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EVALUATION OF PULPAL RESPONSE TO ENDOSEQUENCE ROOT REPAIR VERSUS BIODENTINE AFTER PULPOTOMY IN PRIMARY TEETH OF PUPPIES

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ABSTRACT

Background: Bioceramics are widely used as vital pulp therapy biomaterials given their excellent biocompatible and antibacterial properties.

Aim: the aim of the study was to evaluate the characteristics of the remaining pulp tissue after Endosequence root repair versus Biodentine pulpotomy in puppies' primary molars and canines.

Material and Methods: Twenty-four primary molars and canines in 4 mongrel puppies underwent total pulpotomy procedure using Endosequence root repair and Biodentine. After 4 weeks, areas beneath the pulpotomy sites were subjected to histologic examination and pulpal response evaluation in terms of: inflammatory cell response, tissue disorganization, and hard tissue formation. Mann Whitney test was used for ordinal response variables, to compare between the two groups.

Results: No statistically significant difference was detected between both groups regarding all pulpal response parameters

Conclusions: Both Biodentine and Endosequence root repair presented biocompatibility allowing for preserved pulp vitality and the formation of hard tissue barrier in primary teeth of puppies.

KEYWORDS: Vital pulp therapy, Inflammatory cell response, Hard tissue formation

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INTRODUCTION

Vital pulp therapy is always concerned by maintaining the pulp vitality by protecting the exposed pulp with biocompatible materials [1]. These materials should possess adequate biocompatibility and bioactivity to promote dental pulp stem cells activity and pulp healing [2]. For several decades, mineral trioxide aggregate (MTA) has been considered as the material of choice for pulp vitality conservation. It is widely used for pulp capping and endodontic treatment and is proved high success rates on the short and the long terms [3-5] whether in experimental, clinical, radiographic, or histologic studies with antimicrobial potential, dentine bridge formation [3, 4, 6, 7] and high sealing ability [8-10]. Nevertheless, due to its longer setting time [11], difficult handling characteristics [12] and essential hydration during setting [13], there was an urge for developing new materials with similar ability for dentine bridge formation and sealing effect but with easier handling, faster setting and better physical properties.-

Biodentine is a tricalcium silicate–based restorative cement which is considered a bioceramic material of the second generation. It emerged as an alternative to overcome these drawbacks. It showed better physical properties, higher viscosity, better handling, shorter setting time and reduced staining potential [14, 15]. As a dentin substitute in restorative procedures, it provided good marginal sealing by adhering to both dentin and enamel [15, 16]. It proved efficiency in producing hard tissue bridge in experimental and clinical studies [6, 14, 17, 18]. Whilst it is compatible to dental pulp cells and could stimulate the deposition of hydroxyapatite on its surface when exposed to tissue fluids [6, 13, 19]. Still, the literature is rich with ongoing research on other MTA-like materials and comparable results were achieved with Angelus MTA, Bioaggregate, Micromega-MTA, and Retro-MTA [20].

A promising endodontic material was introduced recently. It is known as Endosequence root repair (ERRM; Brasseler, Savannah, GA) which is a bioactive material used in root repair and as a surgical retrofilling material. ERRM is a premixed putty that has been developed and used in pulp therapy [21]. The manufacturer markets the material as having better consistency, easier handling and quicker application. It is claimed to set in the presence of moisture present in the dentinal tubules. ERRM showed comparable results to ProRoot MTA as both resulted in proliferation of dental pulp cells [22] which could make it a suitable material for pulpotomy in primary teeth [21].

Despite the increase in their use in vital pulp therapy, to the best of our knowledge, there is no sufficient information in the literature about inflammatory cell response to Endosequence root repair after applying directly onto the pulp. Therefore, the aim of our study was to evaluate qualitatively and quantitatively the characteristics of the remaining pulp tissue in terms of inflammatory cell response, tissue disorganization, and calcific barrier formation after Endosequence root repair versus Biodentine pulpotomy in puppies' primary molars and canines. The null hypothesis was that there would be no difference between both groups.

MATERIALS AND METHODS

This experimental animal study was conducted after approval of by the Research Ethics Committee, Pharos University in Alexandria (#PUA0220235283105) consistent with the ethical guidelines and regulations of the Animal Research Ethics Committee and in accordance to ARRIVE guidelines [23]. According to the data collected from a pilot study, the required sample size for creating a statistically meaningful outcome was 11 teeth per group. It was calculated based on 80% power and 0.05 significance level using GPower 3.1. software. To compensate for processing errors, the sample size was boosted to 12 teeth per group to a total sample size of 24 teeth.

TABLE (1) The materials' composition.

