

## EFFICACY OF COMBINATION OF ANTIBIOTICS IN TREATMENT OF INFECTED DECIDUOUS MOLARS

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### Abstract

Dental caries is a significant global health issue, often leading to pulp necrosis and infection in primary teeth. Traditional pulpectomy procedures face limitations due to complex root anatomy and patient cooperation, prompting the search for alternative treatments. This study compares the effectiveness of Lesion Sterilization and Tissue Repair (LSTR) using a modified 3Mixed-MP mortal pulpotomy (ciprofloxacin, metronidazole, amoxicillin in macrogol-propylene glycol) versus conventional formocresol for treating pulpitis and periapical lesions in primary molars. A split-mouth randomized clinical trial was conducted on fifteen children with bilateral non-vital mandibular primary molars. One molar received formocresol treatment while the opposing tooth was treated with the modified 3Mixed-MP mortal pulpotomy. Clinical parameters-pain, swelling, mobility-and radiographic measures of root length and bone density were evaluated at 1-, 3-, and 6-months post-treatment. Both therapies resulted in high clinical success and symptom resolution at 6 months. Formocresol offered slightly higher success rates for pain relief and bone density improvement (86.7%) compared to 3Mix-MP (60%), but both treatments preserved root integrity without marked resorption. The 3Mix-MP technique exhibited transient inflammatory signs, yet its minimally invasive nature and shorter procedure time make it advantageous for uncooperative pediatric patients. Survival analysis indicated longer-lasting benefits for formocresol. In summary, dual-antibiotic LSTR (3Mixed-MP) presents a viable, less traumatic option for managing infected primary molars. Further research is recommended to optimize antibiotic protocols and enhance long-term outcomes for pediatric endodontic care.

**Keywords:** Primary Molar Pulpectomy, Lesion Sterilization and Tissue Repair, Formocresol Pulpotomy, Pediatric Endodontics.

### INTRODUCTION

Dental caries is the leading cause of childhood hospitalization in high-income countries, accounting for 5%-10% of healthcare budgets and posing a significant global health burden [1]. This multifactorial disease involves environmental, genetic, and infectious agents, with pathogenic microorganisms forming dental plaque and biofilm. Untreated caries can progress to pulp necrosis, presenting clinical challenges in primary teeth due to complex root canal anatomy and difficulties in instrumentation. Preserving primary teeth until natural exfoliation is critical, as they maintain space for permanent teeth.

Pulpectomy is the gold standard for treating non-vital primary molars, involving complete removal of infected pulp and filling with absorbable material [2]. However, it is time-consuming, requires patient cooperation, and mechanical cleaning is often incomplete due to variable root canal morphology [3].

Premature extraction eliminates infection but leads to space loss and subsequent orthodontic issues. Previously, formocresol pulpotomy was employed for less cooperative children, but its use has diminished because of concerns over formaldehyde's safety, genotoxicity, and carcinogenic potential [4].

Lesion Sterilization and Tissue Repair (LSTR), also known as Non-Instrumental Endodontic Treatment (NIET), was introduced as a less invasive alternative for infected primary teeth, especially in cases with poor prognosis or difficulty performing pulpectomy. LSTR utilizes a topical mixture of antibacterial drugs-typically Ciprofloxacin, Metronidazole, and Minocycline (3Mix)-in a vehicle such as Macrogol and Propylene Glycol to disinfect root canals and promote tissue repair [5].

The approach focuses on sterilization rather than mechanical removal, relying on the host's natural healing mechanisms, summarized as "do not remove or touch and leave it" [6]. Studies have demonstrated the efficacy of this drug combination against oral bacteria in endodontic lesions of primary teeth both in vitro and in situ [7].

Dental caries is both a disease and a lesion, requiring a cariogenic biofilm and exposure to fermentable carbohydrates for progression [8]. Frequent sugar intake shifts oral biofilm microbiota to an acidogenic and cariogenic state, resulting in dynamic pH fluctuations and hard tissue lesions [9].

Beyond microbiological factors, behavioral, psychological, social factors, and inadequate fluoride exposure also contribute significantly [10]. Caries affects 60%–90% of schoolchildren globally, with prevalence up to 83.3% in some Middle Eastern regions, leading to pain, sleep disruption, impaired learning, nutritional deficits, and social isolation in severe cases [11]; [12]; [13].

This study aims to explore simpler, less invasive restorative options like LSTR for infected primary molars, to improve retention, reduce treatment difficulty and premature tooth loss, and ultimately enhance children's oral health and quality of life.

## MATERIALS AND METHODS

### Research Settings and Ethical Approval

The present study was conducted in the Pediatric Dentistry Department at the Faculty of Dentistry, Suez Canal University<sup>1</sup>. Ethical approval was secured from the Research Ethics Committee (REC) of the faculty, with approval number 64/2017. All clinical procedures were performed in accordance with the REC's guidelines and regulations.

## Subject Selection

Fifteen children aged 4 to 8 years were selected to detect the effect size of 0.25 according to [Cohen (1988); 14], at a power ( $1-\beta=0.90$ ) of 90% at a significance probability level of  $p<0.05$ . Each child had bilateral non-vital lower deciduous molars (first or second molars) suitable for non-vital treatment. Medical and dental histories were obtained, and clinical examinations with preoperative periapical radiographs confirmed eligibility. Clinical symptoms such as pain, abscess, fistula, gingival swelling, and purulent exudates were recorded.

## Inclusion Criteria

Clinical criteria included apparently healthy children of both sexes with bilateral non-vital mandibular deciduous molars that were restorable. Behavior ratings on the Frankel scale were required with excluding rating 1 [definitely negative], with clinical history indicating spontaneous pain, intraoral swelling, or fistula presence. Radiographic criteria [15] included discontinuity of the lamina dura (apical or furcation area), root resorption not exceeding one-third of root length, and limited furcation or apical radiolucency.

## Exclusion Criteria

Children with sensitivity to study drugs or whose parents declined to sign informed consent were excluded [5];[16];[17].

## Informed Consent

The study purpose, benefits, and risks were explained verbally to children and parents/caregivers. Written informed consent was obtained from parents/caregivers prior to any clinical procedures.

## Randomization and Teeth Grouping

A simple randomization using coin tossing allocated the 30 selected non-vital molars from 15 children into two groups in a 1:1 ratio, following the split-mouth technique. Group A, included 15 molars treated with formocresol mortal pulpotomy; Group B, included 15 molars treated with a 3 mix-MP was prepared by using a mixture of Macrogol (M) and propylene glycol (P) to prepare an ointment material (MP); then mixed later with a vehicle (MP) in a ratio of 7:1 that is one part of the vehicle with seven parts of the pulverized drugs in order to obtain an ointment with a consistency that can be formed into a small pellet to form the dual mix.

## Clinical procedures

Benzocaine 20% topical anesthesia gel was applied to the dried mucosa for 2 minutes, followed by local anesthesia with Mepivacaine HCl 2% (Mepivacaine-L®) using a standard technique. The selected molar was isolated with a rubber dam (**Figures 1, 2**). Access opening was performed using a size II round bur in a high-speed handpiece, removing caries, necrotic pulp, and any previous restorations (**Figure 3**). The cavity was irrigated with normal saline.

The treated molars were divided into two groups based on the pulpotomy dressing material:

### I. Group A (Mortal Pulpotomy Group)

Molars received formocresol mortal pulpotomy in two visits. In the first visit, a sterile cotton pellet saturated with Prevest DenPro Formacresol® was squeezed to remove excess solution, then placed over the orifices. The cavity was temporarily filled for 5 days (**Figure 4**). In the second visit, the temporary filling and cotton pellet were removed, the cavity irrigated with 10% sodium hypochlorite, dried, and filled with Reinforced Zinc Oxide/Eugenol (Zinconol: Prevest DenPro®), then covered with a stainless-steel crown (**Figure 5**) [18].

