth may be more likely to experience a failure soon after initial treatment.

While DFC has been shown to have high clinical success rates, ranging from 55 percent to 98 percent, studies have shown that use of DFC can result in chronic inflammation of radicular pulp. Failures of teeth treated with DFC have been proposed to be associated with this long-term chronic inflammation. While DFC is a known irritant that causes inflammation of pulpal tissue, GMTA has been shown to be biocompatible when placed in contact with pulpal tissues. It is, therefore, reasonable to assume that GMTA may be associated with less inflammation vs DFC.

The teeth obtained for histologic processing in this study were collected when they were near exfoliation or presented with clinical symptoms that required extraction. As such, the majority of healthy teeth obtained for sampling lacked appropriate root structure, due to resorption, and had little, if any, pulp tissue remaining for evaluation. Most teeth that had adequate root structure remaining for analysis were extracted due to clinical or radiographic signs of failure. Thus, we considered that those teeth obtained for this study did not represent successful pulpal reactions; however, there are some notable histologic processes, which provide insight into the tissue reactions that occurred subsequent to the selected treatment.

The DFC-treated teeth showed chronic tissue inflammation in three of the 11 samples, which may lead to pulpal necrosis, although pulpal necrosis was only noted in one of the samples obtained. Internal resorption, with the presence of osteoclastic resorption lacuni, was also noted in one of the samples, which has been reported as a common outcome of teeth pulpotomized with DFC. Previous histologic studies have reported chronic inflammation, active resorption, and apposition of hard tissue to be common findings following FC pulpotomies. Interestingly, partial dentin bridge formation was observed in two samples, while complete dentin bridge formation was observed in one sample; however, the sample with complete dentin bridging showed inflammation of adjacent pulpal tissues. This finding, along with the information that very little dentin bridge formation was reported radiographically in the DFC group, is in line with previous findings from Caicedo et al., which showed that the absolute presence of a dentin bridge cannot simply be determined radiographically. In that study, no teeth treated showed radiographic signs of the presence of dentin bridges, but bridges were seen histologically in 62 percent of teeth. These findings may indicate that, while a DFC pulpotomy may result in formation of dentin bridging, these bridges may be poorly organized or lack appropriate thickness to be viewed radiographically. Also, even in the sample that showed complete dentin bridge formation, there was chronic inflammation noted in the adjacent pulpal tissue.

The GMTA-treated teeth obtained for sampling showed irregular tertiary dentin formation in one sample and complete dentin bridge formation in another sample. Also, radicular pulp canal obliteration was noted. These findings agree with previous reports, which describe dentin bridge formation and pulp canal obliteration as common findings in MTA-treated teeth. It is interesting to note that the sample with complete dentin bridge formation showed remaining pulp tissue that appeared healthy. This finding is consistent with findings
of previous studies, which have shown deposition of secondary dentin bridging the pulp
tissues at the site of amputation with preservation of normal pulp architecture.\textsuperscript{11,44} Due to
the small sample size and limitation of sample attainment, we cannot attempt to make any
comparison of the histologic outcomes among the GMTA-and DFC-treated teeth.

This study has demonstrated that GMTA can be used as a material for pulpotomies in
primary molar teeth with a successful 6-, 12-, 18-, 24-, 30-, 36-, and 42-month outcome.
While GMTA offers some advantages, however, there are a few disadvantages associated
with this material. The main surgical advantage of MTA over DFC is the fact that less time
is needed for the procedure. FC requires a 5-minute application after hemostasis is achieved,
but with MTA the pulp chamber is filled immediately after hemostasis. This is particularly
important for practitioners who routinely treat children in the clinic setting, as negative
behavior often may necessitate the use of treatments that can be performed as quickly as
possible. In addition, as the moist cotton pellet in the FC procedure is usually squeezed to
remove the excess of FC before placement over the pulp stumps, it sometimes adheres to the
clot and bleeding reoccurs when the pellet is removed. No such problems were encountered
with DFC in the present study. The other main advantage of GMTA is the decreased
likelihood of an iatrogenic tissue reaction, as GMTA is biocompatible and nontoxic when
placed in contact with human tissue.

