Comparative evaluation of calcium silicate-based dentin substitute (Biodentine®) and calcium hydroxide (pulpdent) in the formation of reactive dentin bridge in regenerative pulpotomy of vital primary teeth: Triple blind, randomized clinical trial

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Abstract

Background: Considering the biological concerns of calcium hydroxide (CH) as a pulpotomy agent, an alternative silicate based dentin substitute i.e. Biodentine (Ca_3SiO_5) was evaluated clinically and radiographically. **Aims:** To evaluate the effectiveness of dentin substitute (Biodentine) in regenerative pulpotomy of vital primary teeth that would giv a biological base to its use in forming reactive dentin bridge and overcoming the drawbacks of calcium hydroxide. **Material and Methods:** Randomised clinical trial on 40 bilateral carious primary molars in 20 participant children (aged 5-10 years) was carried out by same operator using Ca_3SiO_5 (group-1) and CH (group-2) as vital pulpotomy agents. Blinded clinical and radiographic outcomes were observed at 3, 6 and 12 months interval. **Results:** Clinical outcomes of both protocols were analysed using Pearson's chi-square test applied at $P < 0.05$. Descriptive statistics were expressed as mean increase in dentin bridge formation in mms from two reference points in standardized radiographs using paired '*t*'- test at baseline and 12 months and found to be statistically significant ($P < 0.05$) in group-1 when compared with group-2. **Conclusion:** Group-1 revealed statistically favourable regenerative potential along with clinical success compared to group 2 thereby sharing both indications and mode of action with CH, but without its drawbacks of physical and clinical properties.

Keywords: Ca_3Sio_5 - based dentin substitute, calcium hydroxide, dentin bridge, primary molars, regenerative pulpotomy

Introduction

Vital pulp therapy refers to "a treatment which aims to preserve and maintain pulp tissue that has been compromised but not destroyed by caries, trauma, or restorative procedures in a healthy state."[1] The reformation of a protective dentinal bridge by tertiary dentinogenesis is a primary goal of vital pulp therapy. The objective is to stimulate the formation of reparative dentin and to retain the tooth as a functional unit. It may involve the transdentinal (indirect) or direct stimulation of tertiary dentin matrix formation in and by vital dental pulps.[2]

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Although a variety of materials have been suggested as pulpotomy agents, for regenerative pulpotomy technique the most frequently used materials are mineral trioxide aggregate (MTA), calcium hydroxide (CH), and Ca_3SiO_5. CH has been the gold standard for pulp therapy procedures, introduced by Herman *et al.* in 1936, as a biologic dressing and it was found to produce satisfactory results in indirect and direct pulp capping, because of its capacity to induce dentin.[3] However, CH may wound the primary tooth pulp due to its alkalinity leading to drawbacks of internal resorption, dystrophic calcification, and mechanical instability. CH loses its antibacterial capacity when it comes in contact with tissue fluid and is not a good material for sealing against bacterial penetration.

A quest for a new material with better qualities as dentin substitute led to the use of materials such as MTA and tricalcium silicate-based dentin substitute Several new

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calcium silicate-based materials have recently been developed aiming to improve some drawbacks of MTA such as its difficult handling property, long setting time, and potential for discoloration.[4] Biodentine™ (Septodont, Saint Maur des Fosse's, France) is among these materials and is claimed to be used as a dentine restorative material in addition to endodontic indications similar to those of MTA. Ca_3SiO_5-based dentine substitute has shown several advantages which include good sealing ability, adequate compressive strength and short setting time, providing a significant clinical advantage over other comparable materials.[5,6] It shares both its indications and mode of action with CH but does not have its drawbacks.[7]

The present *in-vivo* split mouth triple blind randomized clinical trial was therefore designed to evaluate clinically and radiographically the effectiveness of Ca_3SiO_5-based dentin substitute and compare it with CH in encouraging vital pulpal reaction and dentin bridge formation in vital primary teeth.

Materials and Methods

The present study was conducted at the Outpatient Department of Paediatric Dentistry, Punjab Government Dental College and Hospital, Amritsar, Punjab, India. Ethical clearance was obtained from the Ethical Committee of the Institute/University before the start of the study vide letter no. BFUHS/2K13/P-Th/8083 dated August 06, 2013.

