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Partial pulpotomy on caries-free teeth using enamel matrix derivative or calcium hydroxide: a randomized controlled trial

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Abstract

Kiatwateeratana T, Kintarak S, Piwat S, Chankanka O, Kamaolmatyakul S, Thearmontree A. Partial pulpotomy on caries-free teeth using enamel matrix derivative or calcium hydroxide: a randomized controlled trial. *International Endodontic Journal*, **42**, 584–592, 2009.

Aim To compare the effect of enamel matrix derivative (EMD) and calcium hydroxide [$Ca(OH)_2$] on exposed human pulp.

Methodology Fifteen pairs of human contralateral premolars were intentionally and partially pulpotomized. The exposed pulps were randomly capped with either EMDgel (Emdogain®) or a mix of $Ca(OH)_2$ and sterile water. The subjects recorded pain or discomfort during the first 10 days and were also interviewed and examined by a blinded examiner at 1 day, 2 weeks, 3 and 6 months post-operation. Periapical radiographs were taken prior to the operation, and 3 and 6 months post-operation. After 6 months, the teeth were extracted and processed for histological evaluation. The data were described and analysed using McNemar test and Kaplan–Meier survival analysis.

Results The EMDgel-treated teeth had significantly less tooth hypersensitivity than the $Ca(OH)_2$-treated teeth during the first 2 weeks ($P = 0.031$) but were not significantly different after 2 weeks ($P = 0.125$). No detectable periapical radiographic changes were observed in any teeth and radiographic evidence of dentine bridge formation from both groups were not significantly different during the follow-up periods ($P > 0.05$). Histological evaluation demonstrated that the $Ca(OH)_2$-treated teeth had less inflammation and more dentine bridge formation than those in the EMDgel-treated teeth.

Conclusions After 6 months, healthy pulps capped with $Ca(OH)_2$ had more favourable results than counterparts capped with EMDgel. However, similar clinical and radiographic results were seen in both groups.

Keywords: calcium hydroxide, Emdogain®, enamel matrix derivative, partial pulpotomy.

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Introduction

Vital pulp therapy aims to treat reversible pulpal injury which may involve pulpal exposure. The application of a protective dressing can protect the pulp from additional injury, thereby facilitating healing and repair (Tziafas *et al.* 2000). Exposed vital pulps can be treated by direct pulp capping or pulpotomy to preserve tooth vitality and function (Mass and Zilberman 1993). Direct pulp capping is indicated for small mechanical exposures in young permanent teeth with partially developed roots and should not be used for carious pulp exposure (Baume & Holz 1981, Mass & Zilberman 1993, Mejare & Cvek 1993). Pulpotomy, on the other hand, is treatment for an exposed pulp in a tooth with incomplete root formation. Partial pulpotomy is a vital

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pulp therapy in which only superficial pulp tissue at the exposure site is removed. This technique was suggested by Massler (1959).

Partial pulpotomy is more suitable than direct pulp capping because it removes infected or inflamed pulpal tissue that would increase the success rate of treatment (Baume & Holz 1981). In addition, when compared with coronal or complete pulpotomy, partial pulpotomy preserves cell-rich coronal pulp tissue and thus might enhance healing and continue physiologic dentine deposition. At present, this treatment is an alternative treatment for traumatized or cariously exposed pulp on young permanent teeth. Its success rate has been reported to be 93–94% in cariously exposed young permanent molars (Mass & Zilberman 1993, Mejare & Cvek 1993).

The dental pulp has the potential to heal after exposure. The potential to recover depends on several factors, for example, pulp status, preoperative and postoperative prevention of bacterial infection and the efficacy of treatment strategy (Murray *et al.* 2000, Tziafas *et al.* 2000). Currently, calcium hydroxide [$Ca(OH)_2$] shows favourable clinical and radiographic results because of high rates of dentine bridge formation (>80% of the treated teeth) and its antibacterial properties (Tziafas *et al.* 2000). However, some disadvantages of the $Ca(OH)_2$ include poor sealing ability, degrading over time and tunnel defects in the dentine bridge which makes it questionable for long-term success. Therefore, many new capping materials have been introduced such as mineral trioxide aggregate and bioactive molecules which include enamel matrix protein. (Rutherford *et al.* 1993, Nakashima 1994, Hammarstrom 1997, Koh *et al.* 1997, Torabinejad & Chivian 1999, Decup *et al.* 2000).

