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ORIGINAL ARTICLE

Regenerative Treatment of Mature Teeth with Pulp Necrosis and Apical Periodontitis Using Biodentine Compared with MTA: Randomized Controlled Clinical Trial

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ABSTRACT

Objective: The purpose of this randomized, controlled study was to evaluate the effectiveness of Biodentine compared with MTA used as a pulp space barrier in healing periapical lesions and regaining pulp sensitivity after regenerative treatment in mature single-canal permanent teeth with pulp necrosis and apical periodontitis.

Methods: The study involved 36 patients with mature teeth with necrotic pulp and apical periodontitis. The patient underwent a regenerative treatment that utilized the blood clot technique. Teeth were randomly allocated to either the intervention, Biodentine, group (n=18) or the control, MTA, group (n=18). The healing of periapical lesions and tooth sensibility were evaluated throughout follow-up visits for up to 18 months.

Results: The study analyzed 31 patients; two patients within the biodentine group and three in the MTA group were lost to follow-up. After 18 months, both groups showed effective healing of periradicular lesions; 21 out of 31 patients (67.7%) were healed, ten patients (32.3%) were healing, and no failure cases occurred. There were no significant differences between the groups (p=1.00). More than 70% patients (22 out of 31) regained teeth sensibility, and the groups had no statistically significant difference (p=0.703).

Conclusion: Regenerative treatment using blood clots with either MTA or Biodentine effectively resolved periapical lesions and regained the sensibility of mature teeth.

Keywords: Biodentine, healing periapical lesions mature teeth, procedure, regaining sensibility, regenerative endodontic MTA

HIGHLIGHTS

- Regenerative endodontic procedure (REP) could be a suitable treatment option for mature teeth with necrotic pulp and apical periodontitis.
- REP using blood clot technique with either MTA or Biodentine shows effective healing of periapical lesions.
- REP enables regaining teeth sensibility in teeth with necrotic pulp and apical periodontitis.

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INTRODUCTION

Regenerative endodontic procedure (REP) is considered a potential alternative to conventional endodontic treatment (1), which includes biological agents like blood clots (2). The American Association of Endodontists (AAE) defines regenerative endodontics as “biologically based procedures designed to replace damaged structures, including dentin and root structures, as well as cells of the pulp-dentine complex” (3). REP utilizes a combination of stem cells, scaffolds, and growth factors to aid regeneration (4). It includes cell-homing or cell-based procedures. Cell homing depends on actively recruiting endogenous stem and progenitor cells into root canal space. In contrast, cell-based procedures require transplanting *ex vivo* cultivated stem cells. The current protocol for REP via blood clot (BC) induction is based on cell homing (5).

REP has been focused on immature teeth to regenerate functional pulp tissue and promote the continuation of root development; however, it is suggested that the scope of the procedure should be extended to mature teeth as an alternative to root canal treatment (RCT). REP of mature teeth may face additional difficulties than immature teeth because of the difficulty in achieving adequate bleeding through the narrow apical pathway; narrower apical access of fewer stem and progenitor cells in mature teeth will be the main limitation, together with the fact that it can be challenging to properly disinfect the root canals of mature teeth., mainly necrotic teeth with periradicular infection (6).

Regenerative endodontics has recently attracted much interest and attention since its techniques and outcomes differ from conventional endodontic therapy. The success of REP in mature teeth depends on the resolution of symptoms and the initiation of bone regeneration. These act as functional indicators of long-term tooth retention. Overall, REP restores homeostasis and natural defense, which may aid tooth survival (7). In contrast to RCT, teeth lose their defensive capacity and proprioception after RCT and become prone to fracture by external forces and reinfections (5).

A number of clinical trials (8–14) have shown evidence of the effective use of REP in fully developed teeth; however, they had different parameters and protocols and more research is needed with an extended follow-up period. MTA and Biodentine are the most commonly used coronal barriers in regenerative procedures. Although the literature is available on factors that can affect regenerative outcomes, such as different disinfection protocols (15), scaffolds (16), apical preparation (10), and apical diameter (11), no studies compared the influence of coronal barriers on regenerative treatment in mature teeth.