### II. Group B (Lesion Sterilization Repair Group)

3Mixed-MP was prepared by pulverizing equal parts of ciprofloxacin, metronidazole, and amoxicillin after removing enteric coatings [19]. The powders were mixed with a macrogol and propylene glycol vehicle in a 7:1 ratio to form an ointment shaped into a small pellet [20]. The mixture was freshly prepared for each patient.

Before application, root canal orifices were enlarged to a 1 mm diameter and 2 mm depth medication cavity using a round bur [21]. The cavity walls were chemically cleaned with 37% phosphoric acid gel for 1 minute, rinsed with sterile water, and dried. The cavity was half-filled with the 3Mixed-MP (Figure 6), sealed with glass-ionomer cement (Figure 7), and restored with a suitable stainless-steel crown (Figure 8).



**Figure 1: Selection of eligible molars ( right and left second molars)**



**Figure 2: Rubber dam isolation for the selected molars (a,b)**

**Figure 3: Caries removal and access cavity (a, b)**



**Figure 4: cotton pellet with Foramcresol® 19%**



**Figure 5: Cavity filled with reinforced ZnOE**



**Figure 6: cavity half-filled with 3Mix-MP**



**Figure 7: cavity sealed with glass ionomer**



**Figure 8: Treated molars restored with stainless steel crowns**

#### **IV. Post operative evaluation and follow up:**

##### **1) Clinical assessment:**

Patients were recalled at 1, 3, and 6 months postoperatively, with follow-up dates noted on recall cards. Parents were instructed to report any pain or swelling before scheduled visits. Clinical evaluation included inspection with a mouth mirror and naked eyes, and percussion using the mirror handle tip to assess ligaments and bone. Assessed parameters were spontaneous or dull pain, redness or swelling of soft tissue, and tooth mobility. Mobility was graded using the Grace & Smales index:

- Grade 0: 0–0.25 mm (physiologic)
- Grade 1: 1 mm (horizontal)

- Grade 2: 2 mm (horizontal)
- Grade 3: 2 mm (horizontal + vertical)

Clinical success required absence of spontaneous pain, gingival or mucobuccal fold changes (redness, swelling, or fistula), and tooth mobility. Presence of any sign constituted failure.

## 2) Radiographic Assessment

Digital intraoral parallel periapical radiographs were taken immediately postoperatively and at 1, 3, and 6 months using the CSN RX4 digital X-ray system with a paralleling technique (**Figure 9**). The CCD sensor (23.4×37.4 mm, active area 20×30 mm, pixel size <20 microns) was positioned with a Rinn (XCP) film holder and exposed using Fona® intraoral X-ray unit at 70 kV and 6 mA for 0.06 seconds. Images were automatically read out and stored on the patient archive (**Figure 10**).

Image analysis was performed with Digora 2.7 software, applying image restoration and enhancement for density and contrast adjustments. Parameters evaluated included changes in mesial and distal root lengths (radiometric, mm) and bone density at root apices and furcation midpoint (densitometric, grayscale values).

Root length measurement was standardized (**Figure 11**): a horizontal line (line A) connecting the CEJ at mesial and distal surfaces, a parallel tangent line at the root apex (line B), and a perpendicular vertical line from line B to line A (line C) representing root length in millimeters for follow-up comparison.

### Bone density (densitometric analysis):

The software of Digora program was used for assessment of the radiodensity of the bone at three sites: midfurcation, just below the end of the mesial root and just below the end of the distal root. Density measurements were calculated by quantifying the image on 256 gray scales. Zero scale was given to the totally black regions (totally radiolucent) while 255 gray scales were given to the totally white areas (totally radiopaque). The measurements of the relative density of the bone were measured as follows:

Three equal square areas (2mm×2mm) were identified and drawn just below the apex of the mesial root, below the distal root and at the midpoint of the furcation area of the treated tooth. The numeric value of the bone radiodensity at the drawn square was recorded. The same areas were measured at subsequent radiographs where each reading was taken twice and the mean gray scale value for the reading was recorded for comparisons with follow up radiographs (**Figure 12**).

The radiometric and densitometric measurements were repeated at the successive follow up visits (1, 3 and 6months) for control group A (formacresol) and experimental group B (3Mixed-MP).

All radiographs were evaluated twice by the same examiner, who was blinded to the group being studied, at two weeks intervals. The mean value of each examined criterion was obtained for each reading and used for further evaluation.

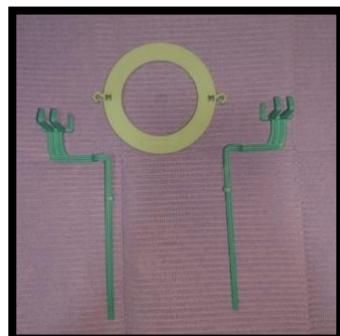
Radiographic success at follow-up visits met the following criteria:

**1) Radiometric analysis:**

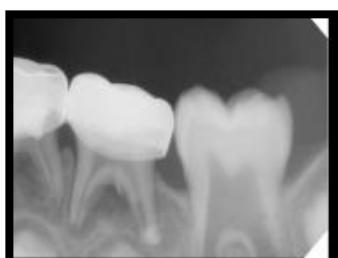
Static value of root length (no root resorption) revealed as no decrease in linear root length (difference measured between baseline root length and 1-, 3- and 6-months follow-up).

**2) Radiographic density analysis:**

Increase in radiographic density (denoting remineralization or increased mineral content of bone) revealed as an increase in gray-scale numerical value throughout the study period.



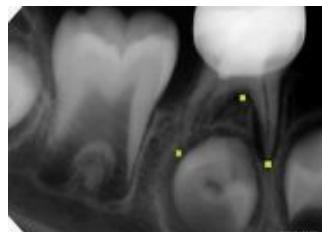
**Figure 9. 24: CSN RX4 X ray cone positioner ring and sensor holders (left & right)**



**Figure 10. 25: Newly read image on CSN Image software system**



**Figure 11. 26: Radiometric analysis for measuring mesial root length using Digora system software**



**Figure 12. 27: Densitometric analysis of periapical mesial, distal and furcation areas using Digora system software**

## Statistical analyses

Data were collected, organized, and checked for outliers using Microsoft Excel 2016 and SPSS (IBM-SPSS ver. 28.0 for Mac OS) [22]. Normality was assessed with Shapiro-Wilk and Kolmogorov-Smirnov tests to determine parametric or nonparametric distribution. Sociodemographic data, pain, swelling/redness, tooth mobility, and success rates were nonparametric, while linear measurements and bone density were parametric.

Nonparametric data were described by frequency (n, %) and compared between treatment groups (formocresol and 3Mix-MP) using Mann-Whitney U or Wilcoxon tests. Differences across time points of investigation (Immediate pre-operative, 1 month, 3 month, 6 month) within each group were analyzed with Friedman's test at a significance level of 0.05.

Parametric data were expressed as mean  $\pm$  standard deviation. Repeated measures ANOVA was used to evaluate differences between treatments and across time points, followed by Duncan multiple range tests (DMRTs) for multiple comparisons. Independent samples t-tests compared treatments at each time point ( $p < 0.05$ ).

## RESULTS

### 1. Descriptive data of the two groups (demographic data):

The present study was conducted on 15 children: eight boys (53.3%) and seven girls (46.7%), the difference between genders was nonsignificant as revealed by Chi-square test. The mean (SD) values for age were 5.6 (1.2) years old with a minimum of four and a maximum of eight years old. Data for age and gender are presented in **Table 1** and **Figure 13**.

