Comparison between biodentine and formocresol for pulpotomy of primary teeth: A randomized clinical trial

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Objective: To assess and compare the clinical and radiographic success rates of biodentine and formocresol for pulpotomy in human primary teeth. Method and Materials: A randomized, split-mouth, double-blind, controlled clinical trial was carried out in 37 healthy 4- to 8-year-old children with 56 pairs (112 teeth) of contralateral primary molars indicated for pulpotomy. Matched teeth in each pair were randomized to undergo either biodentine (n = 56 teeth) or formocresol (n = 56 teeth) pulpotomy. In both groups, the teeth were restored with stainless steel crowns. The teeth were evaluated clinically and radiographically at 3 and 6 months by two blinded, standardized, and calibrated examiners. The data were analyzed using chi-square and McNemar tests with a P value of <.05 considered significant. Results: At both the 3- and 6-month follow-ups, all the 37 children with 112 treated teeth were evaluated. Clinical and radiographic success was similar for biodentine (100%) and formocresol (100%), without any statistically significant difference (P = 1). Pulp canal obliteration was radiographically observed in 10/56 (17.9%) and 7/56 (12.5%) cases in the biodentine and formocresol groups, respectively. Conclusion: Both pulpotomy techniques showed favorable clinical and radiographic outcomes at 3 and 6 months posttreatment without any significant difference. Hence, biodentine has the potential to become a substitute for formocresol in primary molar pulpotomies. (Quintessence Int 2016;47:571–580; doi: 10.3290/j.qi.a36095)

Key words: biodentine, formocresol, primary molars, pulpotomy

Pulpotomy is one of the most frequently used treatments in pediatric dentistry for treating primary teeth with carious pulp exposure without any inflammation of the radicular pulp.1 The technique is based on the removal of the coronal pulp to preserve the vitality of the radicular pulp, leaving the treated tooth asymptomatic until its exfoliation.2,4

Formocresol has been the most popular pulp medicament (gold standard) for pulpotomized primary teeth for the past 75 years due to its ease in use as well as its bactericidal and fixative properties, with success rates ranging from 76% to 97%.4-17 However, concerns have been raised about its toxicity, mutagenicity, and potential carcinogenicity in humans.15,18-23 Because of this, various materials have been formulated, tested, and standardized to carry out primary tooth pulpotomy and overcome the limitations of formocresol.21,24

Mineral trioxide aggregate (MTA) is a material used for pulpotomies with a high rate of success. Clinical
trials show that MTA performs equal to or better than formocresol and may be the preferred pulpotomy agent in the future.\textsuperscript{17,24,25}

Recently, Septodont introduced a new bioactive calcium-silicate based formulation (biodentine) which could combine good mechanical properties with excellent biocompatibility, as well as a bioactive behavior.\textsuperscript{26} Biodentine has been developed and produced (through active biosilicate technology) with the aim of bringing together the high biocompatibility and bioactivity of calcium silicates, resulting in enhanced properties that make it unique compared to other calcium silicate-based materials.\textsuperscript{27-30} It has gained attention in the field of endodontics because of its short setting time, high compressive strength, excellent sealing ability, and ease of handling, as well as versatility; it can be used in both endodontic repair and restorative procedures without causing any staining of the treated teeth.\textsuperscript{27-30} Moreover, it has also been proved that biodentine has excellent antimicrobial properties because of its very high pH (pH = 12). In addition, it eliminates the need for a filling material in the pulp chamber.\textsuperscript{26-31} Accordingly, biodentine might be an interesting alternative to the existing materials for dentin-pulp complex regeneration.\textsuperscript{26}

Many in-vivo and in-vitro studies have provided evidence for the bioactivity of biodentine, as well as its successful performance in pulp therapy.\textsuperscript{26,31-42} Furthermore, all the available clinical studies and case reports revealed excellent results for its use in human primary teeth.\textsuperscript{43-49} This has prompted its use for pulpotomy in human primary teeth.

In the last few years, most of the literature has focused on comparing formocresol to the most recent regenerative materials (such as MTA and bioaggregates) for pulpotomy of primary teeth.\textsuperscript{17,30-54} Due to its major advantages and unique features as well as its ability to overcome the disadvantages of other materials, biodentine has great potential to revolutionize the different aspects of managing both primary and permanent teeth in endodontics as well as operative dentistry. It has the potential of making major contributions to the maintenance of pulp vitality in patients judiciously selected for pulpotomy treatment.\textsuperscript{26}

Unfortunately, the data regarding its clinical and radiographic success in pulpotomy of human primary teeth are scarce. Therefore, prospective clinical studies are necessary to qualify biodentine as a substitute for formocresol for pulpotomy of primary teeth. The purpose of this clinical trial was to assess and compare the success rate of biodentine with that of formocresol clinically and radiographically for pulpotomy of human primary teeth.