Therefore, this prospective, randomized, controlled clinical study aimed to evaluate the effectiveness of Biodentine compared with MTA used as a pulp space barrier on the healing of periapical lesions and regaining pulp sensitivity after REP in teeth with mature roots and single canals diagnosed with pulp necrosis and apical periodontitis.

MATERIALS AND METHODS

This randomized clinical trial followed the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The study was conducted in accordance with the Declaration of Helsinki. The Research Ethics Committee, Faculty of Dentistry, Cairo University, approved the protocol of this double-blind, randomized clinical trial and the informed consent format. The study protocol has been registered at www.clinicaltrials.gov (Identifier No.: NCT04018456). A single operator recruited all the subjects from the Department of Endodontics outpatient clinic at the Faculty of Dentistry starting in August 2021 until the target number met the eligibility criteria. All procedures were described to the patients who were eligible for the trial and accepted to enter the trial, as well as potential outcomes, potential risks, and the desired follow-up period. Then, patients were presented with a printed informed consent form to sign and keep a copy.

Eligibility Criteria

Each patient participating in this study had anterior teeth encasing one root canal with a mature root (closed apex) with necrotic pulp and apical periodontitis, was older than ten years and less than 35 years, and was in good health [American Society of Anesthesiologists (ASA) Class I or II]. A periapical lesion should be shown in the radiograph for more than 3 mm, according to the classification of Ørstavik et al. (17). The exclusion criteria were as follows: patients who had teeth with periodontal pockets more than 3 mm or generalized chronic periodontitis; any teeth with developmental anomalies (i.e., dens invaginatus or a palatogingival groove); teeth with a prior root canal treatment; or teeth that needed a post and core as the final restoration.

Patient Examination

Past medical and dental histories were taken from all patients. A thorough clinical and radiographic examination of the tooth to be treated was done to confirm the diagnosis of necrotic pulp with apical periodontitis. The patients should experience the following: The negative response to cold and electric pulp testing is compared to the contralateral or adjacent tooth if the contralateral one is missing. Each tooth was given a periapical index (PAI) score prior to treatment. The scores for the periapical lesion were as follows:

Score 1: Normal periapical structures

Score 2: Small changes in bone structure

Score 3: Changes in bone structure with some mineral loss

Score 4: Periodontitis with a well-defined radiolucent area

Score 5: Severe periodontitis with exacerbating features

The clinical examination included measuring the depth of periodontal pockets, tenderness to percussion, palpating the affected teeth' apical area, checking the sinus tract's presence, and testing for sensibility. Patients were also examined radiographically using preoperative digital standardized radiographs utilizing the parallel technique to confirm the presence of a periapical lesion.

Randomization

Each participant had the same chance of being assigned to a specific treatment group with a random assignment. All participants were randomly assigned to either the Biodentine intervention group or the MTA control group using a computer-generated sequence by the principal investigator. The allocation ratio was 1:1, with 18 participants in each group. Sealed opaque envelopes with a random sequence from 1 to 36 were used to assign participants to their respective groups. Each participant picked up an envelope during their second visit of treatment.

Regenerative Procedures

One experienced investigator (A.H.R.) performed all clinical procedures (10, 12, 13).

First Appointment

A custom-made index was performed for each patient to obtain standardization of the radiograph using a Rinn film holder, a paralleling device (Dentsply Sirona, Milford, DE, USA), and silicon impression material (Aquasil, Dentsply Sirona) (16, 17). Periapical radiographs were taken with the same index and paralleling device on every visit.