**Table 1: Age and gender distribution in the study**

Variables		No.	%	Significance
Age (years)	Mean $\pm$ SD	5.6 $\pm$ 1.2	46.7%	---
	Range	4-8		
Gender	Girl	7	53.3	0.796 ns
	Boy	8		

NS, non2-significant at  $p>0.05$ , significance checked using Chi-square test

### Clinical assessment:

#### Pain incidence:

The incidence of pain was recorded in the two groups; formacresol and 3Mix-MP group and comparison between pain incidence at successive follow ups is presented in **Table 6** and **Figure 14** in terms of number and frequency (n, %).

In formacresol group, pain was recorded in 6 (40%) patients immediately preoperative, however, no pain was recorded (0.0%) after 1, 3, and 6 months postoperative; respectively. The decrease in pain scores in the formacresol group was highly significant.

On the other hand, in the 3Mix-MP group, pain was recorded in 5(33.3%) patients immediately preoperative and 1 (6.7%) patient only in 3 months postoperative follow ups, however, 1 months and 6 months showed no recorded pain, the difference between follow ups in 3 Mix-MP was significant as revealed by Friedman's test ( $p=0.005$ ). In both groups, there was a statistically significant decrease in prevalence of pain after one month, three as well as six months (**Table 6**) as compared to the baseline (immediate postoperative). Regarding the comparison between both groups, immediately pre-operative; there was no statistical significance difference between two groups. After one as well as six months, none of the cases showed pain in the two groups, so no statistical comparison could be performed. After three months, none of the cases had pain in the formacresol group whereas one case showed pain in the 3Mix-MP group. However, the statistical test result was non-significant, because all cases in one side of the probability equation (one group) had no pain (**Table 2**).

**Table 2: Comparison between pain incidence percentage at different follow-up periods within and between both groups**

Time		Formacresol (n = 15)		3 Mix-MP (n = 15)		Mann-Whitney U
		N	%	N	%	
Immediate pre-operative	Pain	6	40%	5	33.30%	0.775 ns
	No pain	9	60.00%	10	66.70%	
1 month	Pain	0	0%	0	0%	>0.999ns
	No pain	15	100.00%	15	100.00%	
3 months	Pain	0	0	1	6.70%	0.775 ns
	No pain	15	100.00%	14	93.30%	
6 months	Pain	0	0%	0	0%	>0.999ns
	No pain	15	100.00%	15	100.00%	
<i>Friedman's test (p-value)</i>		<0.001***		0.005**		

\*, \*\*, \*\*\*, Significant at  $p<0.05$ ,  $<0.01$ ,  $<0.001$ ; ns, non-significant at  $p>0.05$

#### Redness or swelling of the soft tissue:

The incidence of **redness, swelling or fistula** in the two study groups and comparison between both groups; formacresol and 3Mix-MP groups at different follow ups is presented in **Table 3 and Figure 13** in terms of number and frequency (n, %).

In **formacresol group**, redness, swelling and/or fistulation was recorded in 5 (33.3%), 1 fistula (6.7%), 1 fistula (6.7%), and 1 fistula (6.7%); in immediate, 1, 3, and 6 months postoperative; respectively. There was a statistically significant ( $p=0.008$ ) decrease in prevalence of redness or swelling of soft tissue after one month, three as well as six months.

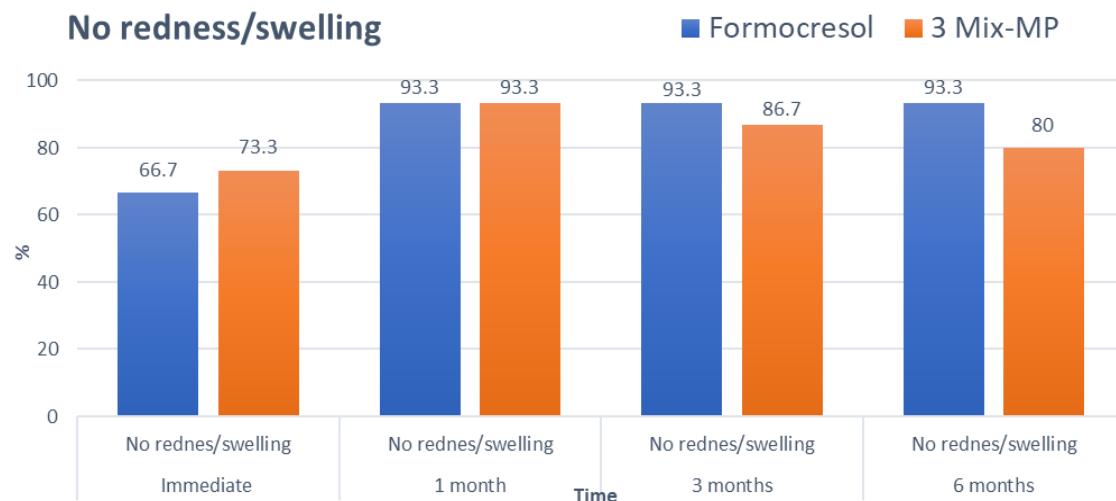
In **3Mix-MP group**; redness, swelling or fistulation were recorded in 4 (26.7%), 1 fistula (6.7%), 2 fistulae (13.3%), 3 fistulae (20%) in immediate, 1, 3, and 6 months; respectively. There was no statistically significant ( $p=0.072$ ) change in percentage of mucobuccal fold changes (redness, swelling or fistula) after one month, three as well as six months (**Table 3**).

Regarding the comparison between both groups, immediately post-operative, one, three as well as six months; there was no statistically significant difference between the two groups at immediate ( $p>0.05$ ), 1 month ( $p>0.05$ ), 3 months ( $p>0.05$  ns) and 6 months ( $p>0.05$ ) (**Table 3**).

**Table 3: Comparison between percentage of redness or swelling of soft tissue at different follow up periods within and between both groups**

Time	Swelling	Formacresol (n = 15)		3Mix-MP (n = 15)		Mann-Whitney U (p-value)
		N	%	N	%	
Immediate post-operative	Yes	5	33.3%	4	26.7	>0.999 ns
	No	10	66.7%	11	73.3%	
1 month	Yes	1	6.7%	1	6.7%	0.775 ns
	No	14	93.3%	14	93.3%	
3 months	Yes	1	6.7	2	13.3%	>0.999 ns
	No	14	93.3%	13	86.7%	
6 months	Yes	1	6.7%	3	20%	0.775 ns
	No	14	93.3%	12	80%	
<b>Friedman's test</b>		<b>&lt;0.008**</b>		<b>0.072 ns</b>		

\*, \*\*, \*\*\*, significant at  $p<0.05$ ,  $<0.01$ ,  $<0.001$ ; ns, non-significant at  $p>0.05$