**METHOD AND MATERIALS**

**Study design**

A randomized, split-mouth, double-blind, controlled clinical trial was performed.

**Patients**

The study population included 4- to 8-year-old healthy and cooperative patients who presented at the Pediatric Dental Clinics, Faculty of Dentistry, King Abdulaziz University (KAU), Jeddah, between 1 May 2014 and 31 October 2014, and had at least two matched bilateral deep carious primary molars indicated for pulpotomy that met specific inclusion criteria. Written consent was obtained from the parent/guardian after explaining the full details of the treatment procedure.

The criteria for inclusion in this study were:

- no history of spontaneous or nocturnal pain
- absence of tenderness to percussion
- absence of physiologic or pathologic tooth mobility
- no clinical evidence of pulpal inflammation or degeneration such as history of swelling or presence of sinus tract
- normal tooth structure
- restorable teeth
- absence of radiographic evidence of internal or external root resorption, pulpal calcification, or osseous disease (periapical or furcation radiolucency)
- presence of at least two-thirds of the root (no physiologic root resorption of more than one-third of the root length).
On the other hand, teeth were excluded if:
• any of the above-mentioned clinical or radiographic inclusion criteria were not satisfied
• hemostasis could not be achieved within 5 minutes by direct contact with a wet cotton pellet, prior to material placement
• the remaining radicular tissue was non-vital (with suppuration or purulence necrosis).

Preoperative periapical radiographic F-speed film of the teeth considered for treatment in the study met the following criteria: proper film density and contrast for radiographic diagnosis; displayed a minimum of 3 mm past the furcation area. The radiographs were obtained using XCP extension cone paralleling technique (Dentsply Rinn).

Patient recruitment was stopped on 31 October 2014, when the number of enrolled patients reached the number specified by the sample size calculation. A sample size of 112 teeth (56 pairs) was determined as the minimum sample size required for validity and 95% power, assuming 10% attrition. Randomization of the pulpal medicament was achieved by using the block randomization technique with sealed envelopes. One tooth in each pair was randomly designated to either the experimental/biodentine (group 1) or control/formocresol group (group 2), with the contralateral-paired tooth being assigned to the other pulp medicament.

Ethical approval was obtained from the Research Ethics Committee, Faculty of Dentistry, KAU, Jeddah, Saudi Arabia.

Procedures
The pulpotomy procedures were all performed by one operator. Local anesthesia was induced using lidocaine hydrochloride 2% with epinephrine 1:100,000, and rubber dam isolation was performed, followed by caries removal and unroofing of the pulp chamber using a #330 high-speed carbide bur with ample water spray. The coronal pulp tissue was amputated using a sterile sharp spoon excavator. The pulp chamber was irrigated with normal saline. Pulp hemostasis was achieved using a sterile wet cotton pellet applied for 2 to 3 minutes.

In group 1 (experimental group), biodentine (Septodont; Lot no. B02049) was used according to the manufacturer’s instructions. The entire pulp chamber was completely filled with biodentine as far as (up to) the occlusal surface. In group 2 (control group), a sterile cotton pellet moistened with 1:5 diluted formocresol (Buckley’s Formocresol, Sultan Healthcare) was blotted dry and placed in contact with the surface of the pulp stumps for 5 minutes. Then the pulp stumps were covered with a thick mix of zinc oxide-eugenol (IRM, Dentsply) paste for hermetic sealing.

In both groups, a stainless steel crown (SSC; 3M Espe) was fitted after the pulpotomy procedure in the same visit and cemented using glass-ionomer cement (Rely-X, 3M Espe) after tooth preparation. A postoperative periapical radiographic F-speed film was acquired immediately after the treatment using the XCP extension cone paralleling technique.

Clinical and radiographic evaluation
All treated patients were followed up at 3 and 6 months after the operation for clinical and radiographic evaluation. Independently, two examiners who were blinded to treatment type evaluated the teeth clinically and radiographically. In case of a disagreement, the two examiners discussed the case to reach a consensus. If an agreement was still not reached, a third blinded examiner was asked to evaluate the case and resolve the disagreement. The examiners were faculty staff members from the Department of Pediatric Dentistry, KAU.

For the purpose of radiographic evaluation, a follow-up periapical radiographic film was obtained using the same specially designed holder that was used immediately after the treatment.