Local infiltration anesthesia was delivered using 1.7 ml of 4% articaine hydrochloride with a 1:200,000 epinephrine local anesthetic agent (Septodont, Saint-Maur-des-Fosses Cedex, France). The tooth was isolated, and endodontic access was performed. The working length was established using an apex locator (Root ZX, J. Morita) and then verified with an intraoral parallel periapical radiograph (Digora, Digital ScaNeo imaging plate size 2). This was done to ensure the length was 0.5–1 mm shorter than the radiographic apex. The canal was shaped using stainless steel hand K files (Mani, Japan) up to the master apical file size with 20 ml of 1.5% NaOCl as an irrigant. The irrigation was performed gently with a closed-end needle and a single-side vent. After the dryness of the canal, it was filled with calcium hydroxide (Metapaste, Metabiomed, Korea) before being temporarily sealed with restorative material (Nucavfil PSP Dental Co. Ltd., Belvedere, Kent, UK). By the end of the first visit, a digital radiograph was taken to ensure the quality of the CaOH dressing. In case of pain, the participant was instructed to take an analgesic of 400 mg of Ibuprofen (Brufen 400 mg tablets, Abbott Pharmaceuticals, Egypt). The patient was discharged for two weeks, during which the patient's response to initial treatment was assessed. If signs or symptoms of persistent infection were present, additional treatment time with antimicrobials or alternative antimicrobials was considered.

Second Appointment

The patient received anesthesia with 3% mepivacaine without a vasoconstrictor (Scandonest, Septodont, France). Dental dam isolation was performed, and 20 ml of 1.5% NaOCl was used to irrigate and flush the calcium hydroxide ($CaOH_2$). Then, the canal was rinsed with saline, irrigated with 20 ml of 17% EDTA, and dried with paper points. Bleeding was induced into the root canals by over-instrumentation and rotation of a pre-curved K-file #25 or #30 beyond the radiographic apex by 2–3mm. The blood was left in the canal for a few minutes to permit clotting. The patients were then randomly assigned to either the intervention group, which received biodentine cement (BD, Septodont, Saint Maur des Fosses, France), or the control group, which received MTA cement (Angelus Indústria de Produtos Odontológicos S/A, Brazil). A collagen sponge (Gelatin hemostatic collagen sponge, Hong Kong Medi CO Limited) was inserted inside the canal over the blood clot to confine the placement of the bioactive material. The case of failure of bleeding induction was excluded from the study.

Then, biodentine or MTA powder and liquid were mixed following the manufacturer's instructions. A 3 mm thickness was carefully placed over the collagen sponge under the cementoenamel junction, and it was gently adapted to dentinal walls using a moistened cotton pellet. A periapical radiograph assessed the position and the cervical plug material's quality.

After the MTA or Biodentine was initially set, which typically takes around 15 minutes per the manufacturer's instructions, a resin composite restoration was performed on the same visit to restore the access cavity. A postoperative standardized radiograph is also taken to monitor the healing of the periapical lesions. The patient is informed about the significance of scheduling a long-term follow-up examination, which is planned accordingly.

Postoperative Examination

All treated teeth were clinically and radiographically evaluated at 6, 9, 12, and 18 months by the principal examiner (A.H.R.), who recalled all patients. Digital radiographs were taken for each case in the same manner as the baseline and re-evaluated by a different examiner (F.M.). The calibration results of the two examiners' calibrations were compared, and re-evaluation was performed in cases of disagreement until an agreement was established.

Outcomes

Healing of periapical tissue

The clinical and radiographic assessments were conducted together throughout the follow-up periods. Clinically, when the case is symptoms-free, i.e., without sinus tract swelling, pain on palpation, or percussions, the case is considered a success. Radiographically, complete healing of the periapical lesion (i.e., scores 1 or 2) or reduction in lesion size was considered successful by comparing each digital radiograph picture at each point in time with the previous one. If the tooth showed symptoms or the radiolucency increased in size, the case was considered unsuccessful (failure) (17).

Restoring the tooth sensibility

A sensibility test was performed at every follow-up point: 6, 12, and 18 months postoperatively. It was assessed by a positive response to the sensibility test using EPT at any point during the follow-up periods. When a tooth responded positively to EPT, it was considered successful. In contrast, if a tooth did not respond to the sensibility test at any point in the follow-up period, it was considered a failure.

The EPT was used to record numerical readings of pulp sensibility in the same manner as preoperatively. The adjacent teeth were isolated and dried, and toothpaste was applied to the affected tooth. Then, the lip clip was placed, and any sensation felt was recorded (10, 12–14).