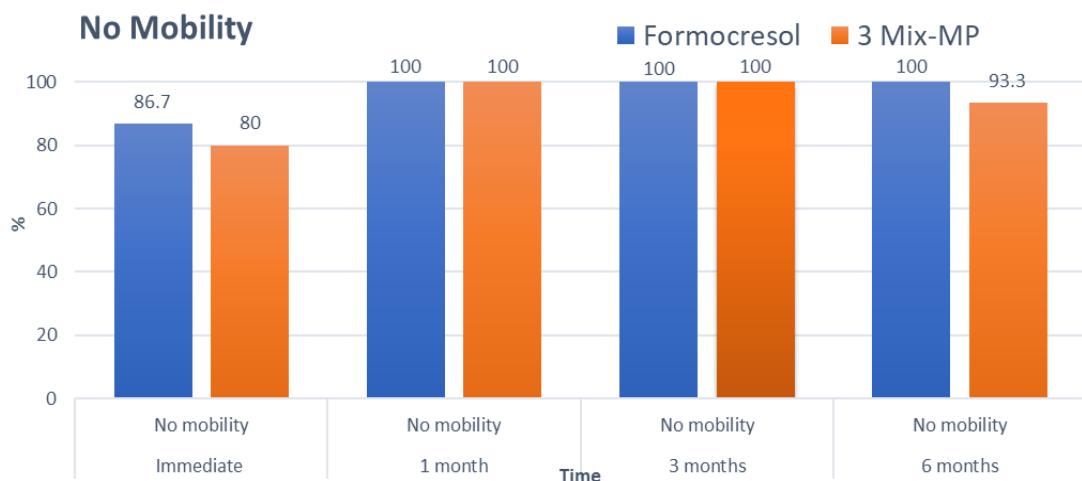
**Figure 13: Bar chart represents percentage of redness or swelling of soft tissue in the two groups throughout the study period**

#### Tooth Mobility:

#### Mobility incidence:

The incidence of mobility was recorded immediately postoperative and after 1, 3, and 6 months as seen in **Table 4** and **Figure 14**. Immediately postoperative 2 (13.3%) and 3 (20%) of patients showed mobility in the formacresol and the 3Mix-MP groups; respectively, however, the difference between two groups was nonsignificant.

After 1 and 3 months, no incidence of mobility was recorded in both groups, therefore, the difference between both groups was nonsignificant. However, after 6 months, only 1 (6.7%) patient in 3Mix-MP group showed incidence of mobility. Upon comparing the incidence of mobility within each group, there was no statistically significant difference in percentage of mobility after one month, three as well as six months in comparison to the baseline (immediate post operative) (**Table 4**). Upon comparing the results of both groups at the different follow up periods, no statistically significant difference was found immediately postoperative, after one and after three months. After one as well as three months, none of the cases had mobility in the two groups, so no statistical comparison could be performed. After six months, none of the cases had mobility in formacresol group and one case had mobility in 3Mix-MP group. Therefore, the statistical test was non-significant because all cases in one group had no mobility. (one side of the probability equation =0) (**Table 4**).



**Figure 14.31: Bar chart representing percentage of mobility incidence in the two groups throughout the study period**

**Table 4: Comparison between percentage of mobility at different follow up periods within and between both groups**

Time	Incidence of mobility	Formacresol (n = 15)		3Mix-MP (n = 15)		Mann-Whitney U P-value
		N	%	N	%	
Immediate post-operative	Yes	2	13.3%	3	20%	0.775 ns
	No	13	86.7%	12	80%	
1 month	Yes	0	0%	0	0%	>0.999 ns
	No	15	100%	15	100%	
3 months	Yes	0	0%	0	0%	0.999 ns
	No	15	100%	15	100%	
6 months	Yes	0	0%	1	6.7%	0.775 ns
	No	15	100%	14	93.3%	
Friedman's test		0.112 ns		0.066 ns		

\*, \*\*, \*\*\*, significant at  $p<0.05$ ,  $<0.01$ ,  $<0.001$ ; ns, non-significant at  $p>0.05$

### Mobility grades:

Results of tooth mobility grading in the two groups; formacresol and 3Mix-MP are presented in **Table 5** and **Figure 15** in terms of number and frequency (n, %).

At **immediately postoperative** time interval, a total of 2 patients (13.4%) of group A (formacresol) showed tooth mobility; one patient was in grade 2 and another patient showed in grade 3 mobility. In group B (3Mix-MP), a total of 3 patients showed tooth mobility; 2 patients were grade 2 while the third patient was grading 3 mobility.

At the different studied postoperative follow ups (1, 3, and 6 months) intervals, in group-I (**formacresol**) no patients (0%) showed any tooth mobility. Which was not significantly changing among time points. Therefore, there was no significant difference in the results within the formacresol group.

However, in the second group (**3Mix-MP**), at 1 and 3 months follow ups, no patients (0%) showed any grade of tooth mobility, whereas after 6 months, 1 patient (6.7%) showed tooth mobility of grade-3, and the difference within the group in comparison to the baseline was non-significant.

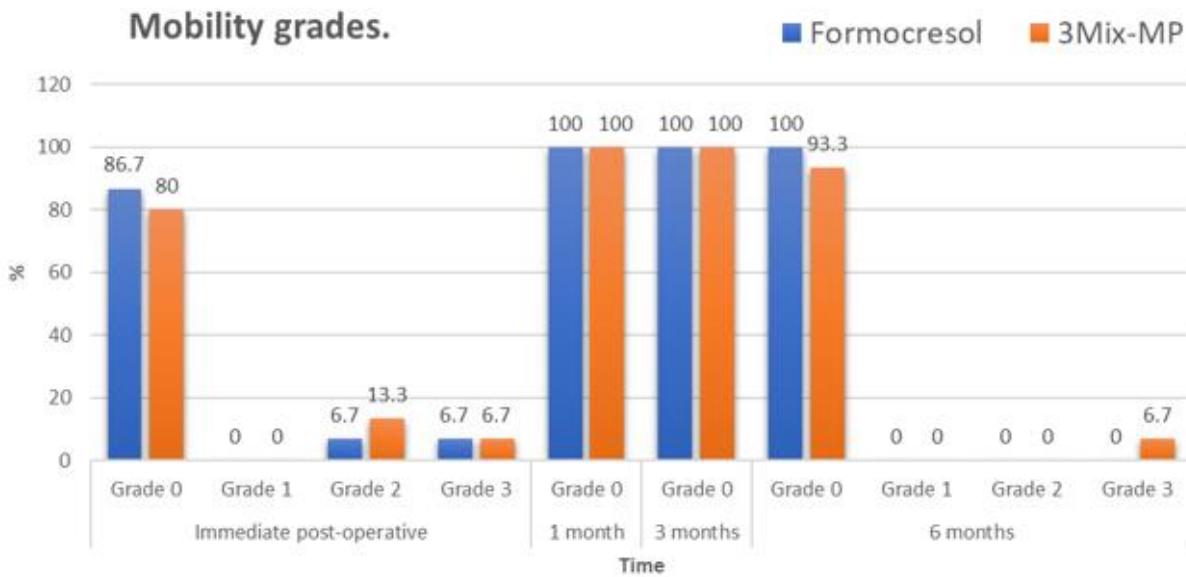
Therefore, within both groups there was a non-significant change ( $p>0.05$ ) in mobility grades after one month, three as well as six months.

Upon comparing both groups at different follow ups, the difference between formacresol group and 3Mix-MP at different time intervals (immediate, 1, 3, and 6 months postoperative), was non-significant ( $p>0.05$ ) as revealed by Mann-Whitney test (**Table 5**).

