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# **Revascularization Procedures in nonvital Immature Permanent Teeth a Comparative Study**

# Ahmed Mahmoud Etman<sup>1</sup>\*; Ibrahim Hassan ElKalla\*\*; Salwa Mohamed Awad\*\* and Hanaa Mahmoud Shalan\*\*\*

## ABSTRACT

Induction of root growth in nonvital immature permanent teeth with revascularization procedures evaluated using triantibiotic paste or Calcium hydroxide paste as a disinfectant intracanal medicament. The coronal seal using Mineral trioxide aggregate or Glass ionomer cement was evaluated. Sixty five permanent non vital immature teeth of 7-13 years old children with signs and symptoms of periapical pathosis were included in the study. Teeth were classified into two main groups according to the disinfectant material Group 1, (triantibiotic paste) and Group 2 (calcium hydroxide paste); each group was subdivided into two subgroups A and B (MTA or Glass ionomer) according to the sealing material. The disinfectant pastes were placed in the first visit and were removed in the second visit using 2.5% NaOCl irrigation. After root canal drying, apical bleeding was induced by over instrumentation in the apical region with 15 K-files. The sealing materials were placed in the coronal third of the root then composite restorations were placed in both subgroups. Children were followed up each three month up to 18 months clinically and radiographically. Standardized digital radiographs were evaluated for thickening of canal walls, continued root development and changes of periapical lesions. At 18 month, the success rate was 70.5%, 33.2%, 26.3% and 22.2% in 1A, 2A, 1B and 2B groups respectively regarding marked thickening of canal wall, while it was 64.7%, 33.3%, 42.1% and 22.2% in 1A, 2A, 1B and 2B groups respectively regarding marked root development. Regarding decrease of periapical lesions it was 88.2%, 66.7%, 57.9% and 55.6% in 1A, 2A, 1B and 2B groups respectively. Thickening of canal wall was significantly increased in 1A, 2A and 2B groups. Root development was significantly increased in 1A, 2A and 2B groups. Periapical lesion was significantly decreased in group 1A, 1Band 2B groups.

### 1. Introduction

Pulp necrosis of an immature permanent tooth due to trauma or caries arrests the tooth development and it becomes prone to fracture. The vitality of dental pulp preserves the capacity of dentin regeneration particularly in case of immature permanent teeth because of their incomplete apical and dentinal wall development <sup>(1)</sup>.

Revascularization treatment of immature necrotic permanent teeth allows continuation of root development has been introduced newly instead of conventional methods that induce formation of barrier against which the obturation materials can pack as apexification with calcium hydroxide <sup>(2)</sup>.

Pulp revascularization success depends on a reliable cell source capable of differentiating into odontoblast, an appropriate scaffold to promote cell growth and differentiation, and signaling molecules as growth factors capable of stimulating cellular proliferation and directing cellular differentiation <sup>(3)</sup>.

The apical end of the pulp, periodontal ligament, apical papilla and bone marrow are rich in dental stem cells so they are considered as a reliable cell source in immature teeth. Blood clot formed after induce bleeding in the apical lesion could act as a scaffold and rich source of growth factors. Growth factors are an extensive group of proteins that can bind the receptors on the cell surface induce cellular proliferation and differentiation <sup>(4)</sup>.

Revascularization procedures begin after relief of all inflammatory reactions and proceeded till good sealant against bacteria and final restoration. These procedures establish a sterilized field in which the stem cells can proliferate into newly formed matrix and differentiate into odontoblasts. The newly formed odontoblasts can lay down a tubular dentine at the apical end, causing elongation of root, as well as on lateral aspects of dentinal walls. This study evaluated the induction of root growth in nonvital immature permanent teeth using different methods of disinfection and sealing materials.

#### 2. Material and methods

Children and their parents were informed about the study, procedures and possible risks then written consents were obtained. Forty nine children were selected from Pediatric Dentistry Clinic, Faculty of Dentistry, Mansoura University. The children comprised sixty five immature and non-vital permanent teeth (upper and lower anterior teeth or lower first permanent molars).