Product	Composition	Company
EndoSequence Root Repair Material-Fast Set Putty	**(Premixed-syringe):** Tricalcium silicate, Dicalcium silicate, Tantalum pentoxide, Zirconium oxide, Proprietary fillers, Thickening agents	Brasseler USA, Savannah, GA, USA
Biodentine	**Powder:** Tricalcium Silicate (Ca_3SiO_5), Dicalcium Silicate (Ca_2SiO_4), Calcium Carbonate ($CaCO_3$), Iron Oxide (Fe_2O_3), and Zirconium Oxide (ZrO_2). **Liquid:** Water (H_2O) with Calcium chloride ($CaCl_2$) and soluble polymer (polycarboxylate).	Septodont, St. Maurdes- Fosses, France

Twenty-four primary molars and canines of 4 Mongrel puppies aging 6-8 weeks weighing 2-4 kg were included in the study and were randomly assigned to one of the 2 study groups according to the material used for pulpotomy: Endosequence root repair and Biodentine. (Table 1) Randomization was achieved by a computerized random sequence generator.

Pulpotomy procedures were performed under general anesthesia using intramuscular xylazine (1 mg/kg; Rompun, Bayer) and ketamine hydrochloride (5 mg/kg; Ketaset, Fort Dodge). The puppies were intubated and 1 L/min 1%–2% isoflurane in oxygen was used as an inhalational anesthetic throughout the procedure. Enrofloxacin (5 mg/kg) was given just before and after the procedure followed by intraoral amoxicillin clavulanate (12.5 mg/kg) for 5 days postoperatively to avoid infection.

One skilled operator performed all dental procedures in the following manner: teeth prophylaxis; rubber dental dam isolation; disinfection of the operative field with 0.2% chlorhexidine gluconate mouth wash; access to the pulp chamber followed by complete deroofing under copious irrigation using a high-speed handpiece and a round bur; full coronal pulp tissue amputation by a sharp and sterile spoon excavator; bleeding stoppage using a dampened cotton pellet with saline; application of the pulpotomy material of choice onto the remaining radicular pulp tissue at the amputation site following the manufacturer's instructions as follows: for Endosequence Root Repair, smoothly extruding small amount of material from the pre-mixed syringe; placing the material into the pulp chamber and compressing it using a sterile plastic instrument; removing excess material with a spoon excavator or disposable microbrush; allowing for setting of 20 minutes dependent upon the presence of moisture in the dentin. While for Biodentine, the capsule is mixed; directly placed on the pulp; allowed for setting of 12 minutes. Both groups were sealed and restored with light cured resin-reinforced glass ionomer filling (Ketac Molar, 3 M ESPE, St Paul, MN, USA); occlusal adjustment.

Adequate measures were considered to minimize pain or discomfort to the experimental puppies. Postoperatively, all puppies were kept at the animal house of the Medical Research Institute where they received soft diet along with intramuscular ketoprofen (2.0 mg/kg once daily) for analgesia for at least 2 days.

After 4 weeks, the 4 puppies were put down with an overdose of pentobarbital sodium solution followed by dissecting and sectioning of their maxillae and mandibles. Treated teeth and their surrounding tissues were prepared as block sections and were fixed in 10% buffered formalin for 48 hours; specimens were washed in running water to

remove formalin; specimens were decalcified in 5% trichloroacetic acid for 8 days [24]; sections were then embedded in paraffin. Sagittal serial sectioning (5 µm thickness) in a mesio-distal direction parallel to the long axes of teeth was performed. The sections were deparaffinized and stained with hematoxylin and eosin (H&E) for histologic analysis. Histologic examination was done with optical light microscopy (Opti 10 Lab, Ray Wild Limited Company, Germany) to evaluate the characteristics of the remaining radicular pulp tissue, inflammatory cell response and presence/absence of hard tissue formation. Images were captured with a charge-coupled device digital camera (TCA-5.0 Color, Ray Wild Limited Company, Germany) coupled with a computer system.

TABLE (2). Scoring system for histological sections [25]

Inflammatory cell response	
Score 0	None or a few inflammatory cells beneath the exposure site
Score 1	Mild inflammatory cells, such as mono- or polymorphonuclear leukocytes beneath the exposure site
Score 2	Moderate inflammatory cell infiltration involving the third coronal radicular pulp
Score 3	Severe inflammatory cell infiltration involving the third coronal or more radicular pulp
Tissue disorganization	
Score 0	Normal tissues beneath the pulpotomy site
Score 1	Lack of normal tissue pattern beneath the pulpotomy site, but a normal deep pulp tissue pattern
Score 2	General disorganization of the pulp tissue pattern
Score 3	Pulp necrosis
Hard tissue formation	
Score 0	No hard tissue formation
Score 1	Slight incomplete hard tissue formation beneath the exposure site
Score 2	Thick hard tissue formation beneath the pulpotomy site considered as a complete calcification

Qualitative histological analysis was done and consisted of describing the features of the remaining radicular pulp tissue, inflammatory response, tissue disorganization and hard tissue formation. Quantitative analysis was performed by scoring all sections of histologic parameters according to the scoring criteria developed by Shayegan et al [25] as described in table 2. Both qualitative and quantitative analyses were carried out by 2 experienced examiners who were blinded to the material used. If any inconsistency in scoring was detected, examiners came to consensus on the score and a final score was determined that was agreed upon by both examiners.