Statistical Analysis

The data were tested for normality using the Shapiro-Wilk test. Continuous data were presented as mean, standard deviation (SD), median, minimum, maximum values, and 95% confidence interval and were analyzed using the Mann-Whitney U test. Categorical data was presented as frequencies and percentages and analyzed using the Chi-square or Fisher exact test when more than 20% of the observed cell counts were less than 5. The significance level for primary tests was set at 0.05 ($p<0.05$). Statistical analysis was performed using SPSS software (IBM Corp., released 2017). IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp.)

RESULTS

For this study, 80 patients were recruited from the outpatient clinic of the endodontic department. A total of 36 patients met the inclusion criteria and were enrolled in the study (n=18) for

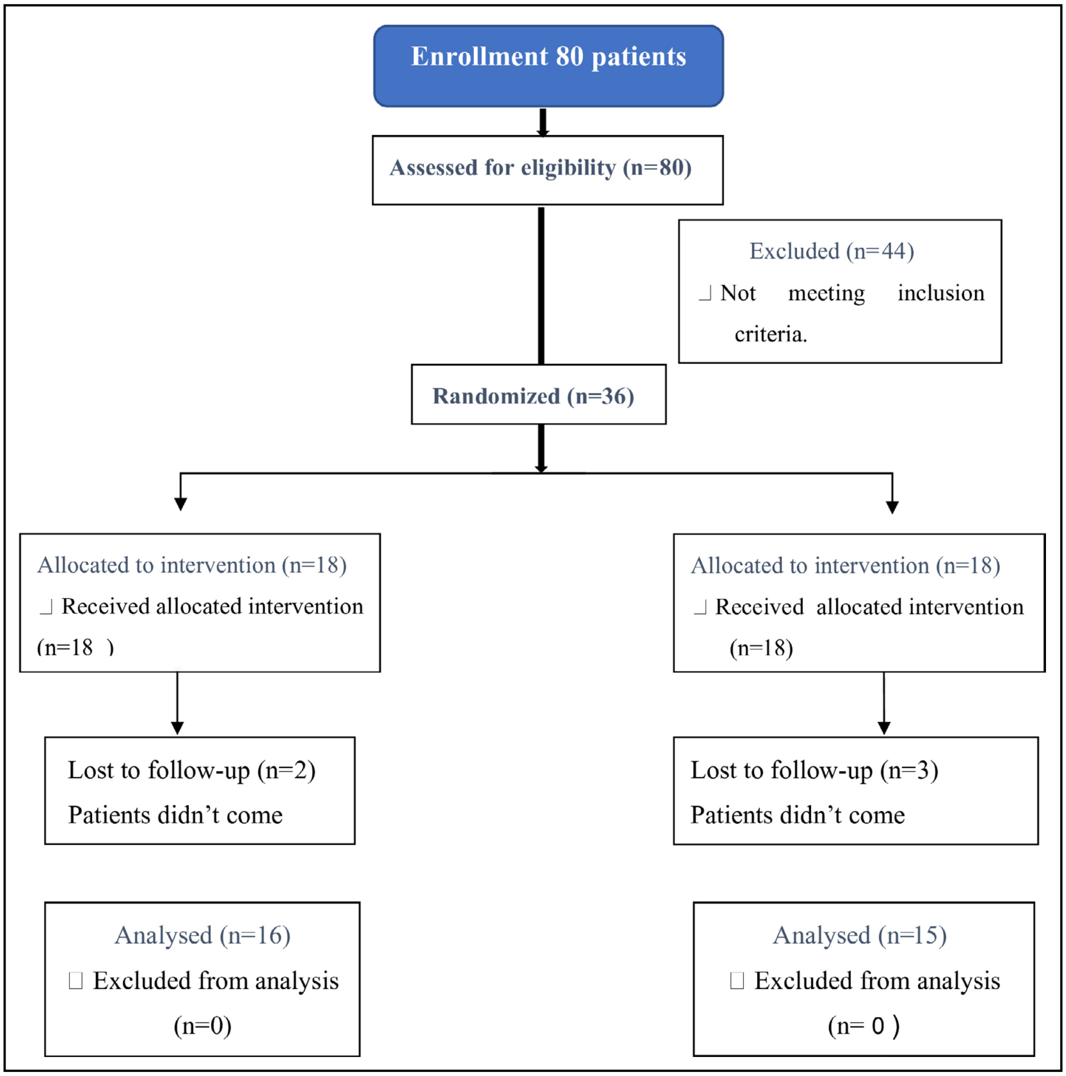

Figure 1. CONSORT flow diagram of the study
CONSORT: Consolidated Standards of Reporting Trials