Enamel matrix proteins are known to play biological roles in the formation of dentine, acellular cementum and alveolar bone during tooth development (Hammarstrom 1997). Based on this concept, a porcine enamel matrix derivative (EMD) compound has been developed and reported to be able to activate the biosynthesis of periodontal tissues and alveolar bone in humans (Heijl *et al.* 1997, Pontoriero *et al.* 1999). The principle component of EMD is amelogenin that has an important role in dentine formation during dentinogenesis (Hammarstrom 1997, Veis *et al.* 2000).

Some studies performed on animal models have demonstrated that EMD, as the capping material, could induce better dentine-like tissue formation with no or less defects compared with $Ca(OH)_2$ (Nakamura *et al.* 2002, 2004). So far, there is only one published report on the effects of EMD on exposed human pulps with a follow-up period of 3 months (Olsson *et al.* 2005).

The aim of this study was to evaluate symptoms, radiographic changes and pulp tissue reactions in humans after the placing of EMDgel or $Ca(OH)_2$ on experimentally exposed pulp in premolar teeth as the capping materials on the partially pulpotomized teeth at the 6 months follow-up period.

Materials and methods

Fifteen pairs of contralateral maxillary first premolars from 15 healthy subjects aged 13–22 years (mean 18.6 ± 2.22 years) scheduled for orthodontic extraction at the Orthodontic clinic, Prince of Songkla University, Thailand, were included. All teeth were clinically and radiographically examined to ensure the absence of dental caries and periapical pathosis. Informed consent was obtained from the subjects or from the parents of the subjects below 18 years old. The study was approved by the Ethical Committee at the Faculty of Dentistry, Prince of Songkla University, Thailand. To ensure the quality of the data collection, blinding of both the subjects and examiner were done in every data collection procedure.

Operative procedures

After local anaesthesia with 2% lidocaine containing epinephrine 1 : 100 000 (Cook-waite, Abbot Laboratories, Wichita, KS, USA), the teeth were isolated with rubber dam and a cavity prepared on the occlusal surface with a cylindrical high-speed diamond bur (ISO size 016) under air–water spray until a small pulp exposure was created. A superficial pulp amputation approximately 2 mm apical from the small exposure area was performed by using a high-speed round diamond bur (ISO size 016) under air–water spray. The pulp wound was carefully irrigated with sterile saline solution to remove operative debris. The bleeding was then arrested by pressing moist sterile cotton pellets on the pulp wound for 1–2 min. Subsequently, the exposed pulp was dressed randomly with either a drop of Emdogain® gel (EMDgel, 30 mg mL^{-1} in propyleneglycol-alginate; BIORA AB, Malmo, Sweden) or a freshly prepared paste of sterile $Ca(OH)_2$ with sterile water on the pulp tissue under gentle pressure. Randomization was achieved by throwing a dye. After placing the capping materials, the cavity was covered in layers with intermediate restorative material (IRM®; Dentsply, Milford, DE, USA), then a resin-modified

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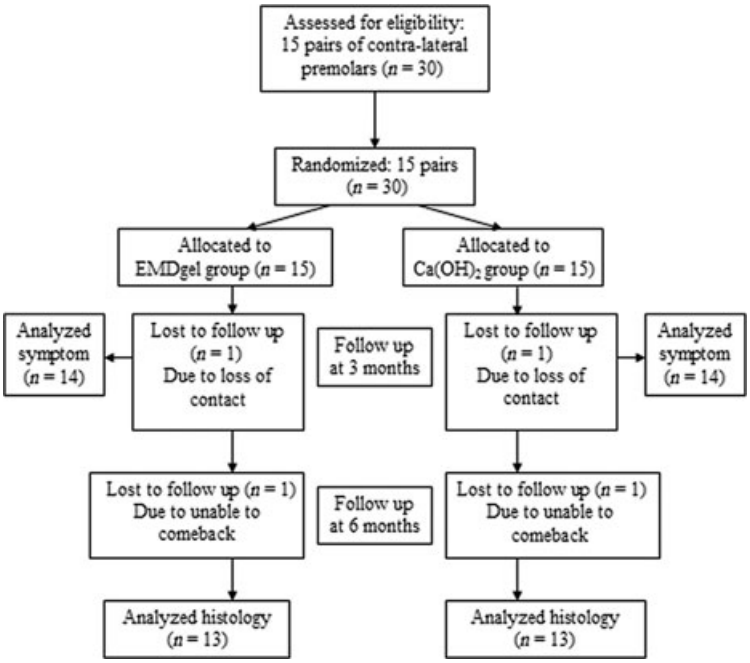

Figure 1 Participant flow.

glass–ionomer cement (Fuji II LC; GC Corp, Tokyo, Japan) and finally with glass–ionomer (Fuji IX GP; GC Corp) (Fig. 1). All treatments were completed by one operator.