Analysis of statistics was carried out using SPSS software package version 20.0. (Armonk, NY: IBM Corp). Mann Whitney test was used for ordinal response variables, to compare between both groups. Significance of the obtained results was judged at the 5% level.

RESULTS

Twenty-four primary molars and canines in 4 puppies underwent pulpotomy procedures and the areas beneath the pulpotomy sites were subjected to histologic examination and evaluation. (Table 3, Figure 1)

Regarding inflammatory cell response: all 12 teeth of both groups showed no or mild inflammatory cells. The difference was not significant between both groups. ($p = 0.755$)

Regarding Tissue disorganization: for ERRM group, 10 teeth showed normal tissue beneath the pulpotomy site while 2 teeth showed lack of normal tissue pattern beneath the pulpotomy site, but a normal deep pattern of pulp tissue. Eight teeth of Biodentine group showed normal tissue beneath the pulpotomy site while 4 teeth showed lack of normal tissue pattern beneath the pulpotomy site while sustaining a normal deep pulpal tissue pattern. There was no statistical difference between both groups. ($p = 0.514$)

Regarding hard tissue formation: All teeth showed hard tissue formation beneath the pulpotomy site in both groups. Completely calcified, thick hard tissue was evident in 11 teeth of ERRM group and in 8 teeth of Biodentine group. There was no statistical difference between both groups. ($p = 0.319$)

TABLE (3) Comparison of scores between both materials

		Endosequence root repair (n = 12)		Biodentine (n = 12)		p
		No.	%	No.	%	
Inflammatory cell response	Score 0	10	83.3	9	75.0	0.755
	Score 1	2	16.7	3	25.0	
	Score 2	0	0.0	0	0.0	
	Score 3	0	0.0	0	0.0	
Tissue disorganization	Score 0	10	83.3	8	66.7	0.514
	Score 1	2	16.7	4	33.3	
	Score 2	0	0.0	0	0.0	
	Score 3	0	0.0	0	0.0	
Hard tissue formation	Score 0	0	0.0	0	0.0	0.319
	Score 1	1	8.3	4	33.3	
	Score 2	11	91.7	8	66.7	

U: Mann Whitney test ***p: p value for comparing between the two groups*** ****: Statistically significant at p ≤ 0.05***