The main disadvantages of GMTA include setting time and cost of material. The setting
time of GMTA is about four hours, and the material should be in contact with moisture
during the setting reaction. The teeth cannot be left unrestored for this time so, as reported
previously, a moistened cotton pellet and an interim restoration are left in the teeth until a
subsequent appointment.\textsuperscript{15,44} In both of these studies, the teeth had to be re-entered to
remove the cotton pellet and a final restoration was required. This was not considered a
problem in this study, as it was hypothesized that adequate moisture was provided from the
amputated pulp to help in the MTA setting. When examining the cost factor for MTA, it
should be noted that Dentsply Pro-Root MTA only supplies the material in a 1-gram
package and claims that, once the package is opened, the humidity will react with the
minerals, causing the material to setup and the contents to prematurely expire.

Since 20 percent of the 1-gram package (0.2 g) is an adequate amount of material for a
primary molar pulpotomy, it was the protocol in this study to split up the 1-gram pack by
preweighting a unit dose amount into air-tight plastic vials in order to prevent humidity from
entering the stored material. The results of this study may indicate that splitting the 1-gram
package of GMTA into smaller amounts, if stored correctly in a humidity-free environment,
is an acceptable practice. Thus, the disadvantage of cost may be reduced to approximately
$10 per tooth. Also, this study showed that the use of GMTA resulted in a significantly
lower number of furcal radiolucencies when compared to DFC pulpotomized teeth. It is
important to consider the potential costs of retreatment, extractions, and space maintenance
that may be required once a pulpotomized tooth is deemed a failure and further treatment is
required. While the initial cost of placement for GMTA may be higher, the decreased need
for future treatment due to failures may be a factor in overall cost consideration.
This study showed that GMTA resulted in increased overall success rates over 42 months for pulpotomized primary molars when compared to DFC. This result, combined with the known negative attributes of DFC, including the fact that some medical facilities are now limiting its use due to the formaldehyde component, suggest that GMTA may be a suitable replacement for DFC for use in primary tooth pulpotomy treatment. Understanding the limitations of the current study and existing literature, we consider that split-mouth studies and comprehensive histologic evaluations are essential future directions.

Conclusions

Based on this study results, the following conclusions can be made:

1. When used as a primary tooth pulpotomy medicament, there was no significant difference in clinical success between gray mineral trioxide aggregate and diluted formocresol at a combined 6- to 42-month follow-up.

2. As a pulpal medicament, GMTA demonstrated a significantly greater success rate radiographically over six to 42 months vs DFC ($P \leq 0.001$).

3. The cumulative proportion of teeth surviving based on clinical assessment over 42 months was 0.98 for the GMTA group vs 0.95 for the DFC group ($P > 0.05$).

4. The cumulative proportion of teeth surviving based on radiologic assessment over 42 months was 0.90 for the GMTA group vs 0.47 for the DFC group ($P < 0.001$).

5. When combining clinical and radiographic observations, teeth treated with DFC were 5.1 times more likely to fail than teeth treated with GMTA over the 42-month survival analysis ($P < 0.001$).

6. Based on 6- to 42-month radiographic results, the pathologies of nonperforated and perforated internal resorption and periapical bone destruction were observed significantly more frequently in the DFC-treated teeth, while within normal limits and dentin bridge formation were observed more frequently in the GMTA group ($P < 0.05$).

7. Variables such as arch type, gender, and locale of treatment did not appear to influence pulpotomy success at the combined 42-month survival analysis; however, maxillary second molars were less likely to fail than any other molar type ($P < 0.05$).