Clinical examination

Every subject was given a 10-day diary and asked to record the use of analgesic drugs and pain or discomfort experienced after the operation. The visual analogue scale was used to record the pain. A 10-cm line marked with 'no pain' at the left end and 'unbearable pain' at the right end was given to the subject who was asked to respond the level of postoperative pain by marking on the line. Then, the distance from the 'no pain' end was measured. Each subject was interviewed via telephone 1 day after the operation and by face-to-face interview and examined at 2 weeks, 3 months and 6 months after the operation. The teeth were evaluated for abnormal signs (gingival swelling, abscess or fistula, pain on percussion, tooth mobility, restorative condition and vitality test) and symptoms (spontaneous pain, tooth hypersensitivity, pain with chewing, abscess or swelling and history of taking analgesics).

Radiographic examination

Radiographs were taken before the procedure and at 3 and 6 months post-operation by using the same X-ray machine (MAXIF1®, J. MORITA Corp, Kyoto, Japan). To control angle and the position of the cone, a silicone jig with a film holder and a posterior bite block were used. The teeth were examined for any pathosis and dentine bridge formation. All radiographs were evaluated by an operator who had been calibrated with an endodontist. The Cohen's Kappa was analysed to determine the inter-examiner agreement using presence or absence of the periapical radiolucency as the outcome variable. The Cohen's kappa coefficient was 0.83 showing very good agreement (Bawson & Trapp 2001).

Histological method

The teeth were extracted after 6 months under local anaesthesia. The root apices were cut off approximately 2 mm to facilitate fixation. All teeth were fixed with 10% neutral buffered formalin for 3 days, then demineralized in 12.5% ethylenediaminetetraacetic acid solution (EDTA, pH 7.01) for 75–120 days and subsequently embedded in paraffin. Serial sections of 5-μm thick were made in the buccolingual direction. Three representative slides were stained with haematoxylin and eosin. They were chosen from the three areas of the pulp wound: the wound edge, the centre, and between wound edge and the centre. One selected slide was stained with Brown and Brenn technique for bacterial assessment. Sections of carious tooth were used as a positive control for staining bacteria.

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Statistical analysis

The McNemar test was used to assess the difference in clinical signs, and radiographic changes between the two groups. Kaplan–Meier survival analysis was used to calculate and test the survival time of the two groups. All the analysis was tested at 95% level of confidence. The histological characteristics were analysed descriptively.

Results

The initial teeth for the study were 15 pairs. However, at the end of the follow-up period, two subjects (two pairs of teeth) could not be contacted, leaving a total of 13 pairs of teeth (Fig. 1).

Clinical signs and symptoms

The data from the 10-day self-assessment diaries showed that the $Ca(OH)_2$-treated teeth presented more frequent pain or discomfort than those in the EMDgel-treated teeth. The severities of pain for both groups ranged from 0.1 to 2.95. Duration of pain or discomfort was 1–2 s and no persistent pain as well as no analgesic use was reported.

During the 6-month follow-up period, only two postoperative symptoms which included tooth hypersensitivity and transient spontaneous pain (1–2 s) were reported. All teeth were free from abnormal signs and were positive to vitality test.

The results of postoperative pain and tooth hypersensitivity are shown in Table 1. The EMDgel-treated teeth had significantly less hypersensitivity than the $Ca(OH)_2$-treated teeth in the first 2 weeks ($P = 0.031$). Transient spontaneous pain was not significantly different between the two groups.