The selected children were apparently healthy, have no chronic systemic diseases. Their age ranged between 7-13 years. The selected children were presented with trauma or badly decayed teeth with symptoms of acute or chronic peri apical periodontitis (pain, tenderness to percussion, diffuse facial and / or mucosal swelling or intraoral sinuses). The selected teeth had the following criteria, immature blunderbuss apices, or moderately developed root; negative response to the pulp vitality test and signs of periapical infection <sup>(5)</sup>.

The selected teeth were classified into two main groups; 32 teeth for group I and 33 teeth for group II, according to the type of medicament. Group I: triantibiotic paste, Group II: Ca (OH) <sub>2</sub> paste. Each group was subdivided into two subgroups according to the material used for coronal seal, Subgroup A: Mineral trioxide aggregate, Subgroup B: Glass ionomer cement.

After isolation and dryness of the tooth surface, the vitality of the selected tooth was evaluated using electric pulp tester; contralateral unaffected tooth was used as a control. Periapical X ray film was taken for each case. All teeth treated according to 2-visit regenerative endodontic protocol <sup>(6)</sup>. The pulp chamber was accessed. Each root canal was irrigated without instrumentation using 5.25 %Naocl. In Group I triantibiotic paste was placed in the pulp chamber and was loosely packed into the coronal portion of the root canals. The tooth was sealed with a temporary filling for two weeks. The same procedures were done in GroupII with Ca (OH) <sub>2</sub> paste. In Second no appointment, where neither signs or symptoms of persistent infection appeared. The tooth isolated, anesthetized locally without vasoconstrictors. The pulp champer reaccessed. Either the triantibiotic paste or Ca (OH)<sub>2</sub> removed with copious 2.5% NaOCl irrigation then the root canals were irrigated with sterile saline and dried using a paper points.

After drying of the root canal, bleeding was induced in the apical region by over instrumentation using 15 Kfiles <sup>(7)</sup>. A tight sterile moist cotton pellet was inserted into the canal for 7-10 minutes to allow blood clot formation in the apical two thirds of the canal. In subgroup A, the moist cotton pellet was removed. MTA adapted over the blood clot as a coronal seal. A wet cotton pellet was placed over MTA. The final coronal restorations were placed in the same visit <sup>(8)</sup>. In subgroup B, after formation of the blood clot, the access opening was sealed with glass ionomer cement followed by final restoration.

For all teeth, immediate postoperative periapical radiograph was taken as a baseline record. The patient was followed up after one week, then three month interval for a period of 18 month. Evaluation was done at each follow – up visit clinically and radiographically. All the results were recoded continuously using image J analysis program for radiographic analysis, further comparison, progress in root length and increase in thickness of root walls<sup>(9)</sup>.

The root lengths were measured as a straight line from cementoenamel junction to the apex of the tooth. Percentage of increase in length = postoperative length – Preoperative length/preoperative length  $\times$  100. Increase in the root thickness was measured by subtracting the width of the pulp space from width of the root at level determined and fixed from the cementoenamel junction. The percentage of increase in thickness = postoperative thickness  $\times$  100. The Mean was determined for results obtained from each group and the results exceed the mean was considered as marked either in progress in root length or thicknesing of canal walls.

#### 3. Results

Forty nine children 25 male and 24 female, with mean age  $8.78\pm1.17$ , were selected from pediatric dentistry clinic. Sixty five immature permanent non vital teeth with signs and symptoms of periapical pathosis were included in the study. The selected teeth completed the study were 45 upper incisors, four lower incisors and 16 lower first molars.

Data in table 1 (figure 1), shows that there was an increasing rate in thickening of canal wall for group 1A along the follow up period. Marked thickening of canal wall was recorded in (70.5 %) of teeth at 18 month follow up. These followed by group 2A (38.9%), then group 1B (26.3 %) and finally in group 2B (22.2 %).

Data in table 2 (figure 2), shows that the Continuation of root development was noted in group 1A with highest percentage of marked root development in 64.7 % of cases at 18 month follow up when compared to the percentage in the other three groups.

