AJDS LAZHAR Al-Azhar Journal of Dental Science
Vol. 27- No. 3- 435:445- July 2024
Print ISSN 1110-6751 | online ISSN 2682 - 3314
https://ajdsm.journals.ekb.eg
Orthodontic & Pediatric Dentistry Issue (Orthodontics and Pediatric Dentistry)

CLINICAL AND RADIOGRAPHIC EVALUATION OF DIFFERENT HEMORRHAGE CONTROL AGENTS AND BASE MATERIAL ON PULPOTOMIZED PRIMARY MOLARS

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ABSTRACT

Objectives: The present study was carried out to evaluate and compare the clinical and radiographic success rates for primary molar pulpotomies with 15.5% ferric sulfate (FS) or 4.8% tranexamic acid (TXA) as hemostatic agents and zinc oxide-eugenol (ZOE) and the antibiotic paste CTZ (chloramphenicol, tetracycline and zinc oxide-eugenol) as base materials. In children aged between 4-8 years. **Subjects and methods:** This study was categorized in 2 main groups and 4 Sub-groups; sub-group A1; FS/ZOE; sub-group A2; FS/CZT; sub-group B1; TXA/ZOE; and sub-group B2; TXA/CTZ. The clinical and radiographic results in this study was evaluated after 3 different follow-up periods of 1-month, 3-months, and 6-months. **Results:** the results of the current study showed non-significant difference in the clinical and radiographic results between the studied groups in regard to the type of the hemostatic agent used as well as regarding to the type of base-material at the different studied time intervals. **Conclusion**: the use of ferric sulfate exhibited relatively better results than tranexamic acid both clinically and radiographically.

KEYWORDS: Pulpotomy, Primary Molars, ferric sulfate (FS), tranexamic acid.

INTRODUCTION

The philosophy of primary tooth pulpotomy is to remove the inflamed or infected coronal pulp tissue and cover the pulp stumps with a therapeutic agent. The success mostly depends on correct diagnosis of pulp status. However, other factors such as control of pulpal bleeding after coronal pulp amputation, and the choice of base material used also contribute to the outcome. Pulpal hemorrhage control is an indispensable step in pulpotomy procedures[(1)]. The most widely used method to control bleeding during pulp therapy is to apply slight mechanical pressure with a cotton pellet wetted with saline over the pulp exposure. Various substances with local hemostatic action can also be used; among these are gelatin sponge, collagen sponge, tannic acid and tranexamic acid (TA) [(2)]. Of these, tranexamic acid which has expanded rapidly for a variety of off-label indications and is now considered the antifibrinolytic of choice in patients who present to the emergency department (ED) with extracranial hemorrhage following a traumatic injury [(3)]. (TA) is one of the most frequently used, both as a mouthwash and locally for topical application. This

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DOI: *10.21608/AJDSM.2023.184715.1399*

second form of application, despite being widely used, still lacks evidence for efficacy in the control of dental hemorrhage [4].

Ferric sulfate (FS) also is a widely known hemostatic agent which has gained considerable popularity in primary tooth pulpotomy. In contrast to other traditional agents, FS provides hemostasis by some chemical retractions in blood. Even though the hemostatic mechanism of FS is questioned, it seems that agglutination of blood proteins occurs due to the reaction of blood with ferric and sulfate ions in acidic PH. [5]. On the other hand, (FS) may cause considerable tissue irritation, postoperative sensitivity due to its acidic nature and also cause tissue discoloration. Moreover, recommendation to be used only with total etch systems due to reducing bonding strength limits its use because of the importance of reduced chair time and technical sensitivity in pediatric patients [6]. Once hemostasis is obtained, the remaining pulp tissue should be covered with a biocompatible material. Zinc oxide–eugenol (ZOE) paste is a common medicament placed over the treated pulp [7].