each group. Two patients from the intervention group (Biodentine) and three from the control group (MTA) dropped out because they could not attend the follow-up visits; therefore, 31 patients were included in the analysis. The CONSORT flow chart illustrates the flow of participants throughout the trial (Fig. 1). There were no significant differences between the groups concerning their baseline characteristics.: age, cause of disease (caries or trauma), tooth type distribution, preoperative lesion score, and preoperative swelling (p>0.05) (Table 1).

The overall healing of the periapical lesion at 18 months postoperatively was 21 out of 31 patients (67.7%) (healed), 10 patients (32.3%) were healing, and no case remained unhealed. The two groups had no significant difference as shown in Tables 2, 3) and Figures 2 and 3.

Regarding regaining sensibility, by the end of the follow-up periods (18 months), 22 out of 31 patients (71%) regained sensibility by a positive response to EPT, and nine (29%) did not. No significant difference was observed between the two groups (Table 4). All patients in both groups showed good coronal restoration.

DISCUSSION

Initially, REPs were recommended for dental pulp revascularization in immature permanent teeth to improve root continuity, dentinal wall thickness, and apical closure (18–20). Evidence suggests that REPs can be an effective treatment for managing mature teeth with pulp necrosis and apical periodontitis and that there is an increased chance of a positive response to EPT when using REPs (1, 4).

This research was a randomized clinical trial with 36 subjects with necrotic pulp and apical periodontitis in the anterior incisors with single canals to standardize the REP of mature teeth (10, 12, 13). Arslan et al. (12) found that age did not significantly affect regenerative outcomes among participants aged 10 to 35.

Endodontic therapy and regenerative treatment aim to preserve and restore periapical health (7). PAI scoring is a reliable and precise measuring method for assessing bone repair in necrotic teeth with apical periodontitis (21). In this study, all teeth had apical radiolucency (PAI score≥3) prior to regenerative treatment (12). Standardized direct digital radiography was used for preoperative, postoperative, and follow-up radio-

TABLE 1. Baseline characteristics of the included study participants within the Biodentine and MTA groups

Variables	Biodentine (n=18)		MTA (n=18)		p
	n	%	n	%	
Age (years)					0.465
Mean (SD)	25.6 (13.7)		22.5 (12.1)		
Median (range)	21.5 (10–35)		18 (10–35)		
Eitology of disease					0.999
Trauma	14	77.8	15	83.3	
Caries	4	22.2	3	16.7	
Tooth type					0.625
Maxillary central	13	72.2	10	55.6	
Maxillary lateral	4	22.2	5	27.8	
Mandibular central	1	5.6	3	16.7	
Preoperative lesion size score					0.999
Score 3	7	38.9	6	33.3	
Score 4	6	33.3	6	33.3	
Score 5	5	27.8	6	33.3	
Preoperative swelling					1.0
Yes	5	27.8	5	27.8	
No	13	72.2	13	72.2	

MTA: Mineral trioxide aggregate; SD: Standard deviation

TABLE 2. Frequencies, percentages, and the result of Fisher exact test for comparison of the incidence of healing between the two groups at 18 months postoperatively

	Biodentine (n=16)		MTA (n=15)			
	Frequency	Percentage	Frequency	Percentage	p	RR (95%CI)
Healed	11	68.8	10	66.7	0.999	1.03 (0.63,1.68)
Healing	5	31.3	5	33.3		
Unhealed	0	0	0	0		

MTA: Mineral trioxide aggregate; CI: Confidence interval; RR: Relative risk.

graphic examinations to overcome the limitations of non-standardized systems. Standardization is necessary to maintain the same horizontal and vertical angulations at each subsequent visit to evaluate the healing of periapical lesions (18). It was reported that a 2-dimensional radiographic assessment, standardized and calibrated, was as practical as cone beam computed tomography in evaluating REP outcomes (18).