The pulpotomized teeth were judged as clinically successful if they met the following criteria:4,50,52,55
• absence of sensitivity, pain, or swelling
• no tenderness to percussion
• no abscess or fistulation
• no tooth mobility.
Radiographic success was defined as:

- presence of a normal periodontal ligament space
- absence of furcation and periapical radiolucency
- absence of internal or external root resorption.

Widening of the periodontal ligament (PDL) was not considered a failure in the absence of other concurrent pathologies. Radiographic evidence of pulp canal obliteration (PCO) was noted, but it was not regarded as a treatment failure.

**Statistical analysis**

Data were collected, revised for completeness and logical consistency, tabulated, and statistically analyzed. Data analysis was performed using the SPSS version 18.0 (IBM). The inter- and intra-rater agreement and correlation between the two examiners was calculated using Cohen’s kappa coefficient. For the two groups, clinical and radiographic findings at 3 and 6 months postoperatively were assessed. The difference in success rate between both groups at the same time point (ie, 3 or 6 months) was evaluated using chi-square analysis. The clinical and radiologic success for each tooth was compared between the third and the sixth months using McNemar’s test. $P < .05$ was considered statistically significant.

**RESULTS**

**Demographic characteristics**

A total of 56 pairs (112 teeth) of primary molars in 37 children (17 boys and 20 girls) were treated in this trial. Of the total number of teeth, 50% (56 teeth) were treated with biodentine and 50% (56 teeth) with formocresol. Overall, 112/112 (100%) teeth were available for the 3- and 6-month evaluations. A CONSORT diagram showing the study protocol up to the 6-month follow-up is presented in Fig 1.

At the time of treatment, the subject’s age ranged between 4 and 8 years with a mean age of $6 \pm 0.75$ years. Since the split-mouth technique was used, there was no difference between the biodentine and formocresol groups in terms of gender distribution and age.
at the time of treatment, as well as in the type of treated molar. Overall, among the treated teeth, the percentage of mandibular molars (79%) was higher than that of maxillary molars (21%). The most frequently treated tooth was the mandibular second molar (45%), followed by the mandibular first molar (34%), maxillary second molar (16%), and maxillary first molar (5%). The distribution of the assessed teeth is presented in Table 1.

Clinical calibration results by the two examiners were found to be in excellent agreement ($\kappa = .98$). For radiographic calibration also, both inter-rater reliability ($\kappa = .97$) and intra-rater reliability ($\kappa = .98$ and .97 for the two examiners) was excellent.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Classification and number treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. treated</td>
<td>37 patients; 56 pairs; 112 teeth</td>
</tr>
<tr>
<td>No. of patients treated in each no. of pairs</td>
<td>1 pair, 18; 2 pairs, 19; 3 pairs, 0; 4 pairs, 0</td>
</tr>
<tr>
<td>No. according to sex</td>
<td>Male 17 patients; 24 pairs; 48 teeth</td>
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<tr>
<td></td>
<td>Female 20 patients; 32 pairs; 64 teeth</td>
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<tr>
<td>No. according to age</td>
<td>4 yrs 5 patients; 8 teeth; 16 teeth</td>
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<tr>
<td></td>
<td>5 yrs 11 patients; 17 pairs; 34 teeth</td>
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<tr>
<td></td>
<td>6 yrs 13 patients; 18 pairs; 36 teeth</td>
</tr>
<tr>
<td></td>
<td>7 yrs 4 patients; 6 pairs; 12 teeth</td>
</tr>
<tr>
<td></td>
<td>8 yrs 4 patients; 7 pairs; 14 teeth</td>
</tr>
<tr>
<td>Mean age</td>
<td>6 ± 0.75 yrs</td>
</tr>
<tr>
<td>No. according to jaw</td>
<td>Maxillary molars 24 (21.4%)</td>
</tr>
<tr>
<td></td>
<td>Mandibular molars 88 (78.6%)</td>
</tr>
<tr>
<td>No. according to molar type</td>
<td>First primary molar 44 (39.3%)</td>
</tr>
<tr>
<td></td>
<td>Second primary molar 68 (60.7%)</td>
</tr>
<tr>
<td>No. according to FDI tooth no.</td>
<td>55 9 (8%)</td>
</tr>
<tr>
<td></td>
<td>54 3 (2.7%)</td>
</tr>
<tr>
<td></td>
<td>64 3 (2.7%)</td>
</tr>
<tr>
<td></td>
<td>65 9 (8%)</td>
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<tr>
<td></td>
<td>75 25 (22.3%)</td>
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<tr>
<td></td>
<td>74 19 (17%)</td>
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<tr>
<td></td>
<td>84 19 (17%)</td>
</tr>
<tr>
<td></td>
<td>85 25 (22.3%)</td>
</tr>
</tbody>
</table>