**Table 5: Incidence and comparison between mobility grades percentage in the two groups**

Time	Mobility Grade	Formacresol (n=15)		3Mix-MP (n=15)		Mann-Whitney p-value
		No.	%	No.	%	
Immediate post-operative	Grade 0	13	86.7%	12	80%	0.775 ns
	Grade 1	0	0%	0	0%	
	Grade 2	1	6.7%	2	13.3%	
	Grade 3	1	6.7%	1	6.7%	
1 month	Grade 0	15	100%	15	100%	>0.999 ns
	Grade 1	0	0%	0	0%	
	Grade 2	0	0%	0	0%	
	Grade 3	0	0%	0	0%	
3 months	Grade 0	15	100%	15	100%	>0.999 ns
	Grade 1	0	0%	0	0%	
	Grade 2	0	0%	0	0%	
	Grade 3	0	0%	0	0%	
6 months	Grade 0	15	100%	14	93.3	0.775 ns
	Grade 1	0	0%	0	0%	
	Grade 2	0	0%	0	0%	
	Grade 3	0	0%	1	6.7%	
Friedman's test		0.112 ns		0.066 ns		

\*, \*\*, \*\*\*, significant at  $p<0.05$ ,  $<0.01$ ,  $<0.001$ ; ns, non-significant at  $p>0.05$



**Figure 15: Bar chart represents the percentage of mobility grades in the two groups throughout the follow up periods**

#### Results of Radiographic assessment:

##### Radiometric analysis (linear analysis) for root length:

##### Mesial linear measurements.

Regarding radiometric results (root length) of the mesial root for the two study groups, **Table 6** and **Figure 16 and 17** represent the mean mesial root length in both study groups, the comparison between the successive follow ups within each group as well as the comparison between both group at each follow up interval.

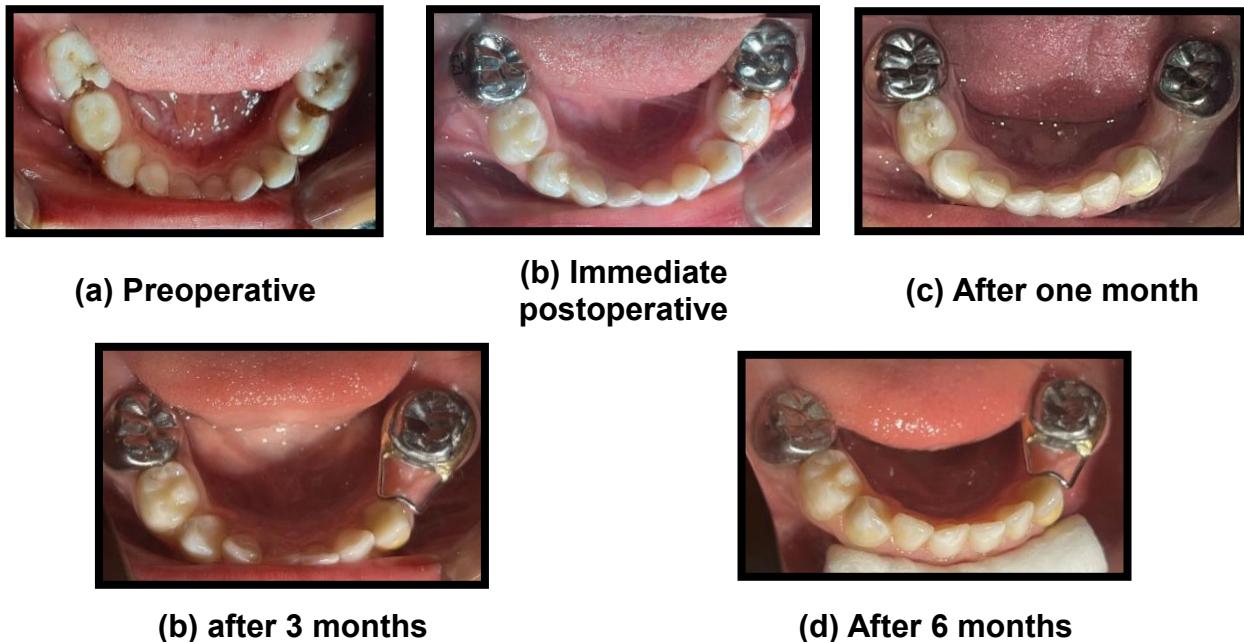
As regards **formacresol group** at the mesial root; the linear measurement at immediate, 1, 3 and 6 months recorded an average ( $\pm SD$ ) of  $8.55 \pm 0.60$ ,  $8.54 \pm 0.59$ ,  $8.53 \pm 0.50$ , and  $8.48 \pm 0.49$ ; respectively. Mesial root length decreased non significantly ( $p > 0.05$ ) from immediate to 6 months as revealed by one-way repeated measure analysis of variance.

While for 3Mix-MP group at the mesial root, the linear measurement at immediate, 1, 3 and 6 months recorded an average( $\pm SD$ ) of  $8.08 \pm 0.48$ ,  $8.10 \pm 0.48$ ,  $8.05 \pm 0.48$ , and  $7.98 \pm 0.47$ ; respectively. There was a statistically high significant decrease in root length by time in 3Mix-MP group as revealed by one-way repeated measures ANOVA.

The difference between both groups; formacresol and 3Mix-MP was significant at all follow-up intervals examined.

The overall effect of variables showed that interaction between time and groups induced non-significant changes in linear measurements throughout the study period.

**Clinical case presentation for treated second molars:**

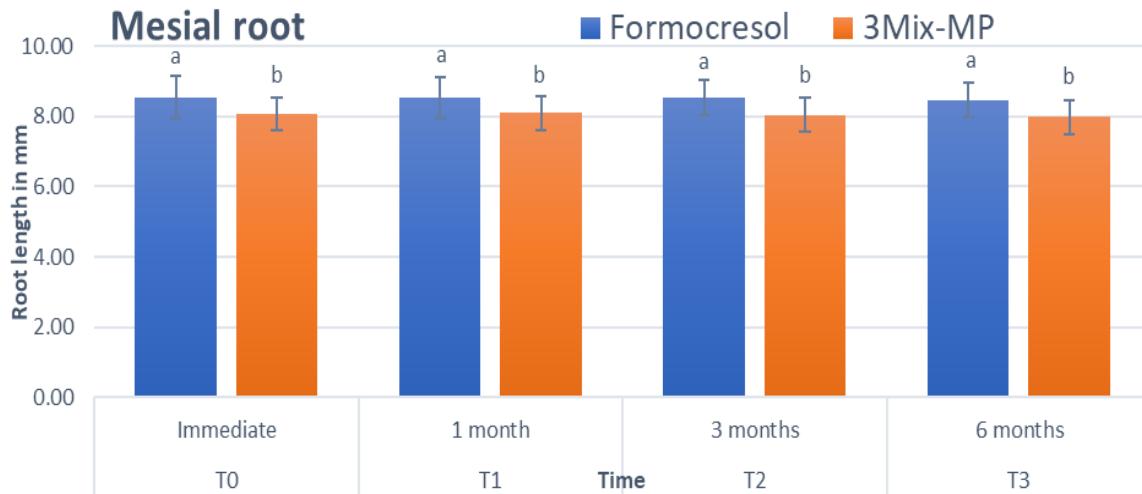


**Figure 16: Photographs show treated primary second molars (The left was treated by formacresol, and the Right was treated by 3Mixed-MP) at different follow up periods (a, b, c, d and e)**

**Table 6: Comparison between the mesial linear measurements at different times within and between groups**

post-operative time points	Mesial root		T-test p-value	
	Formacresol	3Mix-MP		
	Mean	Mean		
Immediate	8.55±0.60 a	8.08±0.48 b	0.023 *	
1 month	8.54±0.59 a	8.10±0.48 b	0.030 *	
3 months	8.53±0.50 a	8.05±0.48 b	0.011 *	
6 months	8.48±0.49 a	7.98±0.47 b	0.009**	
ANOVA RM	0.451 ns	<0.001***		
Two Way repeated measures ANOVA				
Group	0.015 *			
Time	0.071 ns			
Group x Time	0.698 ns			

\*, \*\*, \*\*\*, Significant at  $p<0.05$ ,  $<0.01$ ,  $<0.001$ ; ns, non-significant at  $p>0.05$ . a, b Means followed by different letters vertically or horizontally are significantly different.