Data in table 3 (figure 3), shows that for group 1A, decrease of periapical lesion was the highest. The decrease in size of periapical lesion revealed in 88.2 % of roots at 18 month follows up while decrease of periapical radiolucency in group 1B was the least. There were in 57.9% of roots at 18 month follows up. In contrary, it was

noticed that periapical lesion increased in 11.1 % of cases at 18 months for group 2A.While for group 2B, increase of periapical lesion noticed in 27.7 % at 18 months.

Thickening of canal wall	G1A	G2A	G1B	G2B	Significance			
3 month outcome								
No changes seen	15(78.9)	16(80)	21(100)	21(100)	χ <sup>2</sup> =15.11 p=0.019*			
Thickening of canal wall	4(21.1)	2(10)	0	0				
Marked thickening of canal walls	0	2(10)	0	0				
Total	19(100)© ;	20(100)	21(100)©	21(100);				
	6 r	nonth outcom	e					
No changes seen	13(68.4)	13(65)	16(76.2)	19(90.5)	χ <sup>2</sup> =6.58			
Thickening of canal wall	6(31.6)	5(10)	4(19)	2(9.5)	p=0.36			
Marked thickening of canal walls	0	2(10)	1(4.8)	0				
Total	19(100) ©	20(100)	21(100) ©	21(100)				
	9 r	nonth outcom	e					
No changes seen	8(42.1)	13(65)	14(73.7)	15(71.4)	$\chi^2 = 8.86$			
Thickening of canal wall	10(52.6)	5(25)	3(15.8)	6(28.6)	p=0.18			
Marked thickening of canal walls	1(5.3)	2(10)	2(10.5)	0				
Total	19(100) ©	20(100)	19(100) ©	21(100)				
12-month outcome								
No changes seen	6(33.3)	11(61.1)	12(63.3)	11(57.9)	χ <sup>2</sup> =12.68			
Thickening of canal wall	6(33.3)	4(22.2)	3(15.8)	8(42.1)	p=0.09			
Marked thickening of canal walls	6(33.3)	3(16.7)	4(21.1)	0				
Total	18(100);	18(100)	19(100) ®	19 (100)® ;				
15 month outcome								
No changes seen	No changes seen 5(27.8) 10(55.6) 11(57.9)		11(57.9)	10(52.6)	χ <sup>2</sup> =12.23			
Thickening of canal wall	5(27.8) 1(5.6) 3(15.8		3(15.8)	7(36.8)	p=0.05*			
Marked thickening of canal walls	8(44.4)	7(38.9)	5(26.3)	2(10.5)				
Total	18(100) ©;	18(100) °	19(100) ©	19 (100) °;				
18 month outcome								
No changes seen	2(11.7)	10(55.6)	11(57.9)	9(50)	$\chi^2 = 12.68$			
Thickening of canal wall 3(17.6)		1(5.6)	3(15.8)	5(27.8)	p=0.04*			
Marked thickening of canal walls	12(70.5)	7(38.9)	5(26.3)	4(22.2)				
Total 17(100) ©;		18(100)	19(100) ©	18 (100) ;				

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Small letters showing the internal relation between the studied groups