Table 2 shows the distribution of teeth that presented postoperative pain or hypersensitivity at different observation times. The number of $Ca(OH)_2$-treated teeth with postoperative pain or hypersensitivity was higher than that of the EMDgel-treated teeth at all periods. In the $Ca(OH)_2$-treated group, the postoperative pain or hypersensitivity occurred continuously, more severely and increased with time. These symptoms were reported most frequently at 2 weeks after the operation. However, the highest severity of symptoms presented at 3 months and slightly subsided at 6 months. The severity of these symptoms in the $Ca(OH)_2$-treated group was higher than that of the EMDgel-treated group. In contrast, these postoperative symptoms of the EMDgel-treated teeth showed no pattern and less severity than those of the $Ca(OH)_2$-treated teeth.

The survival analysis indicated that time without tooth hypersensitivity in the EMDgel-treated teeth was significantly longer than that in the $Ca(OH)_2$-treated teeth ($P = 0.046$). Half of the teeth in the EMDgel-treated group were free from hypersensitivity at 82 days post-operation, whereas half of the teeth in the $Ca(OH)_2$-treated group were free from hypersensitivity for only 14 days. However, time without postoperative spontaneous pain was not different between the two groups.

Radiographic findings

There were no periapical and periodontal changes suggestive of pathosis, pulp obliteration, and external and internal root resorption in any of the radiographs. Radiographic evidences of dentine bridge formation from two contra laterally $Ca(OH)_2$- and EMDgel-treated teeth within the same subject were not significantly different at the 3 and 6 month periods. Figure 2 shows radiographs taken at 6 months suggesting the presence of dentine bridges under the capping material of the individual pair of teeth.

Table 1 Number of teeth (%) presenting postoperative transient spontaneous pain and hypersensitivity in both two groups at 2 weeks, 3 months and 6 months

	Hypersensitivity			Transient spontaneous pain		
Follow-up time (*n*)	EMD *n* (%)	$Ca(OH)_2$ *n* (%)	*P*-value[a]	EMD *n* (%)	$Ca(OH)_2$ *n* (%)	*P*-value[a]
2 weeks (15)	6 (40.00)	13 (86.67)	0.031	2 (3.33)	3 (20.00)	1.00
3 months (14)	6 (42.86)	10 (71.43)	0.125	2 (14.28)	2 (14.28)	1.00
6 months (13)	4 (30.77)	9 (69.23)	0.125	0	0	1.00

EMD, enamel matrix derivative.
[a]McNemar test.

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Table 2 Postoperative spontaneous pain and tooth hypersensitivity of each tooth according to the follow-up time in the two groups

Follow-up time													
Subject no.	day 1	day 2	day 3	day 4	day 5	day 6	day 7	day 8	day 9	day 10	2 weeks	3 months	6 months
EMDgel													
1												*	
2											†	†	
3							*						
4													
5											*	†	
6							*	*			*	*	
7													
8								*	*		*		
9													
10													*
11												*	*
12									*	*	*	*	*
13			*								*	†	†
14				*	*								‡
Mean of severity	0	0	0.4	0.27	0.3	0	0.92	1.5	1.97	1	2.16	3.14	2.5
Total	0	0	1	1	1	0	2	2	2	1	6	7	4
Calcium hydroxide													
1											*	*	
2											*	†	
3											*		
4												†	†
5											*	†	
6							*	*	*		*	*	
7											*		*
8						*	*				*	*	†
9	*	*	*	*	*	*	*	*	*	*	*	*	*
10													*
11											*	†	†
12									*	*	*	*	*
13			*	*	*	*		*			*	†	†
14	*			*	*	*		*	*	*	†	†	‡
Mean of severity	1.2	0.25	0.6	1.16	0.8	0.82	1.21	1.46	1.17	1.08	2.8	3.82	3.75
Total	2	1	2	3	3	4	3	4	4	3	12	11	8

*, mild symptom (score ≤ 3); †, moderate symptom (score ≤ 6); ‡, lost to follow up.

Histological findings

Areas of pulp tissue response in both groups were limited in the exposed areas and were not extended over one-third of the coronal pulp. There was no evidence of bacterial infiltration in any of the specimens.

In exposed areas, 10 of 13 $Ca(OH)_2$-treated teeth exhibited complete dentine bridge formation with normal pulpal tissue or a minimal inflammatory tissue response (Fig. 3). The remaining teeth had incomplete dentine bridge formation with mild to moderate pulpal tissue response.