Antibiotic paste CTZ (chloramphenicol, tetracycline and zinc oxide-eugenol) is another used pulpotomy dressing material that was used in this study [8]. There are studies that indicate that the effectiveness of CTZ antibiotic paste is due to its antimicrobial action, mainly due to the presence in its composition of two broad spectrum antibiotics: tetracycline and chloramphenicol[9,10]. The CTZ paste (Chloramphenicol, Tetracycline, Zinc Oxide Eugenol) application technique is easy, simple, can be performed in one session, has antibacterial power, promotes stabilization of bone resorption and does not cause tissue sensitivity [11]. This thesis was conducted to evaluate the success rate of antibiotic paste CTZ as base material and also the success rate of tranexamic acid as heamostatic agent in pulpotomized primary molars.

SUBJECT AND METHODS

Prospective randomized clinical study.

Study Setting and Population:

This clinical study was performed on children aged between 4 and 8 years. The enrolled children were selected from patients attending the outpatient clinic of Pedodontics and Oral Health Department, Faculty of Dental Medicine, Al-Azhar University (Cairo, Boys). This study involved a total of 60 carious mandibular primary molars indicated for pulpotomy in 40 patients.

Eligibility Criteria for Population:

The patient's selection was carried out after preoperative radiographic and clinical evaluation according to the following inclusion and exclusion criteria.

Inclusion criteria:

Age ranges from (4-8) years, the child appear healthy and free of systemic diseases, patients with at least one mandibular primary molar with extensive caries that required pulpotomy treatment, tooth without any previous treatment, the involved tooth has no clinical symptoms or signs of pulp degeneration, such as a history of spontaneous pain or swelling, tenderness to percussion, sinus tract, pathological mobility. Also the involved tooth without radiographical signs of pathological (internal or external) root resorption, widened periodontal ligament space not exceeding one-third physiological root resorption.

Exclusion criteria:

Any tooth with periapical lesion, tooth with a control time of hemorrhage greater than 5 minutes, the tooth with radiographic sign of apical or periapical bone loss. Also patients with allergic reaction to local anesthetics.

Sample size calculation:

Sample size calculation was based on success in hemostasis using different hemorrhage control agents on pulpotomized primary molars retrieved from previous studies for ferric sulfate (FS) and tranexamic acid (TXA) (Atasever et al., 2019)[12]. Using G*power version 3.0.10 to calculate difference of 56.8%, 2-tailed, with α error =0.05 and power = 90.0%.The calculated sample size was 12 in each group and by adding 20% to compensate for drop out then total calculated sample size was 15 in each group at least.

Ethical Consideration:

This study was conducted after approval of Ethical Committee, Faculty of Dental Medicine, Al-Azhar University (Boys, Cairo) with approval reference No. (EC Ref No.536/2682).

Patient Consent:

Before starting of this study, all selected children and his/her parent's / caregiver were informed about all the procedure used in this clinical study. Then, each parent's/care giver was signed an informed consent having details about the whole clinical procedure.

Subject grouping:

After the selection of the involved children and gotten signed informed consent, the enrolled children were randomly divided into two main groups. A total of 60 mandibular primary molars requiring pulpotomy treatment were selected and randomly assigned to two main groups and four subgroups based on the received hemostatic agent and the type of base material used.

TABLE (1) Subject grouping

Group (A)		**Group (B)**	
(A1)	(A2)	(B1)	(B2)
FS-ZOE	FS-CTZ	TXA-ZOE	TXA-CTZ

Preoperative Assessment:

1- Clinical evaluation:

A diagnostic sheet has been made for every patient including the name, age, sex, address, telephone number, treated tooth, and the date of examination. A Complete medical history and personal data was obtained from parents of every selected children [13].

2- Radiographic evaluation:

Periapical radiographs of the intended tooth were obtained prior treatment from every child included in the study to meet all the previously mentioned inclusion criteria and avoid exclusion criteria [14].