Disinfection of the canal is essential for successful REP, particularly in cases of apical periodontitis (6, 20). Mechanical preparation is necessary for infected dentine removal, biofilm disruption, and the creation of space for irrigants (10, 12, 13, 21). A lower concentration of NaOCl 1.5 was used to achieve adequate disinfection while preserving stem cell viability and dentine growth factors (7, 22, 23). As a final irrigant, 17% EDTA was used to stimulate the release of growth factors, including TGF-β, which support stem cell migration, angiogenesis, proliferation, and differentiation (24). NaOCl-EDTA stimulates additional connective tissue formation inside the pulp canal space, improving regeneration capacity (25).

Intracanal medications such as $CaOH_2$ and triple antibiotic paste (TAP) are commonly used for REP, and the AAE (3) advises using one of them. Studies have shown that both medications are equally effective in treating mature teeth (4, 7). $CaOH_2$ is preferred because it releases bioactive growth factors from dentin, encouraging SCAP proliferation (4).

TABLE 3. Frequencies, percentages, and the result of the Chi-square test for comparison of postoperative lesion sizes score between the two groups at 18 months postoperatively

	Biodentine (n=16)		MTA (n=15)		
	Frequency	Percentage	Frequency	Percentage	p
1	8	50.0	7	46.7	0.999
2	3	18.8	3	20.0	
3	5	31.3	5	33.3	

MTA: Mineral trioxide aggregate

The scaffold of the blood clot facilitated the regeneration of dental pulp-like tissue through the proliferation, migration, and organization of mesenchymal stem cells (MSCs). By stimulating bleeding in a well-disinfected root canal, MSCs are in-

Figure 2. Representative case of the Biodentine group revealed complete healing for the upper left central and lateral incisor. (a) Preoperative x-ray; (b) immediate postoperative for Central; (c) regenerative treatment for lateral incisor three months later; (d) 9 months follow-up; (e) 12 months follow-up; (f) 18 months follow-up; (g) 24 months follow-up

troduced, and a fibrin scaffold is formed, which generates a three-dimensional (3D) matrix with growth factors (GFs) to entrap MSCs and start the neoformation of new tissues (23, 25). The researchers used the induced bleeding technique to verify the existence and dispersion of MSCs in the root canal systems of mature permanent teeth. It has been confirmed that there is an influx of MSCs in the root canal system (26). A blood clot is the most common method for regenerative procedures due to its ease of application. Although other scaffolds, such as platelet-rich fibrin (PRF) and platelet-rich plasma (PRP), have been reported, none have been proven to be superior to a blood clot (27, 28). Therefore, the induced bleeding technique remains the standard regenerative procedure (24).

The present study used MTA and biodentine as coronal barrier materials since they are the most commonly used biomaterials for coronal sealing (24). MTA is often a coronal barrier due to its biocompatibility, sealability, and margin adaptability (29). It has been associated with the resolving of apical periodontitis signs and symptoms. MTA promotes the production and release of signaling molecules essential for tissue formation in the pulp space (29). When MTA is mixed with water, it forms calcium hydroxide. This compound breaks down into calcium and hydroxide ions, which raises the pH and releases calcium ions. The calcium ions enhance the osteoblastic viability, proliferation, and differentiation, while the hydroxide ions increase the alkalinity of the environment, which has antimicrobial impact (30). When the phosphate ions of the tissue combine with the calcium ions in the MTA, hydroxyapatite is produced (30). One day after applying MTA, it modifies vascular endothelial growth factor (VEGF) and supports the angiogenic process (31). Biodentine is comparable to MTA in its characteristics. It increases the production of hard tissue bridges and is considered biocompatible with pulp fibroblasts (32). It can enhance the expression of anti-inflammatory cytokines and suppress pro-inflammatory cytokines (33).