Clinical findings
For all treated teeth, both biodentine and formocresol showed 100% clinical success at both the 3- and the 6-month follow-ups (Table 2). Therefore, no statistically significant difference in total clinical success rate was determined between the two groups at 3 and 6 months. All the teeth were clinically asymptomatic at both time points without the presence of any pain, sensitivity, swelling, tenderness to percussion, abscess, fistulation, or tooth mobility.

Radiographic findings
For all treated teeth, biodentine and formocresol showed 100% radiographic success at both the 3- and 6-month follow-ups (Table 3). Therefore, no statistically significant difference in total radiographic success was found between the two groups at 3 and 6 months.
None of the radiographs showed PDL widening, internal resorption, external resorption, furcation radiolucency, or periapical radiolucency (Fig 2). The only observed radiographic finding was PCO, which was observed in 10/56 (17.9%) and 7/56 (12.5%) cases in the biodentine and formocresol groups, respectively.

**DISCUSSION**

The present split-mouth, randomized, double-blind, controlled, clinical trial is one of the recent prospective clinical studies about vital pulpotomy with biodentine on human primary molars. It was intended to assess clinically and radiographically the success rate of biodentine pulpotomy in human primary molars, and compare it to that of formocresol.

Formocresol was selected as the control pulpotomy medicament because in spite of its reported adverse effects, it is still considered by many to be the gold standard for primary tooth pulp therapy. Biodentine was used in this study because it is a relatively new material with documented success in many clinical applications including endodontic and restorative applications. This regenerative material can be used in place of formocresol in the pulpotomy of primary molar teeth. Biodentine has recently been shown to be useful not only as an endodontic material, but also as a restorative material.

Children between 4 and 8 years of age with at least two matched bilateral deep carious primary molars requiring pulpotomy were included in this study, irrespective of their sex, race, and social or economic background. This age group was selected taking into consideration the lack of cooperation of younger children and physiologic root resorption (>½ of the root length) in elder ones. The first and second primary molars of both arches were included in the present study.

Standardization was achieved by using a split-mouth study design and by randomly distributing the treated teeth among the treatment groups so that both techniques (materials) were performed equally in each patient. The split-mouth technique was used in this study to ensure that the patient would have a similar immune reaction in both techniques, thus eliminating inter-patient differences in treatment response. The paired-tooth design also attempted to eliminate possi-
ble confounders regarding the types of teeth involved (maxillary versus mandibular, first molar versus second molar), as both medicaments would have been equally affected by these factors. The block randomization technique used in this investigation (with sealed envelopes for each block of two contralateral teeth) allowed the sides to be equally treated by both materials in order to overcome the limitation imposed by operator preference for a particular side.

The same operator performed all the pulpotomy procedures, thus eliminating intra-operator variations. Group 1 underwent biodentine pulpotomy and group 2 underwent formocresol pulpotomy. Unfortunately, the operator could not be blinded to the type of material used since both materials differ in terms of technique and manipulation.

Filling of the entire pulp chamber up to the occlusal level with biodentine was chosen because this material has been successfully used as a permanent dentine substitute in addition to its documented success in many endodontic procedures. The use of biodentine as a dressing material might ultimately provide long-term benefits that would improve the prognosis and retention of pulpotomized primary teeth.

Since restoration of pulpotomized teeth has been shown to have an impact on the prognosis of pulp therapy, all pulpotomized teeth were finally covered with SSCs, which represent the most effective long-term restoration for pulpotomized primary teeth.

An immediate postoperative radiograph was obtained to document the quality of treatment and serve as a comparative baseline for future follow-ups. Since failure of a primary molar pulpotomy may be evidenced in the furcation or periapical area, radiographs that clearly demonstrate both the inter- and the periradicular areas should be used to monitor prognosis after posterior tooth pulpotomies. Therefore, periapical radiographs were used in this study.

All pulpotomized teeth were followed up clinically and radiographically at 3 and 6 months by two expert pediatric dentists (other than the operator), who were full-time faculty members and did not know which material was being evaluated (ie, blinded study).