Intervention:

1. Pulpotomy Procedure:

- The procedures started with the application of a 20% benzocaine gel (I-Gel, USA) for 5 min.
- An anesthetic solution containing 2% mepivacaine (Mepecaine L: Mepecaine Hcl 3%, Alexandria Co. for pharmaceuticals, Alexandria, Egypt) was administered using aspirating dental syringes and 27-gauge needles.
- After isolation with rubber dam, caries was removed with high-speed diamond fissure burs under copious irrigation.
- Upon pulp exposure, the roof of the pulp chamber was removed with a sterile high-speed diamond round bur (Fig.1).
- Then, the coronal pulp tissue was amputated at the pulp stumps with slow-speed steel round burs, and the pulp chamber was irrigated only with sterile physiologic saline without any attempt of stoppage of bleeding.
- Sterile cotton pellets were slightly compressed against the radicular pulp stamps for 5 min dapped in one of the two previously mentioned hemostatic agents. If the bleeding did not stop after 5 min, the tooth was excluded from the study [15].

2. Restoration Procedure:

In Group A, a cotton pellet soaked in 15.5% FS was applied on the pulp stumps for 15s in accordance with the manufacturer's recommendation. The pulp chamber was then flushed with saline then filled with ZOE paste (Subgroup A1) and CTZ paste (Subgroup A2) [16].

In Group B, a cotton pellet soaked in 4.8% TXA solution was placed in the chamber for 15s. Following hemostasis, the pulp chamber was flushed with saline and filled with ZOE paste (Subgroup B1) and CTZ paste (Subgroup B2) as described above [17].

In all groups, the base materials were covered with glass ionomer cement. SSCs were placed at the same appointment [17].

Observation:

The evaluations comprised clinical and radiographic examinations. Each examination (clinical or radiographic) was performed independently by the same investigator.

The teeth were examined clinically and radiographically by bisecting angle technique at 1, 3, and 6 months. Standardized forms were used to record the following signs and symptoms, any of which were regarded as failure:

a) History of spontaneous pain.
b) A reliable reporting of tenderness to percussion/palpation.
c) Mobility.
d) Swelling.
e) Fistula.

Treatment was recorded as a clinical success if any of these failure parameters were not met.

The evaluation of the radiographs taken at 1, 3, and 6 months (Fig. 2), was made using a standard viewing box. Radiographic success was considered as absence of:

a) Periapical/interradicular radiolucency.
b) Widened periodontal ligament.
c) Loss of lamina dura.
d) Internal/external root resorption.

Data management and Statistical analysis:

Statistical analysis was performed using SPSS statistical version 21 (Statistics statistical procedures companion, Chicago, IL, USA). Chi-square test was used for comparison of all binary outcome data at different time points. One-way ANOVA test was used to compare the mean age in all examined groups. The significance level was set at $p \leq 0.05$. Kappa coefficient to correlate between clinical and radiographic results.