Persistent pulpal tissue responses, such as dense infiltration of chronic inflammatory cells, congested blood vessels and extravasated erythrocytes, were shown in all EMDgel-treated teeth. No evidence of complete dentine bridge formation was observed in this group. However, few calcified tissues could be seen scattering near the underlying vital pulpal tissue (Fig. 4) in 5 of 13 teeth.

Association between clinical, radiographic and histological evaluations

As shown in Table 3, all teeth in both groups exhibited poor correlation between clinical symptom and radiographic and histological appearances. Nevertheless, there was an association between incomplete dentine bridge formation and pulpal tissue responses in the

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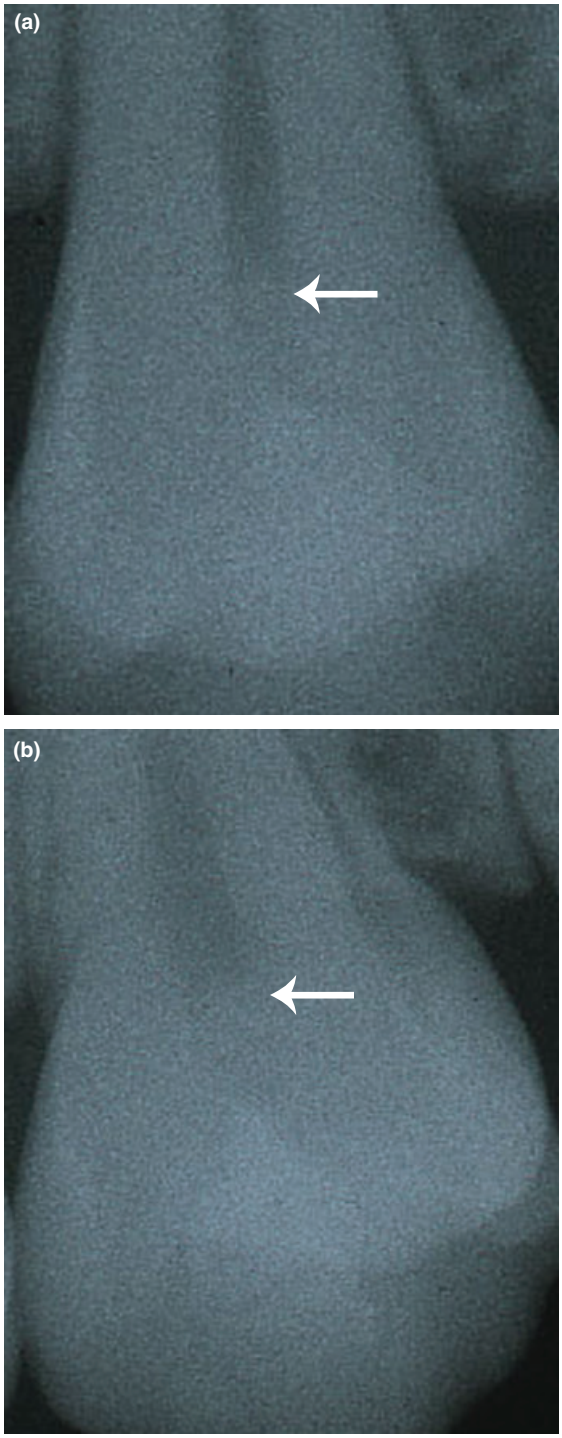

Figure 2 Radiographs taken at 6 months suggesting the presence of dentin bridge (arrow) under the capping material in $Ca(OH)_2$-treated tooth (a) and EMDgel-treated tooth (b).

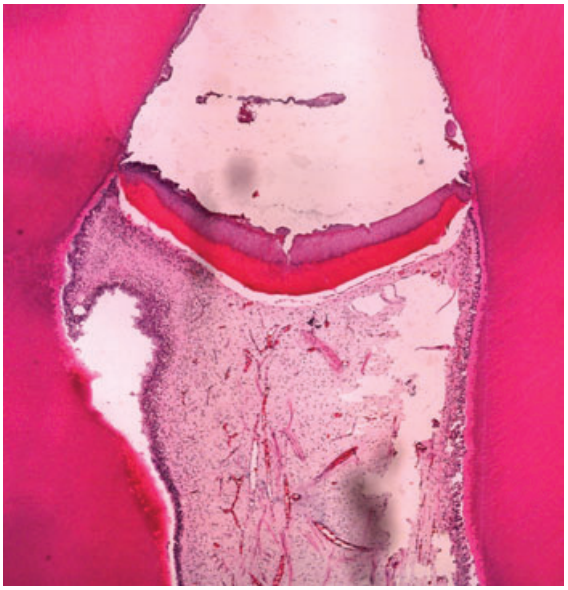

Figure 3 Photomicrograph of a premolar at 6 months after treatment with calcium hydroxide showing a complete dentin bridge formation with normal underlying pulpal tissue (haematoxylin–eosin stain, original magnification 40×).