At all observation time points, the results of the present study showed high (100%) clinical and radio-

Fig 2 Periapical radiographs showing successful (a to d) biodentine pulpotomy of tooth 84 and (e to h) formocresol pulpotomy of tooth 74. (a and e) Preoperative radiographs. (b and f) Immediate postoperative radiographs. (c and g) 3-month radiographs. (d and h) 6-month radiographs.
graphic success rates for both materials used; this could be attributed to proper case selection, proper isolation, high aseptic standards, correct protocol, and appropriate use of medicaments. The results of this trial are in line with the results of a previous randomized controlled clinical trial, which compared biodentine to formocresol in primary teeth pulpotomy with a 6-month follow-up. In that trial, the success rate for biodentine was found to be 100%, while that for formocresol was 94%. It was concluded that there was no significant difference in the success rate between biodentine and formocresol after 6 months of follow-up, and that biodentine seems to be a promising alternative for use in pulpotomies of primary molars.

The high (100%) clinical and radiographic success rates of the formocresol group in this study are in agreement with the success rates observed at 6 months in other studies. This high success rate of formocresol is attributed to its antiseptic (germicidal) and fixative qualities as well as the strict criteria used for selection of teeth in the present study. On the other hand, the high success rate of formocresol in this trial is not comparable with the results of studies by Jabbarifar et al and Holan et al; however, had smaller sample sizes.

The clinical and radiographic success rates of 100% for biodentine in this study were similar to the success rates observed by Cuadros et al. They were also comparable to the results of Rajasekharan et al, who found 94.73% clinical and radiographic success rates for this new product, but with a smaller sample size and a longer follow-up period. Perhaps the higher biocompatibility, alkalinity, regeneration ability, and excellent sealing ability may contribute to this high success rate of biodentine. Additionally, these results are supported and explained on a histologic basis by Shayegan et al, who observed that biodentine promoted beneficial calcification in contact with vital pulp after pulpotomy and direct pulp capping in primary teeth of pigs.

At the 3-month follow-up, no radiographic findings were detected in any of the two groups. PCO was the only observed radiographic finding in both groups at 6 months, which was detected in 15.2% (17/112) of all teeth. In this trial, PCO was observed in 10 (17.9%) teeth treated with biodentine and only 7 (12.5%) teeth treated with formocresol, without significant difference between the two groups.

PCO is a common radiographic finding in pulpotomized teeth treated with formocresol, ferric sulfate, or any calcium silicate-based material, including biodentine. A wide range of incidence has been reported for PCO in teeth treated with formocresol (0% to 52%). In this study, the formocresol group showed PCO in 7 of 56 (12.5%) teeth, which is in the range reported in the literature. The biodentine group in this study showed PCO in 10 of 56 (17.9%) teeth, which is lower than the frequency reported by Rajasekharan et al (40%), who used a smaller sample size and a longer follow-up period. Additionally, our finding of 17.9% for PCO in the biodentine group was in the range reported in the literature for the same class of calcium silicate-based materials (such as MTA).

In spite of the similarity in success rate between biodentine and formocresol observed in this study, one clinical advantage of biodentine over formocresol is that biodentine acts simultaneously as both a dressing and filling material. Formocresol, on the other hand, acts only as a pulpotomy medicament, which needs a restorative material to seal the pulp chamber.

There were some limitations to the present study that were difficult to overcome. The most significant issue was the short follow-up period because of the limited available time. Patient inclusion criteria were strict. Unfortunately, as the two materials were of different types, requiring different protocols and manipulations, the examiners’ cognitive bias for either pulpotomy could not be eliminated in this trial.

The present study is particularly important in that there have been few clinical trials in the recent past using biodentine for primary molar tooth pulpotomy. There was no significant difference in clinical and radiographic outcomes between biodentine and formocresol. The present data indicate that under standardized and optimal clinical conditions and a defined period of observation, biodentine has shown very promising success with all 56 samples without any adverse effects.
The results show that biodentine has the potential to become a substitute for formocresol in primary molar pulpotomies. Even though the sample size was adequate, it is still premature to draw definitive conclusions, as the follow-up period is short. This study might provide a basis for further studies in this field with a long-term follow-up and more participants.

Hopefully, the unique features of biodentine, along with its ease of use, will encourage the general dentist as well as the pediatric dentist to use this new unique material as a routine viable option in pulpotomy procedures.

CONCLUSION

Based on this study’s results, we may conclude that both biodentine and formocresol demonstrate favorable treatment outcomes in the pulpotomy of human primary molar teeth over a 6-month period. Hence, biodentine can be used as a suitable replacement for formocresol in the pulpotomy procedure. Further clinical and histologic studies using a larger sample size and longer observation period should be carried out in future to draw a definitive conclusion.

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