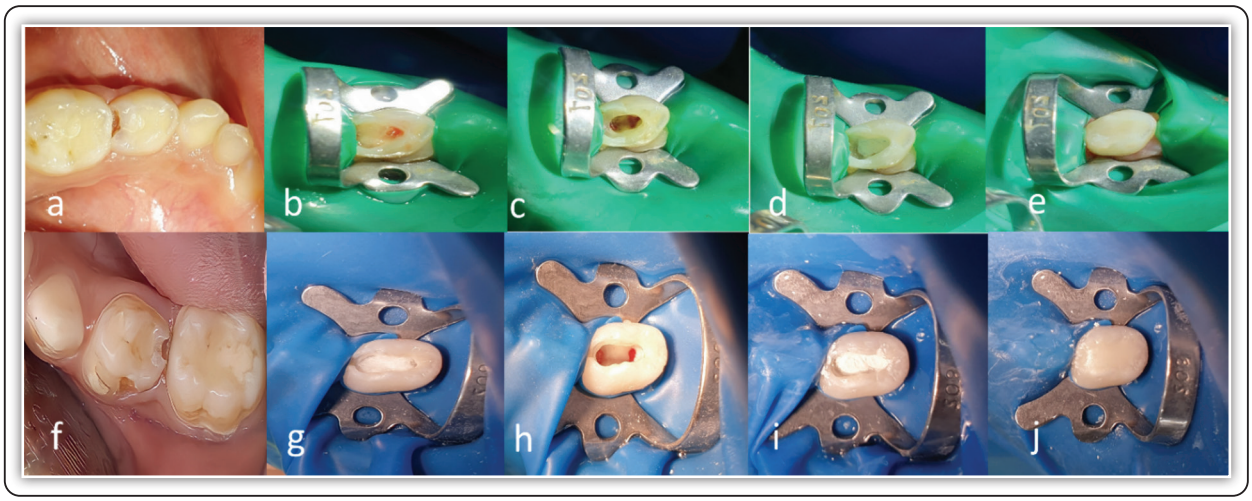

FIG (1) For FS & CTZ: a, Pre-operative situation clinically, b, Access cavity preparation, c, Hemostasis (Bleeding Stoppage), d, Application of base material, e, Glass ionomer cement filling. For FS & CTZ f, Pre-operative situation clinically, g, Access cavity preparation, h, Hemostasis (Bleeding Stoppage), di Application of base material, j, Glass ionomer cement filling.

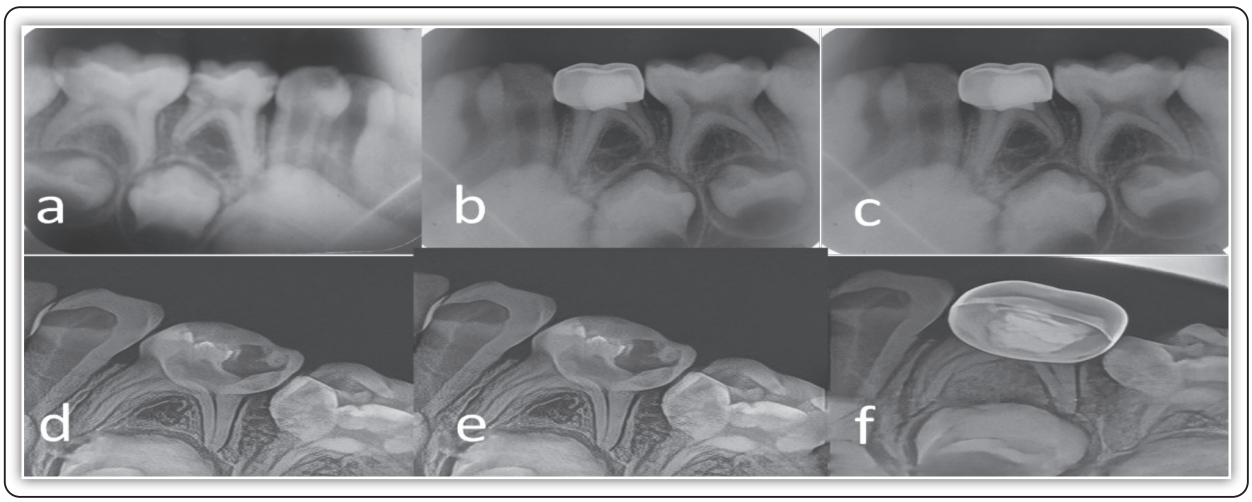

FIG (2) For FS & CTZ: a, Radiographic evaluation after 1 month evaluation, b, Radiographic evaluation after 3 months, c, Radiographic evaluation after 6 montsh. For FS & CTZ f, Radiographic evaluation after 1 month evaluation, b, Radiographic evaluation after 3 months, c, Radiographic evaluation after 6 months.

RESULTS

Clinical evaluation:

After 1-month of clinical follow up the all involved teeth in the all studied groups recorded success rate of (100%) and failure rate of (0%). The results of clinical follow up after 1-months showed non-statistically significant difference in the success and failure rate among the different studied restorative techniques with p-value of (p=1).

After 3-months of clinical follow up the group of teeth those received both of FS-ZOE (Sub-group A1), and TXA-CTZ (Sub-group B2) recorded the same success rate and failure rate of (86.67%) and (13.33%) respectively. While, the group of teeth those received; FS-CTZ (Sub-group A2), recorded the higher success rate of (93.33%) and lower failure rate of (6.67%). However, the group of teeth those received; TXA-ZOE (Sub-group B1) recorded the lower success rate of (80%) and higher failure rate of (20%). The results of clinical follow up after 3-months showed non-statistically significant difference in the success and failure rate among the different studied restorative techniques with p-value of (p=0.6195).