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References


Figure 1.
Flowcharts demonstrate the number of teeth recruited, treated and recalled at each follow up time point at either the UMOPD or MCHC test site.
Figure 2.
Kaplan-Meier plot of clinical survival, in months, by material. DFC=diluted formocresol; MTA=mineral trioxide aggregate; cum survival= cumulative proportion of survival.
Figure 3.
Kaplan-Meier plot of radiographic survival in months by material. DFC=diluted formocresol; MTA=mineral trioxide aggregate; cum survival= cumulative proportion of survival.
Figure 4.
Histologic findings of diluted formocresol-treated teeth. (A) Partial dentin bridge formation with ectopic tertiary dentin (TD) formation present in the pulpal space. Tertiary dentin, with odontoblasts trapped within, is evident lining the radicular walls. Chronic inflammation of pulp cells (CI) with lymphocyte infiltration can be observed. (B) Radicular pulp obliteration with hyalinization of the pulpal tissue. Chronic inflammatory cells are aggregated at the orifice of the pulp canal. (C) Dentin bridge formation (DB) successfully walling off chronic inflammatory and necrosis pulp tissue in direct contact with the pulpal medicament. (D) Healthy pulp tissue with some signs of red blood cell aggregation in the blood vessels and partial DB. (E) Reparative dentin formation along the walls of the pulp canal resulting in pulp canal obliteration. Excessive connective tissue is present in the radicular pulp tissue; however, no signs of inflammation can be noted in this sample. (R) Internal root resorption with osteoclastic activity noted in numerous resorption lacuni of the radicular dentin wall (white arrows).
Figure 5.
Histologic findings of mineral trioxide aggregate (MTA)-treated teeth. (A) MTA material in direct contact with pulpal tissue. Pulpal tissue exhibited a small degree of blood vessel enlargement with aggregation of red blood cells (blue arrow). No odontoblasts were evident in this sample; however, some tertiary dentin was noted adjacent to the MTA material (white arrow). (B) Tertiary dentin formation was highly irregular at the orifice of the pulp canal. No residual pulpal tissue was evident in this sample. (C) Radicular pulp canal obliteration with irregular connective tissue repair. No signs of viable pulp cells. (D) Dentin bridge formation adjacent to residual healthy pulpal tissue.
Table 1

SIX- TO 42-MONTH CLINICAL AND RADIOGRAPHIC OUTCOMES

<table>
<thead>
<tr>
<th>Site</th>
<th>Material</th>
<th>Clinical score</th>
<th>Clinical score Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1 (WNL)</td>
<td>2 (poor OH)</td>
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<tr>
<td>Combined</td>
<td>DFC</td>
<td>407 (96)</td>
<td>14*</td>
</tr>
<tr>
<td>N=865 (%)</td>
<td>GMTA</td>
<td>426 (97)</td>
<td>13 (3.0)</td>
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<table>
<thead>
<tr>
<th>Site</th>
<th>Material</th>
<th>Clinical outcome</th>
<th>Clinical outcome Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>Success</td>
<td>Failure no.</td>
</tr>
<tr>
<td>Combined</td>
<td>DFC</td>
<td>421 (99)</td>
<td>4 (1)</td>
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<tr>
<td>N=865 (%)</td>
<td>GMTA</td>
<td>439 (100)</td>
<td>1 (0)</td>
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<table>
<thead>
<tr>
<th>Site</th>
<th>Material</th>
<th>Radiographic score</th>
<th>Radiographic score Total</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1 (WNL)</td>
<td>2 (DB, PCO, IRR)</td>
</tr>
<tr>
<td>Combined</td>
<td>DFC</td>
<td>165 (39)</td>
<td>207 (49)$^\dagger$</td>
</tr>
<tr>
<td>N=865 (%)</td>
<td>GMTA</td>
<td>205 (47)</td>
<td>207 (47)$^\dagger$</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Site</th>
<th>Material</th>
<th>Radiographic outcome</th>
<th>Radiographic outcome Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Success</td>
<td>Failure no.</td>
</tr>
<tr>
<td>Combined</td>
<td>DFC</td>
<td>337 (79)</td>
<td>88 (21)</td>
</tr>
<tr>
<td>N=865 (%)</td>
<td>GMTA</td>
<td>418 (95)</td>
<td>22 (5)</td>
</tr>
</tbody>
</table>

$^a$DFC=diluted formocresol; GMTA=gray mineral trioxide aggregate; n=no. of evaluations; WNL= within normal limits; DB=dentin bridging; PCO=pulp canal obliteration; IRR=internal root resorption; ERR=external root resorption; PDL=periodontal ligament space widening; IRR-P=internal root resorption perforated; PRL=periradicular lesion; EXF=exfoliated due to eruption of the permanent successor; 1 df=1 degree of freedom; FET=Fisher’s exact test; IRR=internal root resorption.

$^\dagger$The teeth that received a score of 4 were each considered a “failure.”

$^\dagger$IRR=66/207 (32%).

$^\ddagger$IRR=14/209 (7%).

|   | Statistical significance at the $P \leq 0.05$ level. |