A random screening of 1500 school children from different schools in the city of Amritsar, aged 5–10 years was carried out from September 2013 till October 2013. Thirty healthy individuals (19 boys and 11 girls) showing bilateral deep carious lesions fulfilling clinical inclusion criteria indicative of pulpotomy treatment in primary mandibular molars (D or E) were selected for future investigation to make the final selection [Figure 1].

Clinical evaluation for the vitality of pulp in the selected teeth showing a response to thermal pulp sensibility tests was carried out, and a preoperative standardized radiographic evaluation was done to study the extent of carious lesion. Finally, only those children were selected as study group whose parents/guardian gave written consent for being a part of the study. A power calculation indicated that we needed 15 teeth in each group to demonstrate the effect at 90% power of significance. The final convenience sample comprised forty teeth in twenty participant children (aged 5–10 years - weighted mean age of 7.1 years for males and 7.6 years for females) indicated for pulpotomy in bilateral primary molars and fulfilling the inclusion criteria was selected [Table 1].

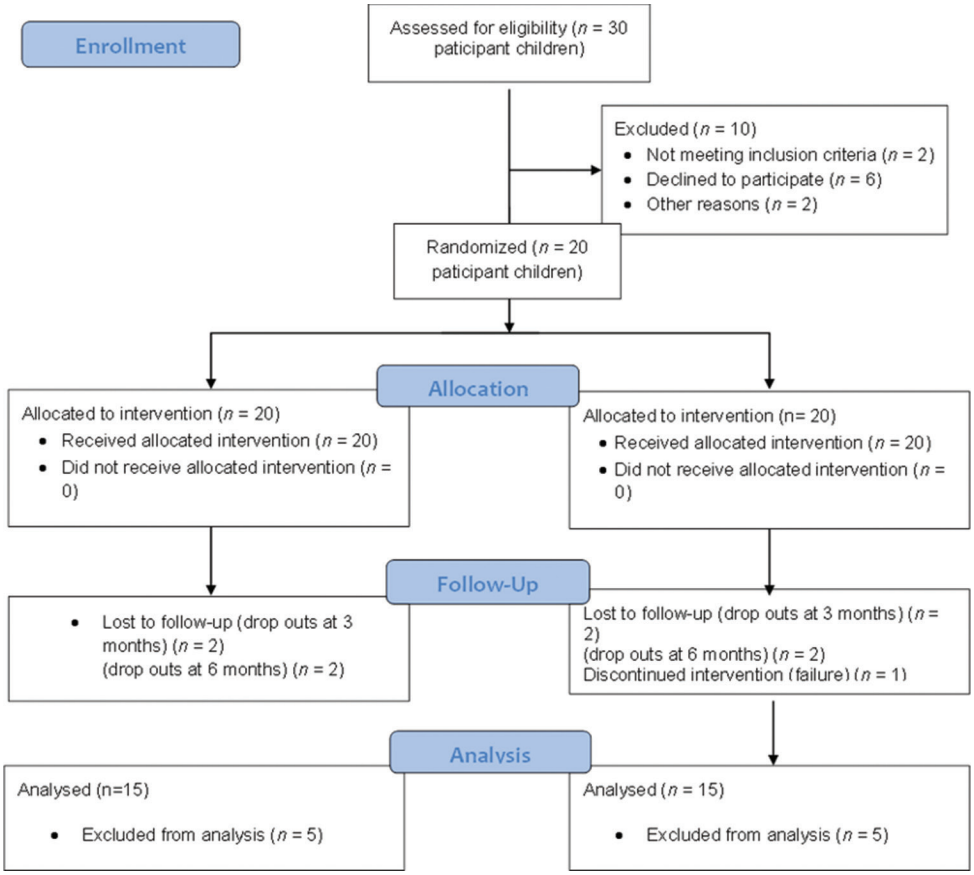

Figure 1: Flow diagram showing study sample selection to final analysis of the sample

Table 1: Distribution of teeth according to age and gender and type of pulp capping material