After 6-months of clinical follow up the group of teeth those received both of FS-ZOE (Sub-group A1), and TXA-CTZ (Sub-group B2) recorded the same success rate and failure rate of (80%) and (20%) respectively. While, the group of teeth those received; FS-CTZ (Sub-group A2), recorded the higher success rate of (86.67%) and lower failure rate of (13.33%). However, the group of teeth those received; TXA-ZOE (Sub-group B1) recorded the lower success rate of (73.33%) and higher failure rate of (26.67%). The results of clinical follow up after 6-months showed non-statistically significant difference in the success and failure rate among the different studied restorative techniques with p-value of (p=0.6195) .

TABLE (2) Comparative of clinical follow-up results after 1-6 months among the studied groups:

Variable		Group (A)		Group (B)		p-value
		(A1)	(A2)	(B1)	(B2)	
		FS-ZOE	FS-CTZ	TXA-ZOE	TXA-CTZ	
1-month	Success; n (%)	15 (100%)	15 (100%)	15 (100%)	15 (100%)	1^{ns}
	Failure; n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
3-month	Success; n(%)	13(86.67)	14 (93.33%)	12 (80%)	13 (86.67%)	0.6195^{ns}
	Failure; n(%)	2(13.33%)	1 (6.67%)	3 (20%)	2 (13.33%)	
6-months	Success; n(%)	12 (80%)	13 (86.67%)	11 (73.33%)	12 (80%)	0.7812^{ns}
	Failure; n(%)	3 (20%)	2 (13.33%)	4 (26.67%)	3 (20%)	

* *Significant at p < 0.05.*

* *Non-significant at p >0.05. ns= non-significant.*

Radiographic evaluation:

After 1-month of radiographic follow up the all involved teeth in the all studied groups; FS-ZOE (Sub-group A1), FS-CTZ (Sub-group A2), TXA-ZOE (Sub-group B1), and TXA-CTZ (Sub-group B2), recorded success rate of (100%) and failure rate of (0%). The results of radiographic follow up after 1-months showed non-statistically significant difference in the success and failure rate among the different studied restorative techniques with p-value of (p=1).

After 3-months follow up; only 4 teeth treated with FS-ZOE (Sub-group A1) and with TXA-ZOE (Sub-group B1) were scored failed radiographically with percentage of (26.67%), and 11 teeth of both treated groups were scored radiographically succeed with percentage of (73.33%). While, after 3-months follow up in group of teeth treated with FS-CTZ (Sub-group A2) only 2 teeth were scored failed radiographically with percentage of (13.33%), and total of 13 teeth were scored success radiographically with percentage of (86.67%). However, in group of teeth treated with TXA-CTZ (Sub-group B2) only 3 teeth were scored failed radiographically with percentage of (20%), and total of 12 teeth were scored success radiographically with percentage of (80%). The results showed non-statistically significant difference in the success and failure rate among the different studied restorative techniques with p-value of (p=0.7818).

After 6-months follow up; only 5 teeth treated with FS-ZOE (Sub-group A1) and with TXA-ZOE (Sub-group B1) were scored failed radiographically with percentage of (33.33%), and 10 teeth of both treated groups were scored radiographically succeed with percentage of (66.67%). While, after 6-months follow up in group of teeth treated with FS-CTZ (Sub-group A2) only 3 teeth were scored failed radiographically with percentage of (20%), and total of 12 teeth were scored success radiographically with percentage of (80%). However, in group of teeth treated with TXA-CTZ (Sub-group B2) only 4 teeth were scored failed radiographically with percentage of (26.67%), and total of 11 teeth were scored success radiographically with percentage of (73.33%). The results showed non-statistically significant difference in the success and failure rate among the different studied restorative techniques with p-value of (p=0.8247).