**Figure 17. 34: Bar chart representing mean and standard deviation values for linear measurement of the mesial root in the two groups throughout the follow up periods. Bars followed by different letters are significantly different**

#### Distal linear measurements

Regarding radiometric results (root length) of the distal root for the two study groups, **Table 7** represents the mean distal root length in both study groups, the comparison between the successive follow ups within each group as well as the comparison between both group at each follow up interval.

As regards formacresol group at the distal root; the linear measurement at immediate, 1, 3 and 6 months recorded an average ( $\pm SD$ ) of  $8.25 \pm 0.46$ ,  $8.28 \pm 0.46$ ,  $8.22 \pm 0.46$  and  $8.19 \pm 0.44$ ; respectively. Distal root length decreased significantly ( $p=0.008^{**}$ ) from immediate to 6 months, however, one case showed lateral root resorption at 6 months follow up. Therefore, it wasn't measured or recorded under this parameter.

Furthermore, regarding 3Mix-MP group at the root; the linear measurement at immediate, 1, 3 and 6 months recorded an average ( $\pm SD$ ) of  $8.63 \pm 0.64$ ,  $8.62 \pm 0.64$ ,  $8.60 \pm 0.64$ , and  $8.57 \pm 0.65$ ; respectively, where it decreased significantly ( $p<0.001^{***}$ ) from immediate to 6 months as revealed by one-way repeated measure analysis of variance.

The difference between formacresol and 3Mix-MP was non-significant ( $p>0.05$ ) at all follow up time intervals as revealed by independent t-test.

The overall effect of groups, time and interaction between groups and time were assessed using two-way repeated measures ANOVA. Time intervals all over the study induced a significant change in distal root linear measures. However, interaction between groups and time showed a non-significant effect on distal linear measures.

**Table 7: Comparison between the distal linear measurements at different times within and between groups**

post-operative time points	Distal root		t-test p-value	
	Formacresol	3Mix-MP		
	Mean	Mean		
Immediate	8.25±0.46 a	8.63±0.64 a	0.075 ns	
1 month	8.28±0.46 a	8.62±0.64 a	0.103 ns	
3 months	8.22±0.46 a	8.60±0.64 a	0.073 ns	
6 months	8.19±0.44 a	8.57±0.65 a	0.071 ns	
ANOVA RM	0.008**	<0.001***		
<b>Two Way repeated measures ANOVA</b>				
Group	0.079 ns			
Time	<0.001***			
Group x Time	0.208 ns			

\*, \*\*, \*\*\*, Significant at  $p<0.05$ ,  $<0.01$ ,  $<0.001$ ; ns, non-significant at  $p>0.05$ . a, b Means followed by different letters vertically or horizontally are significantly different.

### Total (mesial/distal average) linear measurements

Regarding radiometric results (root lengths) of both mesial and distal roots for the two study groups, **Table 8** represents the mean mesial and distal root lengths in both study groups, the comparison between the successive follow ups within each group as well as the comparison between both group at each follow up interval.

As regards the mean of mesial/distal roots in the formacresol group; the linear measurement at immediate, 1, 3 and 6 months recorded an average ( $\pm SD$ ) of  $8.40\pm0.45$ ,  $8.41\pm0.45$ ,  $8.37\pm0.43$ , and  $8.33\pm0.43$ ; respectively, where it decreased non-significantly ( $p=0.099$ ) from immediate to 6 months.

Furthermore, regarding the mesial/distal roots in the 3Mix-MP group; the linear measurement at immediate, 1, 3 and 6 months recorded an average ( $\pm SD$ ) of  $8.35\pm0.50$ ,  $8.36\pm0.50$ ,  $8.32\pm0.50$ , and  $8.28\pm0.50$ ; respectively.

Total root length decreased significantly ( $p<0.001***$ ) from immediate to 6 months as revealed by one-way repeated measure analysis of variance.

The difference between formacresol and 3Mix-MP were non-significant ( $p>0.05$ ) at all time intervals studied.

The overall effect of groups, time and interaction between groups and time were assessed using two-way repeated measures ANOVA. Time intervals all over the study induced a significant change in average mesial/distal side linear measures. However, interaction between groups and time showed a non-significant effect on mesial/distal linear measures.

**Table 8: Comparison between mesial and distal linear measurements at different times within and between groups**

post-operative time points	Average (Mesial, Distal)		p-value	
	Formacresol	3Mix-MP		
	Mean	Mean		
Immediate	8.40±0.45 a	8.35±0.50 a	0.781 ns	
1 month	8.41±0.45 a	8.36±0.50 a	0.760 ns	
3 months	8.37±0.43 a	8.32±0.50 a	0.759 ns	
6 months	8.33±0.43 a	8.28±0.50 a	0.737 ns	
ANOVA RM	0.099 ns	<0.001***		
<b>Two Way repeated measures ANOVA</b>				
Group	0.758 ns			
Time	<0.001***			
Group x Time	0.904 ns			

\*, \*\*, \*\*\*, Significant at  $p<0.05$ ,  $<0.01$ ,  $<0.001$ ; ns, non-significant at  $p>0.05$ . a, b Means followed by different letters vertically or horizontally are significantly different.

### Densitometric analysis for bone density:

#### Bone density at mesial root apex:

The radio-densitometric measures of bone density at mesial root apex were recorded in the two studied groups formacresol and 3Mix-MP at four different time intervals, immediately postoperative, 1, 3 and 6 months follow ups and are presented as mean and standard error in **Table 9**.

Regarding the formacresol group at the mesial root apex; the bone density at immediate, 1, 3 and 6 months recorded an average( $\pm$ SD) of  $110.99\pm6.51$ ,  $128.51\pm6.00$ ,  $127.86\pm5.57$ , and  $118.40\pm7.80$ ; respectively. Where density increased significantly ( $p<0.001$ ) till 3 months, then decreased at 6 months in comparison to immediate postoperative. However, regarding the 3Mix-MP group at the mesial root; the bone density at mesial root at immediate, 1, 3 and 6 months recorded an average( $\pm$ SD) of  $97.96\pm4.91$ ,  $105.85\pm4.90$ ,  $96.33\pm7.77$ , and  $76.51\pm11.99$ ; respectively. There was a statistically significant ( $p=0.012$ ) decrease in bone density in mesial root apex by time in 3Mix-MP group with the exception of the one month follow up. Upon comparing between bone density at each follow up, the mean difference between formacresol and 3Mix-MP were significant at 1, 3 and 6 months post-operative follow ups as revealed by t-test. The overall effect was checked using two-way repeated measures ANOVA, which showed that groups, time intervals, and interaction between groups and time intervals induced significant differences in bone density in the mesial root all over the two groups.

#### Bone density at distal root apex:

The radio-densitometric measures of bone density at the distal root apex was recorded in the two studied groups formacresol and 3Mix-MP at four different time intervals, immediately postoperative, 1, 3 and 6 months follow ups and are presented as mean and standard error in **Table 10**. Regarding the formacresol group at the distal root apex; the bone density at immediate, 1, 3 and 6 months recorded an average( $\pm$ SD) of  $109.10\pm5.87$ ,

129.81±4.51, 131.92±4.67 and 117.26±7.35; respectively. Where the density increased significantly ( $p<0.001$ ) till 3 months then decreased at 6 months in comparison to immediate postoperative. However, regarding the 3Mix-MP group at the distal root; the bone density at immediate, 1, 3 and 6 months recorded an average(±SD) of 96.03±6.27, 123.05±7.25, 121.71±6.64 and 101.91±10.16; respectively. There was a statistically significant ( $p=0.010$ ) decrease in bone density in distal root apex by time intervals in 3Mix-MP group with the exception of one month follow up. Upon comparing between density at each follow up, formacresol and 3Mix-MP was non-significant ( $p>0.05$ ) at immediate, 1, 3 and 6 months post-operative follow ups. The overall effect was checked using two-way repeated measures ANOVA, which showed that groups, time intervals, and interaction between groups and time intervals induced significant differences in bone density in the distal root all over the two groups.