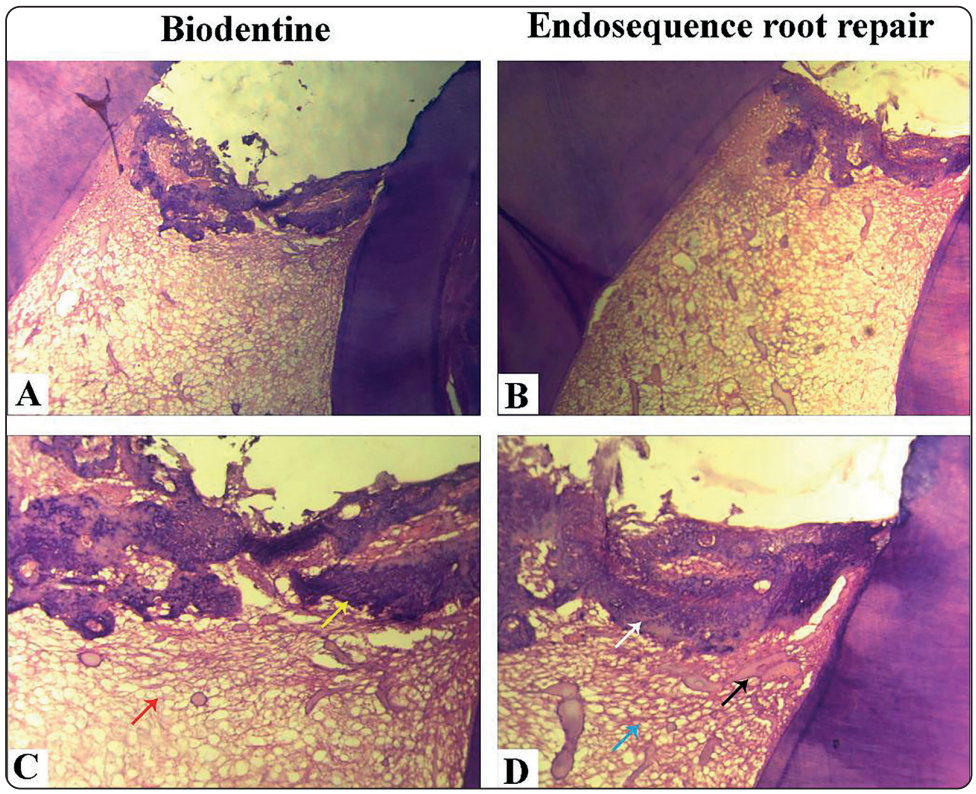

Fig. (1) Hematoxylin-eosin staining for histologic evaluation of the area beneath the pulpotomy site. Biodentine group (A&C); A: Represents newly formed calcified tissue occupying large area of the regenerating pulp tissue with rich blood supply (H&E stain x100). C: Represents normal pulpal architecture pattern with small to medium sized blood vessels and with no inflammatory cell infiltration is seen (Inflammatory cell response & Tissue disorganization: score 0) (red arrow). Newly formed tertiary dentine is noticed (Hard tissue formation: score 2) (yellow arrow) (H&E stain x400). ERRM group (B&D); B: Newly formed calcified tissue is noticed with mineralization foci and with a regular odontoblast layer seen in the relatively normal pulp tissue underneath (H&E X100). D: Higher magnification of newly formed dentin bridge (Hard tissue formation: score 2) (white arrow) with normal organization of the pulp (Tissue disorganization: score 0) (blue arrow). Fibrous tissue with high vascularity is also apparent (Inflammatory cell response: score 0) (black arrow) (H&E X400).

DISCUSSION

Success of vital pulp therapy is dependent on multiple factors among which are the sealing capacity of the material, its antimicrobial potential and its biocompatibility. Whilst all pulpotomy materials may be initially irritant to the pulp leading to an inflammatory reaction, the shorter the inflammatory period, the faster the healing process takes place [26]. This explains the importance of studying the pulp behaviour in response to variable materials.

The present study evaluated the histologic response of the persisting pulp tissue after applying Biodentine and ERRM as pulpotomy biomaterials in primary puppy molars and canines. Both Biodentine and ERRM showed favourable pulpal response represented by sparse inflammatory cell infiltration, persistence of normal pulpal tissue organization either right beneath the pulpotomy site or at a deeper level within the pulp along with hard tissue formation. Such findings support their use as pulpotomy materials over the primary pulp and were in harmony with the findings of Tomas Catala et al. who reported Biodentine to be a biocompatible material with the dental pulp [27]. Likewise, De Rossi et al. reported pulp compatibility and evidence of calcified tissue formation in 100% of pulpotomized teeth after Biodentine [14]. As well, Mahgoub et al. in their systematic review of literature concluded that ERRM was a biocompatible material that enhanced the human pulpal cells to proliferate and stimulate the formation of hard tissue [28].

Although our findings showed no statistically significant difference between both groups regarding all pulpal response parameters, ERRM showed better healing process than Biodentine. The results reported by Muruganandhan et al. confirmed that ERRM was significantly better than Biodentine regarding hard tissue formation and inflammatory response [29]. Another previous study reported similar patterns of hard tissue formation with ERRM pulpotomy [30]. Conversely, Parikh et al. in their clinical study reported different outcomes where the clinical performance of Biodentine was superior to ERRM after 12 months. However, their clinical trial differed from our study in more than one aspect since they tested the materials on permanent human teeth with deep caries and the procedure was direct pulp capping [31]. The dissimilarity in findings could be for the reason that the current study was conducted on primary pulps which are known to have different responses than permanent pulps to external stimuli [32].

The present data should be cautiously interpreted since only healthy pulps were included and procedures were done under controlled conditions with absence of bacterial invasion and pre-existing inflammation unlike real-life clinical situations. Moreover, another limitation of this study is that only histologic assessment was done disregarding clinical and radiographic assessments. Also, follow up was done after only one interval which was 4 weeks without considering the shorter- or longer-term periods on pulpal response.

The null hypothesis of the current study was not rejected where both Biodentine and ERRM showed comparable and favourable results regarding pulpal response to their use as pulpotomy biomaterials in primary teeth of puppies which was assessed in terms of inflammatory cell response, tissue disorganization and hard tissue formation.

CONCLUSION

Both Biodentine and ERRM presented biocompatibility allowing for preserved pulp vitality and the formation of hard tissue barrier in primary teeth of puppies. Further research is recommended to investigate the response of primary human pulp to ERRM.

LIST OF ABBREVIATIONS

ERRM: Endosequence root repair

MTA: Mineral trioxide aggregate

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