Figure 1: The progress in thickening of canal wall of the four studied groups



Figure 2: The progress in root development of the four studied groups

# Table (2): radiographic findings of the four studied groups during follow up period:

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Continued root	G1A	G2A	G1B	G2B	Significance			
aevelopment 3 month outcome								
Ne charges even 15/79.0) 16/90 10/71.4) 21/1004								
No changes seen	15(78.9)	16(80)	18(/1.4)	21(100)	$\chi^2 = 11.004$			
Not development	4(21.1)	2(10)	3(14.3)	0	p=0.08			
Marked root development	0	2(10)	0	0				
Total	19(100);	20(100)	21(100)	21(100);				
· · ·		6 month out	come		•			
No changes seen	13(68.4)	13(65)	15(71.4)	19(90.5)	χ <sup>2</sup> =9.53			
Root development	5(26.3)	5(25)	3(14.3)	2(9.5)	p=0.15			
Marked root development	1(5.3)	2(10)	3(14.3)	0				
Total	19(100)	20(100)	21(100)	21(100)				
9 month outcome								
No changes seen	7(36.8)	13(65)	12(63.2)	15(71.4)	$\chi^2 = 11.29$			
Root development	10(52.6)	5(25)	3(15.8)	6(28.6)	p=0.08			
Marked root development	2(10.5)	2(10)	4(21.1)	0				
Total	19(100) ©;	20(100)	19(100) ©	21(100);				
12 month outcome								
No changes seen	5(27.8)	10(55.6)	9(47.4)	11(57.9)	$\chi^2 = 12.68$			
Root development	6(33.3)	3(16.7)	3(15.8)	8(42.1)	p=0.04*			
Marked root development	7(38.9)	5(27.8)	7(36.8)	0				
Total	18(100);	18(100) °	19(100) ®	19(100) °®;				
15 month outcome								
No changes seen	4(22.2)	9(50)	9(47.4)	10(52.3)	$\gamma^2 = 12.68$			
Root development	5(27.8)	2(11.1)	2(10.5)	7(36.8)	p=0.04*			
Marked root development	9(50)	7(38.9)	8(42.1)	2(10.5)	I III			
Total	18(100);	18(100)	19(100) ®	19(100) ®;				
18 month outcome								
No changes seen	3(17.6)	9(50)	9(47.4)	9 (50)	$\chi^2 = 11.59$			
Root development	3(17.6)	2(11.1)	2(10.5)	5(27.8)	p=0.07			
Marked root development	11(64.7)	7(38.9)	8(42.1)	4(22.2)	1			
Total	17(100);	18(100)	19(100)	18(100);	1			

Small letters showing the internal relation between the studied groups

Changes of PL	G1A	G2A	G1B	G2B	Significance		
3month outcome							
No changes seen	9(47.4)	8(40)	18(85.7)	21(100)	$\chi^2 = 24.26$		
Decrease of PL	10(52.6)	12(60)	3(14.3)	0	p<0.001*		
Total	19(100) ©;	20(100) ° a	21(100) © <sup>a</sup>	21(100) °;			
		6 month outcor	ne				
No changes seen	8(42.1)	8(40)	15(71.4)	21(100)	$\chi^2 = 23.25$		
Decrease of PL	11(57.9)	12(60)	6(28.6)	0	p<0.001*		
Total	19(100);	20(100) ° a	21(100) ® ª	21(100) °®;			
		9 month outcor	ne				
No changes seen	3(15.8)	6(30)	12(63.2)	17(81)	$\chi^2 = 24.26$		
Decrease of PL	16(84.2)	14(70)	7(36.8)	4(19)	p<0.001*		
Total	19(100) ©;	20(100) ° a	19(100) © <sup>a</sup>	21(100) °;			
12month outcome							
No changes seen	3(16.7)	5(27.8)	9(47.4)	5(26.3)	χ2=16.67		
Decrease of PL	15(83.3)	13(72.2)	10(52.6)	10(52.6)	p=0. 01*		
Increase of PL	0	0	0	4(21.1)			
Total	18(100) ©;	18(100)	19(100) ©	19(100);			
15 month outcome							
No changes seen	2(11.1)	3(16.7)	9(47.4)	3(15.8)	χ <sup>2</sup> =16.67		
Decrease of PL	16(88.9	13(72.2)	10(52.6)	10(52.6)	p=0.002*		
Increase of PL	0	2(11.1)	0	6(31.6)			
Total	18(100) ©;	18(100)	19(100) ©®	19(100) ®;			
18 month outcome							
No changes seen	2(11.8)	3(16.7)	8(42.1)	3(16.6)	χ <sup>2</sup> =12.69		
Decrease of PL	15(88.2)	13(72.2)	11(57.9)	10(55.6)	p=0.048*		
Increase of PL	0	2(11.1)	0	5(27.8)			
Total	17(100) ©;	18(100)	19(100) ©	18(100);			

Table (3): radiographic findings of the four studied groups during follow up period:

Small letters showing the internal relation between the studied groups



Figure 3: The progress in changes of periapical lesion of the four studied groups



A- Preoperative Periapical x ray film of left upper central incisor showing wide root canal and open apices with periapical lesion.