$Ca(OH)_2$-treated group. All teeth in this group with incomplete dentine bridge formation showed signs of pulpal tissue response.

Discussion

At the present, $Ca(OH)_2$ is still the material of choice for pulp capping. Its use on the exposed pulp can induce a reparative dentinogenic response leading to dentine bridge formation. However, $Ca(OH)_2$ may not be an ideal capping material because there were discontinuities, so-called 'tunnel defects' in dentine bridge formation (Cox *et al.* 1996). The presence of tunnel defects could impair the properties of the bridge as a permeability barrier. Therefore, many bioactive pulp capping agents including EMD have been developed. In animal studies, EMD was shown to induce pulpal wound healing and dentine bridge formation in pulpotomized teeth (Igarashi *et al.* 2003, Nakamura *et al.* 2004). This study investigated the effects of EMD on experimentally exposed pulp tissue of human premolar teeth.

All teeth included in this study were free from caries and were scheduled for extraction for orthodontic purposes. Therefore, it is difficult to compare the results of this study with those using cariously exposed teeth.

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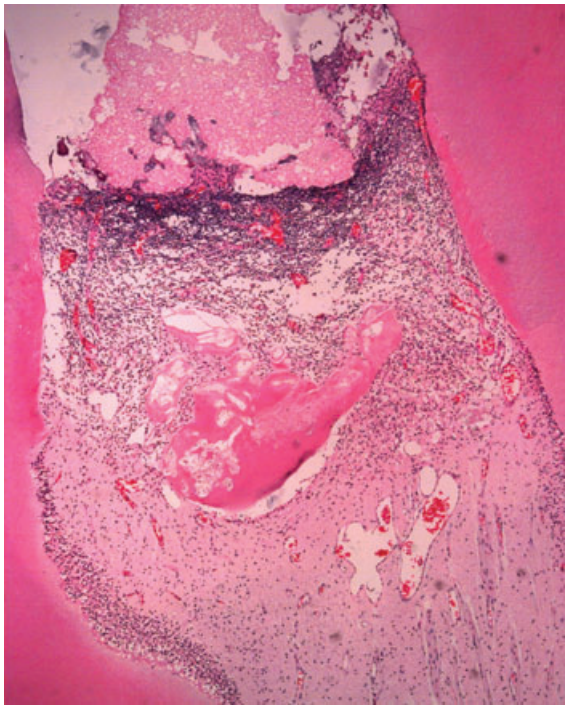

Figure 4 Photomicrograph of a premolar at 6 months after treatment with Emdogain® (Biora AB) gel showing a thick zone of chronic inflammatory pulpal response at the exposed area with few calcified masses formation near the underlying vital pulp (haematoxylin–eosin stain, original magnification 40×).

Data on postoperative pain and tooth hypersensitivity are subjective and difficult to compare between subjects. To eliminate this problem, a split mouth technique and visual analogue scale were used to compare contralateral teeth of the same subject. In addition, the double-blinded technique and only one examiner were used to control the quality of data collection.

This study showed that the EMDgel-treated teeth exhibited less postoperative hypersensitivity than the $Ca(OH)_2$-treated teeth, especially in the first 2 weeks. However, there was no significant difference after 2 weeks. Hypersensitivity in the $Ca(OH)_2$-treated teeth may be because of pulpal irritation from the pressure of placing the $Ca(OH)_2$ paste on the pulpal wound, or from alkalinity of the $Ca(OH)_2$ itself (Schroder & Granath 1971). In contrast, EMD is a mild acid and is prepared in a gel form. Pressure of applying the gel and pulp irritation may be slight. This tooth hypersensitivity is not considered to be a sign of treatment failure; in contrast, it may be a protective response of the pulp tissue to trauma (Mjor 2002).