**Table 9: Comparison between bone density at the mesial root apex at different times within and between groups**

post-operative time points	Bone density: Mesial		independent t-test p-value	
	Formacresol	3Mix-MP		
	Mean ±SE	Mean ±SE		
Immediate	110.99±6.51 ab	97.96±4.91 b	0.121 ns	
1 month	128.51±6.00 a	105.85±4.90 ab	0.007**	
3 months	127.86±5.57 a	96.33±7.77 bc	0.003 **	
6 months	118.40±7.80 ab	76.51±11.99 c	0.007**	
ANOVA RM	<0.001***	0.012 *		
Two Way repeated measures ANOVA				
Group	0.007 **			
Time	<0.001***			
Group x Time	0.011 *;			

\*, \*\*, \*\*\*, Significant at  $p<0.05$ ,  $<0.01$ ,  $<0.001$ ; ns, non-significant at  $p>0.05$ . a, b Means followed by different letters vertically or horizontally are significantly different.

**Table 10: Comparison between bone density measurements at the distal root apex at different times within and between groups**

post-operative time points	Bone density: Distal		Independent t-test p-value	
	Formacresol	3Mix-MP		
	Mean ±SE	Mean ±SE		
Immediate	109.10±5.87 bcd	96.03±6.27 d	0.139 ns	
1 month	129.81±4.51 ab	123.05±7.25 abc	0.436 ns	
3 months	131.92±4.67 a	121.71±6.64 abc	0.219 ns	
6 months	117.26±7.35 abc	101.91±10.16 cd	0.232 ns	
ANOVA RM	<0.001***	0.010 **		
Two Way repeated measures ANOVA				
Group	0.168 ns			
Time	<0.001***			
Group x Time	0.667 ns			

\*, \*\*, \*\*\*, Significant at  $p<0.05$ ,  $<0.01$ ,  $<0.001$ ; ns, non-significant at  $p>0.05$ . a,b Means followed by different letters vertically or horizontally are significantly different.

### Bone density at the furcation area:

The radio-densitometric measures of bone density at the midfurcation was recorded in the two studied groups formacresol and 3Mix-MP at four different time intervals, immediately postoperative, 1, 3 and 6 months follow ups and are presented as mean and standard error in **Table 11; Figure 14 and 15**.

Regarding the formacresol group at the furcation, the bone density at immediate, 1, 3 and 6 months recorded an average( $\pm$ SD) of  $57.70\pm5.06$ ,  $71.03\pm4.62$ ,  $85.42\pm4.91$ , and  $70.81\pm4.27$ ; respectively. Where density increased significantly ( $p<0.001$ ) till 3 months, then decreased at 6 months in comparison to immediate postoperative.

However, regarding the 3Mix-MP group at the furcation; the bone density at the furcation at immediate, 1, 3 and 6 months recorded an average( $\pm$ SD) of  $59.28\pm4.52$ ,  $68.90\pm4.34$ ,  $59.25\pm6.02$ , and  $49.84\pm7.93$ ; respectively. There was a statistically significant ( $p=0.015$ ) change in bone density in furcation by time intervals in 3Mix-MP group with the exception of the one month follow up.

Upon comparing between density at each follow up, the difference between formacresol and 3Mix-MP was non-significant ( $p>0.05$ ) at immediate, and 1 month, however, it was significant after 3 and 6 months post-operative follow ups.

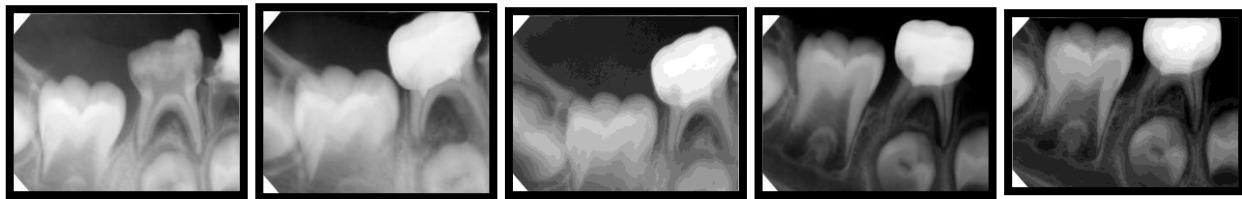
The overall effect was checked using two-way repeated measures ANOVA, which showed that groups had non-significant effect on furcation bone density, however, time intervals, and interaction between groups and time intervals induced significant differences in bone density in furcation area all over the two groups.

**Table 11: Comparison between bone density measurements at the furcation area at different times within and between groups**

post-operative time points	Bone density Furcation (mean, SE)		p-value	
	Formacresol	3Mix-MP		
	Mean $\pm$ SE	Mean $\pm$ SE		
Immediate	$57.70\pm5.06$ bc	$59.28\pm4.52$ bc	0.818 ns	
1 month	$71.03\pm4.62$ ab	$68.90\pm4.34$ b	0.739 ns	
3 months	$85.42\pm4.91$ a	$59.25\pm6.02$ bc	0.002**	
6 months	$70.81\pm4.27$ ab	$49.84\pm7.93$ c	0.027 *	
ANOVA RM	<0.001***	0.015 *		
Two Way repeated measures ANOVA				
Group	0.088 ns			
Time	<0.001***			
Group x Time	<0.001***			

\*, \*\*, \*\*\*, Significant at  $p<0.05$ ,  $<0.01$ ,  $<0.001$ ; ns, non-significant at  $p>0.05$ . a,b Means followed by different letters vertically or horizontally are significantly different.

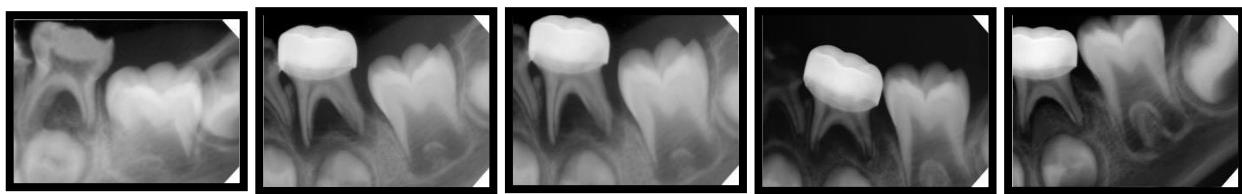
### Radiographic case presentation for a second molar in group A:



(a) Pre-operative      (b) Immediate post-operative      (c) After 1 month      (d) After 3 months      (e) After 6 months

Figure 14: Radiographs show formacresol pulpotomy at different follow up periods (a, b, c, d and e)

### Radiographic case presentation for a second molar in group B:



(a) Pre-operative      (b) Immediate post-operative      (c) After 1 month      (d) After 3 months      (e) After 6 months

Figure 15: Radiographs show 3Mixed-MP treatment at different follow up periods (a,b,c, d& e)

### Success rate:

#### Clinical success

Regarding all combined clinical parameters assessed in the current study, the success rate after 6 months follow-up period was recorded as number and frequency (n, %) and presented in **Table 12**.

Concerning the success rates of pain scores, the formacresol group recorded a success rate of 100% starting from 1 month follow up, however 3Mix-MP showed 93.3 % success rates; the difference between two groups was non-significant ( $p=0.317$ ) (**Table 12**).

