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Clinical observation and histopathological evaluation of pulp after pulpotomy of primary teeth with formocresol and biodentine

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ABSTRACT

Pulpotomy is the typical treatment for keeping deciduous teeth until exfoliation. Formocresol is one of the most common materials used in dental pulpotomy. Due to the side effects of this drug, its replacement with other substances seems necessary. Therefore, this study compared clinical and histopathological evaluations of primary pulpotomy molars with formocresol and biodentine. In this clinical trial, 66 second-mandibular deciduous molars of children aged 6 to 9 years who met the criteria for pulpotomy were selected. Pulpotomy of the teeth was performed using formocresol and biodentine. For each patient, one tooth was randomly placed in the pulpotomy group with formocresol. The other tooth was placed in the pulpotomy group with biodentine. Then the crowns of the teeth were restored with stainless steel veneer. We recorded clinical and radiographic results of these teeth over six months and one year. The teeth were then extracted after 12 months, and hematoxylin-eosin staining was performed for histopathological evaluations. The obtained data were analyzed by Fisher test and SPSS software version 22. The results showed that clinical success of 6 and 12 months of pulpotomy in both groups was 100%. The 6-month radiographic evaluation of the formocresol group was 84.8%, and the biodentine group was 93.9% ($p = 0.21$). The success of 12-month radiographs of the formocresol group and the biodentine group were 81.8 and 93.9, respectively ($p = 0.13$). Also, the histopathological evaluation showed that in the biodentine group, there was mild inflammation in two teeth, two teeth showed moderate inflammation, and two teeth showed severe inflammation. In the formocresol group, severe inflammation was seen in two cases. Mild inflammation was not seen in any of the teeth. Moderate inflammation was seen in one tooth. It was found that there was no significant difference between the two groups in terms of inflammation ($P > 0.05$). No necrosis was seen in any of the biodentine group teeth, and there was necrosis in four teeth of the formocresol group. There was a significant difference between the two groups regarding necrosis ($P = 0.032$). There was no significant difference between the two groups regarding abscess ($P > 0.05$). According to the obtained results, biodentine could be a suitable alternative for mandibular second molar pulpotomy.

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Introduction

Pulpotomy is one of the most common treatments for asymptomatic deciduous teeth in which the pulp is exposed to decay (1). The philosophy of pulpotomy is that the radicular pulp remains healthy or can repair after amputation of the infected pulp. Numerous drugs are used in the pulpotomy of deciduous teeth. The suitable drug for covering the radicular pulp should be bactericidal, harmless to the surrounding pulp and tissue, stimulate radicular pulp repair, and not interfere with the physiological flow of root resorption (2).

The most common drug is formocresol, which contains 19% formaldehyde, 35% cresol, glycerin, and water. The success rate of formocresol pulpotomy has been reported to be 70-98% (3). However, studies have shown the possibility of local and systemic side effects such as inflammatory reactions, necrosis, and cytotoxicity for the pulp, its mutagenic and carcinogenic potential and immunological responses (3-6). There are also concerns about using formocresol in deciduous tooth pulpotomy on permanent replacement enamel. Due to the side effects of formocresol, its replacement with a healthier substance seems necessary (5). For this reason, various materials such as ferric sulfate, calcium hydroxide, MTA, electrosurgery, and laser have been developed and tested for deciduous tooth pulpotomy (7). After the application of formocresol, one-third of the corpus pulp is fixed, in the middle third, chronic inflammation occurs, and in the apical third, there is living tissue, and its benefits are bactericidal, and the structures that provide it are harmless. Also, it does

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not interfere with the process of physiological root analysis (8).

Another new ingredient in treating young dental pulp and restorative therapies today is biodentine. Biodentine is a non-metallic, inorganic material, tri-calcium-silicate-based restorative cement. Biodentine is commercial inorganic restorative cement based on tricalcium silicate called bioactive dentine substitute (9). In studies, this material has shown favorable biological and physical properties such as more straightforward application of the material, faster hardening time, higher compressive strength, higher liquefaction resistance, and faster formation of dentin bridges than MTA. After using biodentine, mineralization is induced, and mineralization occurs in osteodentin, which produces restorative dentin (9, 10).

In recent years, the focus has been on comparing formocresol with other substances such as MTA and Bio-aggregates for deciduous tooth pulpotomy (3). Clinical evaluation and radiographic pulpotomy of pediatric deciduous teeth with MTA and biodentine showed that biodentine has similar clinical and radiographic results to MTA in deciduous molar pulpotomy (9). The study of clinical success and radiography in pulpotomy of deciduous teeth showed that this substance's clinical and radiographic success was very high (11). Due to the favorable properties of biodentine and the disadvantages of formocresol, ferric sulfate, and MTA, and the lack of clinical and long-term studies on the use of biodentine in deciduous teeth, this study performed a clinical, radiographic, and histopathological comparison of pulpotomy deciduous teeth with formocresol and biodentine.