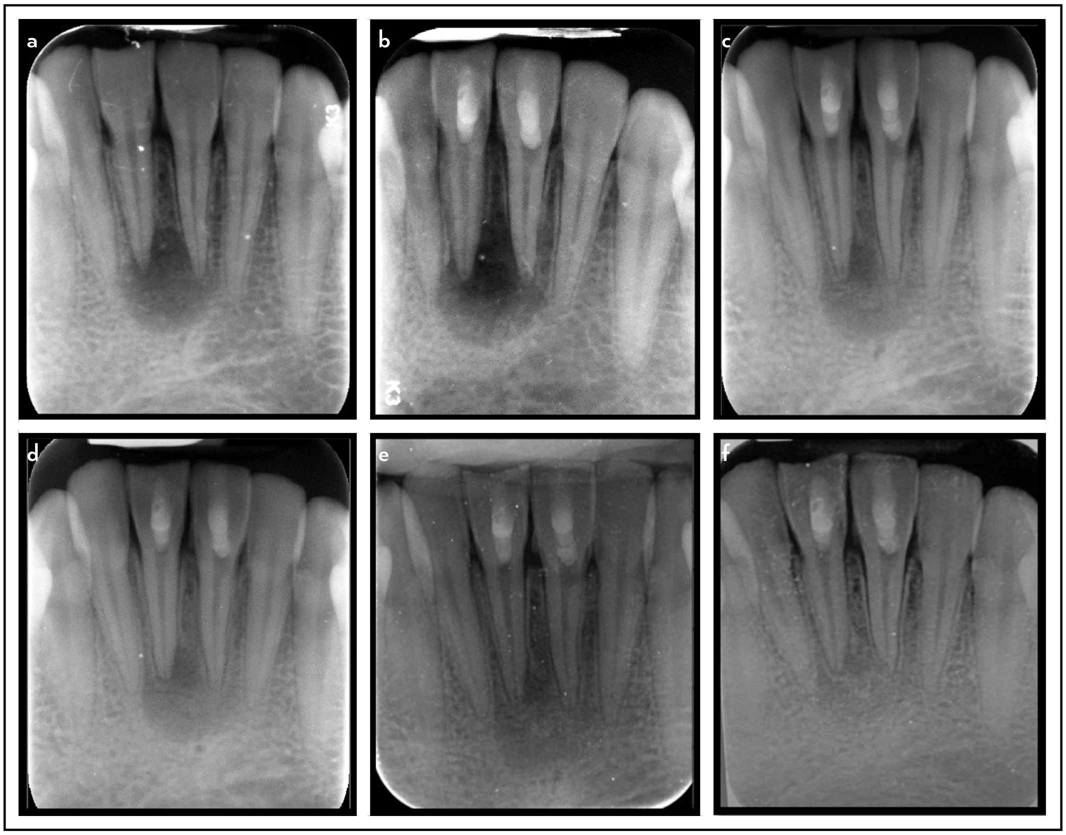

Figure 3. Representative case of MTA group for both lower central incisors revealed healing, (a) preoperative x.ray, (b) immediate postoperative, (c) 6 months follow-up, (d) 9 months follow-up, (e) 12 months follow-up, (f) 18 months follow-up

MTA: Mineral trioxide aggregate

Even though both Biodentine and MTA are tricalcium silicate-based cement and have similar properties, Rathinam et al. (34) demonstrated that they have different gene expression profiles that may be responsible for different histological outcomes after regenerative treatment. They suggested these variations in gene expression profiles may be attributed to differences in composition, purity, and calcium kinetics between the two cements (34).

The adhesive-bonded resin composite restoration was performed in all cases as a definitive final restoration, according to the guidelines of AAE (3), to prevent any possibility of coronal microleakage that may confound the results and affect the regenerative outcomes.

Regarding the results of the current study, the radiographic healing of the periapical lesion was promising. It showed either complete healing or a notable decrease in the size of the periapical lesions for both groups, and no failure occurred during 18 months of follow-up after REP. These results confirmed previous findings by Arslan et al. (12), El-Kateb et al. (10), and Youssef et al. (13), which demonstrated a decrease in the extent of periapical lesions after 12 months of REPs compared to the baseline score in mature permeant teeth.