B- post-operative



C-After 18 month Maturation and root lengthening noticed



Figure 4: A, B, C: Radiographic outcome of 1A group



A- Pre-operative B- post-operative Lower left central incisor showing Matura wide root canals and open apices Fig 5 A, B, C: Radiographic outcome of group 2A

C-At18 month Maturation and marked root lengthening

#### **4- Discussions**

Injury to immature permanent teeth may lead to arrest in dentin deposition and root maturation leaving a root with an open apex and thin dentinal tubules that is prone to fracture. Conventional methods of treatment as apexification with calcium hydroxide were unable to stimulate regeneration of pulp tissue so the teeth remain at fracture risk. Pulp revascularization is an emerging therapy appears to be effective in treatment of immature teeth as it allows root development by a relatively simple technique <sup>(10)</sup>.

In the present study, we try to induce root growth in nonvital immature teeth by stimulating autologous cells from the apical region to avoid potential immune reaction. The teeth were selected with special criteria including necrosis and presence of apical lesion with different signs and symptoms. In this study, teeth were subjected to the revascularization procedures with mean age  $8.78\pm1.17$ . In this age there is a degree of vascularity and cellularity in the apical region which facilitate cellular proliferation and differentiation<sup>(11)</sup>.

In the present study the root canals were not debrided to avoid fracture susceptibility of thin dentinal tubules and avoid formation of smear layer that could occlude the dentinal tubules. Gates Glidden drills were used in the coronal one third of canals to facilitate irrigation and placement of disinfectant material <sup>(12)</sup>. Irrigation of the root canals was passive directed toward the walls of the canals to prevent irritation to periapical tissues. Sodium hypochlorite used alone for irrigation of canals instead of sodium hypochlorite + chlorhexidine irrigation, as chlorhexidine have cytotoxic effects on human cells and affect the attachment of pulp stem cells to the root canal walls <sup>(13,14)</sup>.

Calcium hydroxide the wide intracanal medicament was compared to triantibiotic paste commonly used in regeneration of immature teeth for decontamination of root canals. Lentulo spiral was used for homogenous spread

of both materials inside the canal. MTA and glass ionomer were used for coronal seal. The importance of a tight coronal seal against bacteria for successful revascularization was documented in several studies confirmed the sealing ability and biocompatibility of MTA <sup>(15, 16)</sup>. White MTA was used as it produces a significant reduction in discoloration when compared to gray MTA by using spectrophotometric analysis method <sup>(17)</sup>. In this study glass ionomer was compared to MTA as it has the ability to form chemical bond with tooth structure. Hana <sup>(18)</sup> showed that glass ionomer cement has biocompatibility and good sealing ability either in vivo or in vitro.

Our Radiographic finding showed a statistical significant difference between groups 1A and 1B regarding thickening of canal wall, root development and changes of periapical lesion which can be attributed to the biocompatibility and reparative dentingenesis of MTA. It involves a complex cellular and molecular events leading to hard tissue repair by newly differentiated odontoblast like cells <sup>(19)</sup>. These results are in accordance with a number of in vitro and in vivo studies revealing that the biocompatibility of MTA and its ability to produce reparative dentingenesis was higher than other dental materials used for the same purpose <sup>(20, 21)</sup>.

A statistical significant difference between groups 2A and 2B was showed also regarding thickening of canal wall, root development and changes of periapical lesion size revealed the role of MTA in success of revascularization process. These results are in accordance with Seok-woo<sup>(22)</sup> who showed that MTA is not affected by presence of blood where Tricalcium oxide in MTA reacts with tissue fluids to form calcium hydroxide resulting in apical barrier, Torabinejad<sup>(23)</sup> who revealed that MTA reduce root fracture risk, better patient compliance and showed early results and better long term effect. Also in accordance with a study compare MTA with osteogenic protein and calcium hydroxide who revealed that MTA has the highest capacity to produce apical barrier during apexification process<sup>(24)</sup>.