Materials and methods

Studied patients

In this clinical trial, 30 children aged 6 to 9 years with a mean age of 7.2 years who had two-second deciduous molars that needed a mandibular pulpotomy were selected. The crown of these teeth (which had to be removed due to orthodontics) was intact and physiological resorption of the root was observed up to a maximum of 1/3 apical.

Inclusion criteria included general health and proper physical and mental development in the child, lack of adverse clinical signs in the target teeth such as spontaneous pain or nocturnal pain, swelling of pulpal origin, pathological sagging, fistula, pulp calcification, lack of adverse radiographs symptoms of the target teeth, such as internal root resorption, external root resorption, periapical lumen, or forca area.

Sixty teeth were randomly divided into two equal groups of pulpotomy with formocresol (Maquira, Brazilia) and biodentine (Septodont, French). In each patient, pulpotomy was performed with both formocresol and biodentine. After selecting the patient and filling out the consent form before the treatment, a file or checklist was prepared for each patient. OPG radiography of the patient, which was prepared for orthodontic treatment, was used to evaluate the condition of the tooth roots.

Pulpotomy procedure

For pulpotomy, 2% lidocaine anesthesia and infusion of the inferior alveolar nerve block were performed, and all caries were removed by milling (Brasseler, USA) to minimize bacterial contamination after exposure. The roof of the pulp chamber was also removed. Then, using a sharp exciter, the coronal pulp was cut. Then one or more cotton balls impregnated with normal saline were placed at the site of pulp rupture for 2-3 minutes. In case of cessation of bleeding, treatment was randomized in 2 groups formocresol and biodentine.

In the formocresol group, a cotton ball impregnated with formocresol was placed on the pulp for 5 minutes. After browning the canal entrance, zonalin (Kemdent, England) was placed in the cavity. The tooth crown was reconstructed with stainless steel crown (SSC; 3M Espe).

In the biodentine group, after mixing the powder and five drops of liquid and placing it in the amalgamator for 30 seconds, the biodentine was placed in the whole cavity. The tooth crown was reconstructed after 10 to 12 minutes (to harden the material).

The patient presented for treatment in two sessions. Because in each child, pulpotomy with formocresol was performed on one mandibular second molar, and pulpotomy with biodentine was performed on the mandibular second molar on the other side. All treatment steps in each session were recorded in a

patient-specific form. It should be noted that one practitioner performed all treatment steps.

Clinical and radio-graphical evaluations

In 6-month and 12-month recall examinations, the target teeth were examined first, and the clinical condition of the teeth was assessed. Then periapical radiography was obtained by the parallel method. Clinical success included the absence of pain, looseness, swelling, fistula, and radiographic success included the absence of internal occlusion, external occlusion, PDL (Periodontal ligament) widening, and absence of periapical radiolucency. 6-month and 1-year clinical and radiographic examinations were performed by two experts who were not aware of the use of the relevant substance.

Histopathological evaluation via hematoxylin-eosin staining

All teeth were extracted after 12 months (due to orthodontics). The teeth were immediately immersed in 10% neutral formalin after the extraction. Then, the samples were placed in a 10% formic acid solution.

To stain the samples with hematoxylin-eosin, the samples were first immersed in 70, 80, 90, and 96% alcohol for 2 minutes. They were then washed with distilled water.

The samples were then soaked in hematoxylin for 15 minutes. They were washed again with distilled water. They were immersed in calcium carbonate solution for 5 seconds and then immersed in eosin for 10 seconds. Finally, they were rinsed with distilled water and immersed in 70, 80, 90, and 96% alcohol for 5 seconds. Finally, they were placed in xylol for 5 minutes.

Histological changes were then examined by a pathologist who was unaware of the above groups. Each of these samples was examined twice. This evaluation was performed based on Horsted et al.'s modified criterion (12). Number zero was mild inflammation, number one was moderate inflammation, number 2 was severe inflammation, number 3 was necrosis, number 4 was an abscess, and number 5 was internal resorption. Ivory dam formation was also examined in these groups.

Statistical analysis

The obtained data were analyzed using the Fisher test and SPSS software (version. 22). Significance level was considered $\alpha = 0.05$.