Capping material	Gender	Number of teeth (D/E)	Age (years)			*t*-test* (*P*)
			Minimum	Maximum	Mean±SD	
Biodentine (Group-1)	Male	13	6	9	7.115±2.102	0.626
	Female	7	6.5	9.5	7.643±3.055	
	Total	20	6	9.5	7.3±0.933	
$Ca(OH)_2$ (Group-2)	Male	13	6	9	7.115±2.012	0.626
	Female	7	6.5	9.5	7.643±3.055	
	Total	20	6	9.5	7.3±0.933	

**T*-test between males and females in each pulp-capping material group. SD: Standard deviation

Selection criteria

Bilaterally placed carious primary mandibular molars (D or E) with not more than one wall defect (buccal or lingual) and history of sensitivity to cold impulses and recent history of transient, sharp, lancinating, and momentary type of pain were selected for the study. Only those teeth where no previous treatment therapy was done such as restoration or secondary caries at the margins of the previous restoration were included. Restorable or nonrestorable deeply carious teeth with more than one wall defect and medically compromised subjects and teeth with a history of spontaneous pain or tenderness to percussion were excluded from the study. No clinical evidence of soft tissue pathology, mobility around or adjacent to the tooth in question was noted.

Radiographically, teeth fulfilling Ekstrand's criteria no. 4, i.e., presence of carious lesion radiolucency in pulpal one-third of the dentin and absence of radiographic signs of widened periodontal ligament space, any furcation/apical radiolucency, pathological internal or external root resorption, and absence of pulp canal obliteration were selected for the study. Physiological root resorption not more than one-third of the root length if present was considered in the radiographic inclusion criteria.

Twenty participant children with bilaterally placed carious molars indicated for pulpotomy were recruited for two study groups. Simple randomization, without any restriction of teeth indicated for pulpotomy in each participant children, was done through computer generated allocation ratio of 1:1. Thereby allocating equal number of teeth for both study groups bilaterally. Ca_3Si0_5-based dentin substitute vital pulpotomy procedure was carried out in twenty teeth (Group-1) and CH regenerative pulpotomy was carried out in 20 teeth on contralateral side (Group-2).

After ruling out any history of allergies to local anesthetic agents, all teeth were treated under local anesthesia and with rubber dam isolation. Straight line access with water-cooled high-speed handpiece was made for caries removal, and ablation of the coronal pulp was carried using round burs no. ½ and ¼ or spoon excavator. The entire cavity was flushed with sterile normal saline solution, and pulp hemostasis was achieved using a dry sterile cotton pellet applied for 2–3 min.

Procedure for mixing of Ca_3SiO_5-based dentin substitute: Group-1

Ca_3SiO_5-based dentin substitute in capsular form was used. Before the capsule was opened, it was tapped gently on a hard surface to diffuse the powder. Five drops of liquid from the single-dose dispenser were poured into the capsule, after which the latter was placed in a triturator for 30 s.

The material was then transferred with the aid of the manufacturer supplied spatula and placed inside the cavity with the aid of an amalgam carrier or spatula. To adjust it against the walls without excessive compression a plugger or sterile cotton pellet was used. The entire cavity was filled with Ca_3SiO_5 till the second appointment.

In the recall visit after 24–48 h, the following primary clinical outcomes were assessed:

The absence of spontaneous pain or pain on pressure/biting assessed on the basis of Universal Pain Assessment Tool of Visual Analogue Scale for pain on a scale of 1–10.

The absence of any inflammation or swelling was done by double-blind assessment of soft tissue by two different caliberated examiners.

Participant children fulfilling the above criteria were further given final restoration. Leaving half depth of the cavity with Ca_3SiO_5 material without any voids or lack of marginal adaptation checked under a surgical operating microscope, the final restoration was done with nanohybrid composite resin. The presence of intact marginal adaptation of composite restoration was checked under ×9 magnification and was assessed by double-blind examiners clinically soon after restoration. The values were noted as standard baseline values as per Cvar and Ryge criteria.[8]

Calcium hydroxide pulpotomy: Group-2

CH paste (Pulpdent) was gently applied with the help of disposabe tip topped by light cured CH, and the cavity was

restored with glass ionomer cement. In the recall visit after 24–48 h, after removing top layer of GIC up to half of cavity depth, teeth were restored with nanohybrid composite resin. The presence of intact marginal adaptation of composite was checked under 9x magnification and was assessed as per Cvar and Ryge criteria similar to that in Group-1 by double-blind examiners.