Table (3) Comparative of radiographic follow-up results after 1-6 months among the studied groups:

Variable		Group (A)		Group (B)		p-value
		(A1)	(A2)	(B1)	(B2)	
		FS-ZOE	FS-CTZ	TXA-ZOE	TXA-CTZ	
1-month	Success; n (%)	15 (100%)	15 (100%)	15 (100%)	15 (100%)	1^{ns}
	Failure; n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
3-month	Success; n(%)	11 (73.33%)	13 (86.67%)	11 (73.33%)	12 (80%)	0.7818^{ns}
	Failure; n(%)	4 (26.67%)	2 (13.33%)	4 (26.67%)	3 (20%)	
6-months	Success; n(%)	10 (66.67%)	12 (80%)	10 (66.67%)	11 (73.33%)	0.8247^{ns}
	Failure; n(%)	5 (33.33%)	3 (20%)	5 (33.33%)	4 (26.67%)	

** Significant at $p < 0.05$.*

** Non-significant at $p > 0.05$. ns= non-significant.*

Correlation between clinical and radiographic results:

After 1-month: Among the total number of 60 examined teeth, 60 (100%) exhibited clinical and radiographic success rate. While, 0 (0%) of the examined teeth exhibited clinical and radiographic failure rate. Number of observed agreements: 120 (100.00% of the observations). While, Number of agreements expected by chance: 60.0 (50.00% of the observations). The Kappa agreement index was 1.000, indicating an almost perfect agreement between the two examinations, with a confidence interval excluding (1.000 to 1.000).

After 3-months: Among the total of 60 teeth examined clinically, 53 (88.33%) exhibited clinical success rate, while, 7 (11.67%) exhibited clinical failure rate. However, Among the total of 60 teeth examined radiographically, 47 (78.33%) exhibited radiographic success rate, while, 13 (21.67%) exhibited radiographic failure rate. The number of observed agreements: 60 (50.00% of the observations). While, the number of agreements expected by chance: 64 (53.33% of the observations). The Kappa agreement index was 0.071, indicating substantial agreement between the two examinations, with a confidence interval excluding (-0.211 to 0.068).

After 6-months: Among the total of 60 teeth examined clinically, 47 (78.33%) exhibited clinical success rate, while, 13 (21.67%) exhibited clinical failure rate. However, Among the total of 60 teeth examined radiographically, 43 (71.67%) exhibited radiographic success rate, while, 17 (28.33%) exhibited radiographic failure rate.

The number of observed agreements: 60 (50.00% of the observations). While, the number of agreements expected by chance: 62.0 (51.67% of the observations).

The Kappa agreement index was 0.081, indicating almost perfect agreement between the two examinations, with a confidence interval excluding (-0.194 to 0.125).

TABLE (4) Correlation between clinical and radiographic results 1-6 months among the studied groups:

Variable		Clinical evaluation	Radiographic evaluation	Kappa index	Confidence interval (CI)
1-month	Success; n (%)	60 (100%)	60 (100%)	1.000	(1.000 to 1.000)
	Failure; n (%)	0 (0%)	0 (0%)		
	Total	60	60		
3-month	Success; n(%)	53(88.33%)	47 (78.33%)	0.071	(-0.211 to 0.068)
	Failure; n (%)	7(11.67%)	13 (21.67%)		
	Total	60	60		
6-months	Success; n(%)	47(78.33%)	43 (71.67%)	0.081	(-0.194 to 0.125)
	Failure; n (%)	13(21.67%)	17 (28.33%)		
	Total	60	60		

- Kappa < 0: No agreement
- Kappa between 0.00 and 0.20: Slight agreement
- Kappa between 0.21 and 0.40: Fair agreement
- Kappa between 0.41 and 0.60: Moderate agreement
- Kappa between 0.61 and 0.80: Substantial agreement
- Kappa between 0.81 and 1.00: Almost perfect agreement.

DISCUSSION

In this study in order to allow comparison with the CTZ pulpotomy, we chose the traditional pulpotomy technique having ZOE paste as an intermediate base material. Zinc oxide–eugenol paste is a common medicament placed over the treated pulp. Moreover, it was reported that ZOE, provides analgesic properties and a potent antibacterial action against bacteria for more than 30 days [18]. Also, Heyder et al [19]. reported that ZOE has a bactericidal effect and not only a bacteriostatic effect. Therefore, ZOE was selected in the present study as a tested material.