Results

Clinical and radio-graphical evaluations

In the clinical trial, all specimens in both groups had clinical success in 6-month and 1-year follow-ups, and no tooth had any symptoms of induction, swelling, fistula, and pain. In the six-month radiographs of the formocresol group, treatment failure was observed in five cases, which included three cases of internal resorption and two cases of radiolucency, and other symptoms of failure such as external degradation PDL widening and periapical radiolucency were not observed. (Table1). In a 6-month study of the biodentine group, only two samples showed treatment failure, which included one case of internal resorption and one case of radiolucency (Table 1).

Table 1. Frequency distribution of radiographic findings in two groups in a 6-month follow-up

Variable	Biodentine Group	Formocresol Group	P-value
Internal Resorption	1 (3%)	3 (9.1%)	0.31
External Resorption	0 (0%)	0 (0%)	1
PDL Widening	0 (0%)	0 (0%)	1
Radiolucency	1 (3%)	2 (6.1%)	0.50
Periapical Radiolucency	0 (0%)	0 (0%)	1

One-year radiographs of the formocresol group showed treatment failure in six samples, including three cases of internal resorption and three cases of radiolucency, and other symptoms, such as external degeneration, PDL widening, and periapical radiolucency were not seen (Table 2). In a one-year study of the biodentine group, only two samples showed treatment failure, including one case of internal degradation and one case of radiolucency (Table 2).

At the 6-month radiographic follow-up, 30 cases (93.9%) were observed in the biodentine group and 28 cases (84.8%) in the formocresol group. Fisher's exact test did not show a significant difference between the two groups (p-value = 0.21). At 1-year follow-up, in the biodentine group, 30 cases (93.9%) and in the formocresol group, 27 cases (81.8%) were

successfully observed. Still, Fisher's exact test did not show a significant difference between the two groups (p-value = 0.13) (Figure 1).

Table 2. Frequency distribution of radiographic findings in two groups in the one-year follow-up

Variable	Biodentine Group	Formocresol Group	P-value
Internal Resorption	1 (3%)	3 (9.1%)	0.31
External Resorption	0 (0%)	0 (0%)	1
PDL Widening	0 (0%)	0 (0%)	1
Radiolucency	1 (3%)	3 (9.1%)	0.31
Periapical Radiolucency	0 (0%)	0 (0%)	1

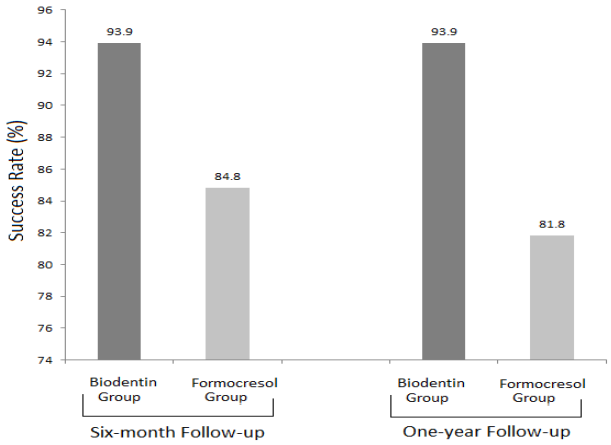

Figure 1. Success rate (percentage) of radiographic findings in two groups in six-month and one-year follow-ups

Histopathological evaluation

In the biodentine group, there was mild inflammation in two teeth, two teeth showed moderate inflammation, and two teeth showed severe inflammation. In the formocresol group, severe inflammation was seen in two cases (Figure 2). Mild inflammation was not seen in any of the teeth. Moderate inflammation was seen in one tooth. It was found that there was no significant difference between the two groups in terms of inflammation (P >0.05). No necrosis was seen in any of the biodentine group teeth, and there was necrosis in four teeth of the formocresol group. There was a significant difference between the two groups regarding necrosis (P = 0.032). There is no significant difference between the two groups regarding abscess (P> 0.05). Ivory bridges were seen in one tooth of the formocresol group and one tooth of the biodentine group. Table 3 shows the results of tooth tissue changes in the two groups.

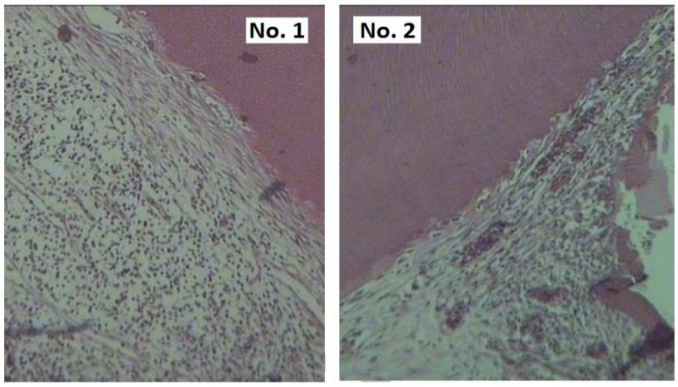

Figure 2. Observation of Internal resorption and severe inflammation twelve months after formocresol treatment in two cases through histopathological evaluation