Radiographic findings did not reveal a statistical difference in dentine bridge formation between the two groups. It is known that evaluation of dentine bridge formation from radiographs is difficult because of the overlapping of the objects on the image. It is concluded that radiographic evaluation alone cannot be used to determine the formation of dentine barrier.

Table 3 Clinical symptom, presence of radiographic and histological dentine bridge formation, and pulp tissue response from each tooth at 6 months post-operation

	EMDgel-treated teeth				Calcium hydroxide-treated teeth			
Subject no.	Clinical symptom	Dentine bridge (X-ray)	Dentine bridge (histology)	Pulp response	Clinical symptom	Dentine bridge (X-ray)	Dentine bridge (histology)	Pulp response
1	–	?	–	+	–	?	C	–
2	–	?	–	+	–	?	C	–
3	–	–	–	+	–	?	C	–
4	–	–	–	+	++	?	I	+
5	–	?	–	+	–	?	C	–
6	–	?	–	+	–	?	I	+
7	–	–	–	+	+	–	I	+
8	–	?	–	+	++	–	C	–
9	–	?	–	+	+	?	C	+
10	+	?	–	+	+	–	C	+
11	+	–	–	+	++	–	C	–
12	+	–	–	+	+	?	C	–
13	++	?	–	+	++	?	C	–

Clinical symptom: –, no symptom; +, mild symptom; ++, moderate symptom.
Dentine bridge (X-ray): –, no dentine bridge formation; ?, questionable dentine bridge formation.
Dentine bridge (histology): –, no dentine bridge formation; C, complete dentine bridge formation; I, incomplete dentine bridge formation.
Pulp response: –, no; +, yes.

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Calcium hydroxide-treated teeth had favourable histological results by showing more complete hard tissue bridge formation with subjacent normal pulpal tissue than the EMDgel-treated teeth. In contrast to the $Ca(OH)_2$-treated teeth, the pulpal tissue responses with chronic inflammatory cell infiltration was observed in all EMDgel-treated teeth after 6 months. The possible explanation for the persistence of inflammatory pulpal responses in the EMDgel-treated teeth may be that the pulpal tissue was contacted with IRM® (Dentsply). The major component of IRM® (Dentsply) is zinc oxide eugenol. It has been shown that exposed pulps capped with zinc oxide eugenol showed persistent chronic inflammation interfering the pulpal healing process (Zander & Glass 2005). The possible factors that promoted pulpal tissue to contact with the IRM® (Dentsply) were: (i) the gel form of EMD is not stable and does not adhere well to the dentinal wall; (ii) the effect of increased intrapulpal pressure during the inflammatory process; (iii) the pressure from insertion of the filling materials; and (iv) pulpal proliferation because of the proliferating effect of the EMD (Lyngstadaas *et al.* 2001).

A previous study by Olsson *et al.* (2005) had a similar study design except they followed their subjects for only 3 months and used a Teflon disc between the EMD and restorative material. Teflon is an inert material which prevents pulp tissue contacting other materials and the discs might eliminate or minimize pressure from material insertion. In that study, all EMDgel-treated teeth had hard tissue formation. However, pulpal inflammation was also observed in all EMDgel-treated teeth similar to this study. Therefore, the presence or absence of the Teflon disc may not be causal for this inflammation. In addition, two EMDgel-treated teeth showed abscess or extended lesions not localized only to the proliferated pulp tissue. In this study, all EMDgel-treated teeth had pulpal inflammatory responses in the wound area only. The pulpal inflammation should not be considered as a naturally protective response because it should not persist 6 months after treatment. The possible cause for the persistent inflammation may be due to the composition in the EMD. Further characterization of the EMD components and their role in pulp healing is needed.

At 6 months, most EMDgel-treated teeth were asymptomatic, despite the persistent inflammation demonstrated in the histological studies. This confirms the lack of a relationship between clinical symptoms and histological pulp tissue characteristics (Lundy & Stanley 1969, Taintor *et al.* 1981). Therefore, clinical formation alone cannot predict the histological success for vital pulp therapy.

Conclusions

Less frequent postoperative pain and hypersensitivity in the EMDgel-treated teeth did not correlate with the persistent chronic inflammatory response. EMDgel may not be an effective capping material for partial pulpotomy. Further investigations should be conducted over a longer follow-up period (>6 months) and on more stable vehicles of EMD as well as on other new materials for the most effective pulpal treatment.

Acknowledgement

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