Regarding thickening of canal wall and root development, there was a statistically significant difference between groups 1B and 2B. These results may be attributed to presence of calcium hydroxide remnants in the dentinal walls after irrigation of root canals. These remnants of calcium hydroxide may affect the ability of glass ionomer to produce a good sealing <sup>(25)</sup>.

Our results come in accordance with several studies in which removal of calcium hydroxide was difficult with using different irrigation methods <sup>(26, 27)</sup>, and disagree with other studies that revealed the ability of its removal by various irrigation techniques <sup>(28, 29)</sup>. However, Julie et al <sup>(30)</sup> showed that removal of either triantibiotic paste or calcium hydroxide completely after disinfection is difficult. Triantibiotic paste has a high diffusion and retention, penetrate deeply in the dentinal tubules while calcium hydroxide remnants remain superficial within dentin that affects the physical properties of sealing material.

These results may be attributed also to the effect of disinfectant material on the stem cells in apical region. These results are not in accordance with several studies determining the effect of disinfecting material on stem cells. Ruparel et al <sup>(31)</sup> showed that calcium hydroxide not affecting the viability of stem cells while triantibiotic paste reduces the viability of stem cells. Nagata <sup>(32)</sup> found no difference in bacterial reduction between triantibiotic paste and calcium hydroxide after the process of disinfection. Hachmeister et al <sup>(33)</sup> found that one or two weeks use of calcium hydroxide therapy had no adverse effect on the sealing ability of MTA for 70 days, but the effect of calcium hydroxide remnants on sealing materials may differ from sealing material to another. Yesilyurt et al <sup>(34)</sup> revealed that the combination of glass ionomer cement and antibiotics was compatible and produce better antimicrobial effects and adequate physical and bonding properties.

A statistical significant difference between groups 1A and 2B was noted regarding all variables. Concerning the disinfectant materials, these may be attributed to the drawbacks of calcium hydroxide as cause weakening dentinal walls, inducing tissue necrosis, and decrease in its effectiveness by infectious exudate <sup>(19)</sup>. While in triantibiotic paste the three antibiotics cover a broad spectrum of root canal bacteria and show minimum cytotoxicity on stem cells <sup>(35, 36)</sup>. Melanie and Stephanie <sup>(37)</sup> showed that the triantibiotic paste seems to be more compatible disinfectant material. Concerning the sealing materials, glass ionomer cement could be affected by the remnants of calcium hydroxide and cytotoxic effect of fluoride released from it during follow up period.

Regarding changes of periapical lesion size, a statistical significant difference was shown between groups 2A and 1B. Concerning the disinfectant materials, these results can be attributed to the use of calcium hydroxide as medication before MTA that helps drying the canal and keeping it free from infection and microorganism.

Concerning the sealing materials, MTA can reduce the duration for apical healing more than any other material <sup>(38)</sup>. Louping et al <sup>(39)</sup> showed that MTA used after calcium hydroxide would be repairable over time regarding weakening of canal wall. Alhaddad et al <sup>(40)</sup> proved that materials potentially inducing mineralization such as MTA can avoid drawbacks of calcium hydroxide when used as coronal seal after it.

We can arrange the success rate in descending order as follow; the group 1A was superior during follow up period regarding all the variables followed by groups 2A, 1B and 2B. These results come in accordance with many studies and reports that revealed success of revascularization process by using triantibiotic paste and MTA <sup>(41, 42)</sup>. Concerning the disinfectant materials, these were attributed the presence of three antibiotics in triantibiotic paste and to the deep penetration of it into the dentinal tubules so can deal with most of the microorganisms. Concerning the sealing materials, MTA represent a cause for high rate of success, not only due to its antimicrobial properties but also because fine hydrophilic particles in it, set in the presence of tissue fluids, sealing the pathways of communication between the outer environment and the root canal space<sup>(39)</sup>.

Potential clinical and biological limitations were observed during the revascularization procedures, as crown discoloration, induce bleeding difficulties. The amount of bleeding to form blood clot differs from a case to another and the time to form clot also differ from one to another. Manipulation and application of the sealing materials to the desired level within coronal third of the root represented a challenge particularly in the presence of blood inside the canal. The time needed for complete disinfection and relief of signs and symptoms differ from case to another.

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