Table 3. Results of tooth tissue changes in the two groups

Inflammation Rate	Biodentine Group	Formocresol Group	P-value
Mild Inflammation	2 (4%)	0 (0%)	0.085
Moderate Inflammation	2 (4%)	1 (2%)	0.067
Severe Inflammation	2 (4%)	2 (4%)	1
Necrosis	0 (0%)	4 (8%)	0.032
Abscess	1 (2%)	1 (2%)	1

Discussion

Pulpotomy is the most common treatment for preserving decayed deciduous teeth with pulp involvement. With this method, the teeth will keep their space, and future problems in this field will be prevented (13). Formocresol, commonly used as a pulpotomy drug in deciduous teeth, has side effects. Biodentine, a hemostatic agent, can be used in the pulpotomy of deciduous teeth (14). This study aimed to evaluate the impact of Biodentine and formocresol on the pulp of deciduous teeth after pulpotomy with these substances. The present study results showed that there was no difference between the clinical success rate and radiography of formocresol and biodentine. Despite the proven harms of formocresol and its toxic properties, this substance was used due to its gold standard in the pulpotomy of deciduous teeth. The reason for using biodentine is its success in endodontic and restorative applications. This regenerative substance can be used on the pulp of pulpotomies deciduous teeth instead of formocresol. In Cohn (15), Allazzam et al. (16), And Akhtar et al. (17), biodentine has been introduced as a suitable material for pediatric dental treatments such as pulp cap, pulpotomy, perforation, and oxidation.

The mean age of the children was 6-9 years, who had bilateral and symmetrical deep caries in their primary molars. The reason for not choosing younger children was their lack of cooperation while doing work. The present study performed treatment on symmetrical and bilateral caries in children, and biodentine and formocresol, were placed randomly. The advantage of this method was that their immune systems matched to cause possible interference in the research results considered in this study.

In a 6-month and 1-year clinical trial, no failure was observed in any samples. In the 6-month radiographic study in the formocresol group, the success rate of radiography was 84.8% and the success rate of one-year radiography was 81.8%. In the biodentine group, the 6-month success of radiography was 93.9%, and the one-year success was 93.9%. There was no statistically significant difference between the clinical success rate and radiography of formocresol and biodentine in this study. In the present study, both materials' clinical and radiographic success was 100%, which is due to the selection of the appropriate case, adequate isolation, correct treatment, and use of proper materials. The results of this study are in line with the study of Rubanenko et al. (18), in which the success of biodentine was 100%, and the success of formocresol was 94%, which were not statistically significant.

In the study of El Sadek et al. (13), there was no statistically significant difference between the clinical and radiographic success of formocresol and biodentine, which was consistent with the present study results. Although performed in children 3 to 8 years of age and followed by 3 to 6 months, it can be concluded that the use of biodentine instead of formocresol is possible in primary pulpotomy. The 100% clinical success and radiography of formocresol in this study were consistent with other studies that had a 6-month follow-up due to the appropriate case selection and the antimicrobial and fixative properties of this substance. Also, the successful results of formocresol in this study were not consistent with the study of Holan et al. (19). This discrepancy could be related to the difference in the number of samples. The clinical and radiographic success of 100% biodentine in the study of Cuadros et al. (20) was similar to the present study. In the study of Rajasekharan et al. (21), the clinical and radiographic success of biodentine was 97.73%, which had a smaller number of samples and a more extended follow-up period than the present study. The reason for the success of biodentine in clinical and radiographic follow-ups can be related to the unique properties of this material, such as biocompatibility, regenerative properties, and excellent sealing.

In general, due to the lack of significant differences between formocresol and biodentine in this study, biodentine is superior to formocresol because biodentine has two properties (covering and filling). While formocresol acts only as a drug, and after fixation, a restorative substance is necessary to fill the chamber pulp. According to the present study results, if the treatment is performed in ideal and clinical standard conditions, biodentine is a practical and valuable substance that can be considered a suitable alternative to formocresol in pulp treatments for deciduous teeth. The limitations of this study include the preparation of biodentine, its high cost (almost 100 times), and follow-up longer than one year.

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Authors' contribution

This study was done by the authors named in this article, and the authors accept all liabilities resulting from claims which relate to this article and its contents.

Conflicts of interest

There are no conflicts of interest.

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Availability of data and materials

The data used to support the findings of this study are available from the corresponding author upon request.

Statements and Declarations

The author declares that no conflict of interest is associated with this study.

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