Follow-up

The clinical observations were followed up over a period of 3, 6, and 12 months whereas the radiographic outcomes were followed soon after the procedure and after 6 months and 12 months interval.

Standardization of the radiograph

To standardize the serial radiographs to be taken at 6 months and 12 months interval, the angulation of X-ray tube and head position of the participant children had to be kept constant. For this purpose, the endo-ray film holder (dentsply) was used to facilitate the use of paralleling technique and prevent distortion of radiographic images. Fixott-Everett lead grid with gradations (one gradation = 1 mm) was used with an added benefit of less stray radiations and increased resolution of the radiographic image.

Measurement of the image

Radiographs were scanned, and an increase in dentin thickness was measured through sequential imaging. Software named Digora® (Orion Corporation Soredex, Helsinki, Finland) was used for measurements by digitalizing the scanned image. To rule out the interpersonal variation in measurement, triple blind evaluation of the images was carried out by three different examiners at 95% confidence interval (CI). These examiners were first trained in measurement methodology and were calibrated by statistically analyzing their mean observations of ten different radiographs. The mean of computed value from the three measurements was taken as the final reading. Intraclass Correlation Coefficient (ICC) of different observers was computed at 95% CI. Cronbach's alpha test value between 0.9 and 1 indicated optimum interexaminer variability.

All the images were studied carefully for an increase in dentin thickness keeping the reference point constant from the furcation area (Point-B) [Figure 2]. Digital measurements of radiographic change in distance from reference Point-A (base of the material) and Point-B at baseline was done in mms and on postoperative radiographs [Figure 3a] at 6 months and 12 months interval [Figure 3b and c], thereby giving a measure of reactive dentin band increase.

Statistical analysis

Statistical analysis was performed with SPSS 20.0 software (Inc. Chicago, IL). Descriptive statistics were expressed as mean increase in dentin thickness in millimeters using paired *t*-test on digitalized scanned radiographic images using a PNG format at $P > 0.05$ - not significant, $P < 0.05$ - significant

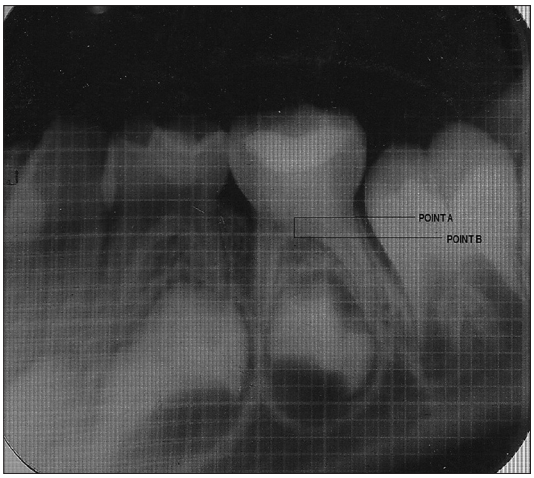

Figure 2: Reference points for measurements: Point-A (base of the material) to Point-B (furcation area)

up to 5% level, $P < 0.001$; highly significant up to <5% level. Coefficient of observer variability was checked by paired *t*-test, ANOVA, Interclass Correlation Coefficient (ICC) and Cronbach's alpha test. ICC of different observers was found to be 0.989 when computed at 95% CI. Cronbach's alpha test value of 0.989 indicated optimum interexaminer variability. Pearson's Chi-square test was applied at $P < 0.05$ or at 5% level of significance.