Regarding redness and swelling scores, formacresol showed success 93.3%, which was higher than 3Mix-MP which showed a success rate of 80%, however, the difference was non-significant ( $p=0.157$ ) as revealed by Wilcoxon's singed rank test for nonparametric data (**Table 12**).

Moreover, regarding tooth mobility, formacresol showed 100% success, which was higher than 3Mix-MP which showed a success rate of 93.3%, however, the difference was non-significant ( $p=0.317$ ) (**Table 12**).

**Table 12: Comparison between clinical success rates in the two groups in pain scores, redness or swelling and tooth mobility**

Clinical parameters		Success rate (%)				Wilcoxon's	
		Formacresol		3Mix-MP			
		Success	Failure	Success	Failure		
Pain scores	n, %	15.0 (100.0%)	0.0 (0.0%)	14.0(93.3%)	1.0(6.7%)	0.317 ns	
	Chi	>0.999 ns		<0.001***			
Redness/swelling	n, %	14.0(93.3%)	1.0(6.7%)	12.0(80.0%)	3.0(20.0%)	0.157 ns	
	Chi	<0.001***		0.020*			
Tooth mobility	n, %	15.0(100.0%)	0.0(0.0%)	14.0(93.3%)	1.0(6.7%)	0.317 ns	
	Chi	>0.999 ns		<0.001***			
Total	n, %	14.0(93.3%)	1.0(6.7%)	12.0(80.0%)	3.0(20.0%)	0.157 ns	
	Chi	<0.001***		0.020*			

\*, \*\*, \*\*\*, Significant at p<0.05, <0.01, <0.001; ns, non-significant at p>0.05

### Radiographic success

Regarding all radiographic parameters assessed in current study, the success rate after 6 months follow-up period is presented in **Table 13**. The success rate based on linear measures recorded a radiographic success rate of 100% in both formacresol and 3Mix-MP groups due to absence of any evidence of aggressive root resorption with a nonsignificant difference between groups.

However, regarding bone density measures, the formacresol group showed a success rate of 86.7% and 3Mix-MP showed a success rate of 60 %, which was significantly higher in formacresol group than in 3Mix-MP group (**Table 13**).

**Table 13: Radiographic success rates in the two groups in overall of linear measurement and bone density at different follow ups**

Clinical parameters		Success rate (%)				Wilcoxon's	
		Formacresol		3Mix-MP			
		Success	Failure	Success	Failure		
Linear measurements	n, %	15.0(100.0%)	0.0(0.0%)	15.0(100.0%)	0.0(0.0%)	>0.999ns	
	Chi	>0.999 ns		>0.999 ns			
Bone density	n, %	13.0(86.7%)	2.0(13.3%)	9.0(60.0%)	6.0(40.0%)	0.046*	
	Chi	0.005 **		0.439 ns			
Total	n, %	13.0(86.7%)	2.0(13.3%)	9.0(60.0%)	6.0(40.0%)	0.046*	
	Chi	0.005 **		0.439 ns			

\*, \*\*, \*\*\*, Significant at p<0.05, <0.01, <0.001; ns, non-significant at p>0.05

### Kaplan-Meier survival function:

Kaplan-Meier estimate is one of the best options to be used to measure the fraction of subjects living for a certain amount of time after treatment. The survival estimate showed a remarkable difference between formacresol and 3Mix-MP groups at different follow-ups.

Initially both groups, formacresol and 3Mix-MP showed the same K-M curve length which indicate the same survival duration of both groups. Both groups at start showed good survival rate, however, end results indicate that formacresol showed a better survival.

The formacresol group showed a mean K-M survival of  $25.67 \pm 13.27$  days to reach success however, 3MixMP showed an average( $\pm SD$ ) of  $52.80 \pm 20.78$  days to reach success (**Table 14**).

**Table 14: Survival rate of both study materials within the time frame of the study**

	Mean	SD	95% Confidence interval	
			Lower	Upper
Formacresol	25.67	13.27	0.00	51.68
3MixMP	52.80	20.78	12.08	93.53

## DISCUSSION

Management of infected primary teeth presents considerable challenges due to behavioral issues in young patients, complex root canal anatomy, root resorption, mechanical debridement difficulties, and the polymicrobial nature of infections [23]; [24]. Parental dental anxiety often delays treatment until symptoms become severe, complicating management [25]. Various antibacterial drug combinations have been explored to control infections and minimize microbial resistance in nonvital primary teeth [26].

This study compared the efficacy of a 3Mixed-MP antimicrobial mixture with formocresol for treating infected deciduous molars. While formocresol remains a standard pulpotomy agent, it raises safety concerns such as enamel defects in permanent successors and systemic toxic effects including impacts on internal organs and vascular flow [27]; [28]. Its mutagenic and carcinogenic risks underscore the urgent need for safer alternatives [29].

The 3Mix mixture, used in Lesion Sterilization and Tissue Repair (LSTR), has demonstrated promise in sterilizing necrotic pulps and infected dentine without mechanical preparation, reducing treatment time and trauma [30]. The current study targeted children aged 4-8 years due to the onset of physiological root resorption near seven years and the high caries prevalence within this group [31]. Only restorable mandibular primary molars were included to standardize clinical and radiographic assessments [32], enrolling children with acceptable behavior ratings to facilitate cooperation [33]. The split-mouth design minimized intersubject variability and selection bias [34].

Use of stainless-steel crowns in both groups helped achieve a biological seal, reducing microleakage and supporting mucosal and bone healing, consistent with prior reports on their effectiveness in restoring primary molars with multisurface loss [35]. Digital radiography, particularly direct digital intraoral periapical imaging, enhanced diagnostic accuracy while minimizing radiation exposure [36]; [37]; [38]. Standardized imaging and densitometric bone analysis allowed objective evaluation of treatment outcomes [39].

Clinically, both groups showed symptom resolution (pain, redness, swelling, mobility) by 6 months, aligning with previous studies [40]. The formocresol group experienced slightly fewer pain episodes, though the 3Mix-MP group's transient symptoms likely reflected inflammatory exudate [40]. High regression rates of tooth mobility were consistent with **Luengo-Fereira's** findings (2019)<sup>[41]</sup>. Radiographically, both treatments showed 100% linear success and no aggressive root resorption. Increased periapical bone mineral content suggested effective healing, with formocresol achieving 86.7% bone density success, like **Yildirim et al.**'s 84.44% (2016)<sup>[42]</sup>. The 3Mix-MP group's 60% radiographic success matched prior LSTR success rates [43], although recurrent lesions and furcation radiolucencies were more common, potentially due to drug-induced inflammatory responses (e.g., amoxicillin, ciprofloxacin, metronidazole).

Notably, formocresol demonstrated a longer survival time compared to 3Mix-MP, indicating greater efficacy in this cohort. Its germicidal and fixative properties may contribute to this outcome [44]. Differences with prior formocresol studies reporting lower success rates may be attributable to the shorter follow-up period in this study [45]; [46].

Limitations included challenges in assessing external root resorption, discomfort from rubber dam placement, difficulty using rigid radiographic sensors, and technical issues during LSTR medication placement in cases with root divergence or limited mouth opening. These factors may have influenced outcomes and patient compliance.

In conclusion, LSTR emerges as a promising minimally invasive treatment for infected primary molars with extensive root resorption or furcation radiolucency, offering a viable alternative to extraction. Formocresol remains effective in non-instrumental endodontic therapy, but its safety concerns demand cautious use. Future research should focus on safer, biocompatible antimicrobial agents, detailed histomorphological evaluations, improved radiographic parameters, and refinement of LSTR protocols including canal excision, with the aim of establishing 3Mix-MP as a preferable alternative to formocresol due to its simplicity, reduced treatment time, and safety profile.

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