In the present study the clinical and radiographic follow-up intervals of 1,3, and 6 months were selected. This is because accordingly to the American Academy of Pediatric Dentistry's (AAPD) guideline on pulp therapy the pulpotomies treated teeth should evaluate clinically and radiographically at least every 3 months [20]. Also, it was reported that the radiographic infectious process of pulpotomies teeth should resolve in 6 months, which is evidenced by bone deposition in the pretreatment radiolucent areas [21].

Results of clinical findings at different follow-up periods in this study showed no statistically significant difference between the tested groups in terms of success and failure rate. This finding may be due to the both tested hemostatic agents have nearly the same action via the formation of blood clots without significant antibacterial action [22]. Moreover, both used base materials in the present study have free eugenol which is able to come in direct contact with the pulp tissue which is able to produce an inflammatory change in the pulp and hence failure [23].

The higher initial success rate (100%) of all restoration protocols tested in the present study in the first follow-up period (after 1-month) could

be attributed to the use of hemostatic agents in all tested groups. Where, it was reported that in pulpal procedures, a clot formed at the pulp surface upon contact with the hemostatic solution, and it was suggested that this clot may also act as a barrier for irritative substances that cause inflammation and internal resorption [24]. Also, the results of the present study showed that the use of ferric sulfate as a hemostatic agent has better clinical and radiographic follow-up results (after 3 and 6-months) when compared to tranexamic acid, however, these results were statistically insignificant [25].

This could be because the FS was able to form a more effective clot barrier on the pulp surface when compared to TXA. This is due to the mechanism of action of FS depending on protein precipitation [26]. However, the mechanism of action of TXA depends on its antifibrinolytic effect and coagulation of the existent protein [27].

Moreover, the bitter results of FS over TXA could be attributed to the higher concentration of FS (15.5%) used in the present study when compared to the relatively lower concentration of TXA (4.8%) used in this study. This is in accordance with the finding of the previous studies which reported that the ability of the hemostatic agent to form a proper barrier against microorganisms may be related to its concentration and time of application [28].

Also, the finding of this study revealed that the use of CTZ paste as base material over the pulpotomies pulp showed better clinical and radiographic results when compared to ZOE paste after 3 months and 6-months of the follow-up period. However, these results were non-significant statistically. This may be due to the CTZ paste containing ZOE in addition to two broad-spectrum antibiotics: tetracycline and chloramphenicol [29]. Therefore, it presents an effective antimicrobial activity, biocompatibility, and satisfactory clinical and radiographic results [30].

Moreover, it was found that CTZ has higher antimicrobial activity than ZOE paste in both agar diffusion and direct contact tests. This corroborates with Amorim which used the same method and observed that CTZ paste had a more effective antimicrobial activity than ZOE paste for all the micro-organisms [31].

However, the comparative results of both ZOE and CTZ in the present study were due to the both of these materials have an antibacterial effect. As the antibacterial effect of ZOE is mainly attributed to the action of eugenol that causes protein denaturation[32].

Additionally, it has been suggested that after placement of ZOE paste, ongoing hydrolysis of zinc eugenolate may result in free eugenol coming in direct contact with the pulp tissue. This could cause moderate to severe inflammatory changes in the pulp leading to chronic inflammation and necrosis. Internal resorption is known to be one of the common responses of the pulp to chronic inflammation. This could explain the relatively higher radiographic failure results of ZOE when compared to its clinical counterpart results [33].

The clinical result of the present study was confirmed by the radiographic results as the Kappa results revealed a substantial to almost perfect agreement between the clinical and radiographic examinations after 1-month, 3-months, and 6-months of follow-up with kappa index of 1.000, 0.071, and 0.0.081 respectively. This is because the aim of the scoring assessment was to reveal the severity of changes, and pulpotomies molars were not only counted as 'successful' or 'failed' based on clinical signs or symptoms [34].

CONCLUSION

Ferric sulfate as hemostatic agent showed relatively better clinical and radiographic results compared to tranexamic acid during pulpotomy treatment of primary molars.

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