Several variables may have contributed to the healing of periapical lesions caused by REP. It is suggested that stimulating bleeding in periapical tissue initiates the process of natural wound healing (35). Introducing bleeding into a disinfected canal is believed to help strengthen the clearance of antimicrobial agents. This is because blood contains components of both the innate and adaptive immune systems, such as cytokines and immunoglobulins, which promote phagocytosis by enabling the localization and opsonization of bacteria (36).

TABLE 4. Frequencies, percentages, and the result of Fisher exact test for comparison of the incidence of regaining sensibility by EPT between the two groups at 18 months postoperatively

	Biodentine (n=16)		MTA (n=15)			
	Frequency	**Percentage**	**Frequency**	**Percentage**	**p**	**RR (95%CI)**
Yes	11	68.8	11	73.3	0.999	0.94 (0.60,1.47)
No	5	31.3	4	26.7		

MTA: Mineral trioxide aggregate; CI: Confidence interval; RR: Relative risk.

In the current research, more than 71% of patients responded positively to EPT after 18 months. Equivalent findings were observed in the studies of Arslan et al. (12) and El-Kateb et al. (10), where 50% and 77% of adult teeth respond favorably to EPT after 12 months of REP using MTA. In addition, Nageh et al.(14) reported that 60% of their patients treated with PRF restored tooth sensitivity after 12 months, and Youssef et al. (13) reported that 20% of the blood clot group and 50% in the PRF group restored sensibility. These differences might be because of the smaller sample size compared to the current study [10 patients in Youssef et al. (13)], as well as different regenerative technique (PRF) as used in Nageh et al.(14), and PRF with a blood clot as followed in Youssef et al. (13). However, the findings of the current investigation contradicted Saoud et al. (36), who showed a negative response to sensibility tests in adult teeth after a follow-up period of 26 months; however, that report was limited to seven teeth.

The current study showed that there was a significant drop in EPT readings, and the response to the sensibility test improved over time. This suggests that a more extended observation period may be necessary to assess sensibility in mature teeth after REPs. It also indicates that by time, there is a higher chance for the formation of more organized nerve-like tissue (10). In addition, the regenerated pulp-like tissue may have an underdeveloped nervous system, which could cause a delayed positive response (37). This delayed sensitivity response can be attributed to the coronal plug material, making it difficult to immediately feel the necessary pulp-like tissue reaction (36). It is important to note that a negative pulp response does not necessarily mean that the tooth has lost its vitality; a positive response does not guarantee tissue regeneration (10). El-Kateb et al. (10) used MRI to find no difference in regenerated pulp tissue between treated and untreated mature teeth. Lei et al. (38) confirmed the regeneration of nervous tissue in an immature tooth treated with REPs.

The mechanism where the tooth is able to respond back to different stimuli is a matter of debate. One possible explanation is that the blood clot may induce nerve regeneration by providing endogenous growth factors (10). Another mechanism is that dental pulp stem cells from viable apical pulp tissue may survive even in the presence of periradicular lesion (39). These stem cells can initiate axon guidance and develop into neuronal cells (40). Another theory suggests that stimulation of periapical bleeding may cause periodontal ligament , or bone marrow mesenchymal stem cells, to develop into stem cells. Nerve ingrowth in the pulp canal may lead to collateral reinnervation (38).

This study has limitations. Maxillary and mandibular incisors with single canals were only included in this study. Further studies are needed with that include other teeth types with extended follow-ups.

CONCLUSION

Under the conditions of this study, regenerative treatment using the blood clot technique with MTA and Biodentine significantly resolved patients' symptoms and periapical lesions and restored teeth sensibility. It could be considered a suitable treatment for mature permanent teeth with pulp necrosis and apical periodontitis.

Disclosures

Ethics Committee Approval: The study was approved by the Faculty of Dentistry Cairo University Research Ethics Committee (no: 19759, date: 28/07/2019).

Authorship Contributions: Concept – A.H.A.R., S.M.I.; Design – A.H.A.R., S.M.I.; Supervision – S.M.I., F.M.A.N.; Data collection and/or processing – A.H.A.R., F.M.A.N.; Data analysis and/or interpretation – A.H.A.R., F.M.A.N.; Literature search – A.H.A.R.; Writing – A.H.A.R.; Critical review – A.H.A.R., S.M.I., F.M.A.N.

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