Results

A total of forty lower primary molars in twenty study subjects, aged 5–10 years (weighted mean age of 7.3 years) were treated with pulpotomy procedure where twenty teeth were randomly selected for pulpotomy procedure with Ca_3SiO_5-based dentin substitute (Group-1) and twenty teeth were selected for pulpotomy with CH (Group-2). Randomization was done using a computer-generated sequencing of teeth belonging to the left or right side of the patient by an independent observer. Clinical outcome was assessed at 3, 6, and 12 months interval whereas radiographic outcomes were assessed at 6 and 12 months.

Resolution of clinical signs and symptoms occurred in all except one case in Group-2 which reported back in 2 months with symptoms of pain without swelling and underwent conventional root canal treatment. This led to one failure in the CH group reducing the total sample size to 19 in Group-2. There were two dropouts within 3 months, who did not show up for treatment after resolution of initial signs and symptoms, bringing a fall in a number of teeth in both groups to a total of six with 17 teeth in each group. Further, at the 6 months follow-up visit, two cases in Group-1 and two cases in Group-2 did not report back and were considered as dropout cases, bringing the final sample size to 15 (15 teeth in each group). This fall in sample size due to drop-out cases showed no statistical differences in the results of a final sample size of 15.

There was a statistically significant increase in mean dentin thickness in Ca_3SiO_5-based dentin substitute group (Group-1) as compared to CH group (Group-2) at 12 months follow-up. Internal resorption was found to be present in two cases in Group-2 at 6 and 12 months follow-up and in none of the case in Group-1.

The mean change in distance between Point-A to Point-B in Group-1 showed an increase of 0.910 ± 0.319 from baseline to 12 months which was statistically significant (up to 5% level), concluding that there was greater deposition of tertiary dentin in Group-1 as compared to Group-2 (0.668 ± 0.259). The change in mean dentin thickness at any time interval in sequential images at 6 months and 12 months did not differ significantly in both groups ($P > 0.05$) but the difference in total increment from baseline to 12 months in Group-1 was more than Group-2, and this value was found to be statistically significant [Tables 2 and 3].

Internal resorption was found to be present in two cases in Group-2 at 6 and 12 months follow-up, but none of the cases in Group-1 showed any changes. However, in the present study, internal root resorption was not considered as a failure and the teeth were followed up once in every 3 months, since they were asymptomatic, similar to that stated by Smith *et al*. and Holan *et al*.[9,10]

Based on Cvar and Ryge criteria, 13.3% teeth showed slight marginal discoloration (Score-B) in both Group-1 and Group-2 at baseline whereas 14.4% teeth in Group-1, and 16.7% teeth in Group-2 showed marginal discoloration (Score-B) at 12 months follow-up [Tables 4 and 5]. 6.7% teeth in Group-1 and 13.3% teeth in Group-2 showed slight loss of contour (Score-B) at baseline and 9.3% teeth in Group-1, and 18% teeth in Group-2 showed slight loss of contour at 12 months follow-up. Slightly rough or pitted surface texture (Score-B) was noticed in 19% teeth in both Group-1 and Group-2 at 12 months. Marginal integrity was disrupted (Score-B) in 4% teeth in Group-1 and 2% teeth in Group-2 at baseline and 3% teeth showed disruption in marginal integrity at 12 months follow-up. Any rough or pitted surface texture and disruption in marginal integrity was corrected by polishing it with the help of composite polishing kit (Shofu). Although loss of marginal integrity, surface texture, and contour was noticed from baseline to 12 months follow-up, clinical findings did not affect the radiographic success indicating the selective importance of pulpotomy agent to be used instead of the type of restoration used.

Table 2: Average thickness of tertiary dentin at baseline, 6 and 12 months according to the pulp capping material

Pulp capping material	Follow-up duration (months)	
	6	12
Ca_3SiO_5		
n	15	15
Mean±SD (mm)	1.62±0.692	1.25±0.625
CH		
n	15	15
Mean±SD (mm)	1.53±0.587	1.29±0.578
t	0.549	−0.350
P	0.592^{NS}	0.732^{NS}

SD: Standard deviation; ^{NS}: Not significant; CH: Calcium hydroxide

Discussion

In the present study, only lower primary molars were selected to ensure that radiographic evidence of all pathology would be detected without overlapping of underlying permanent teeth. Since the selected teeth were only those with not more than one walled defect the final restorations were a

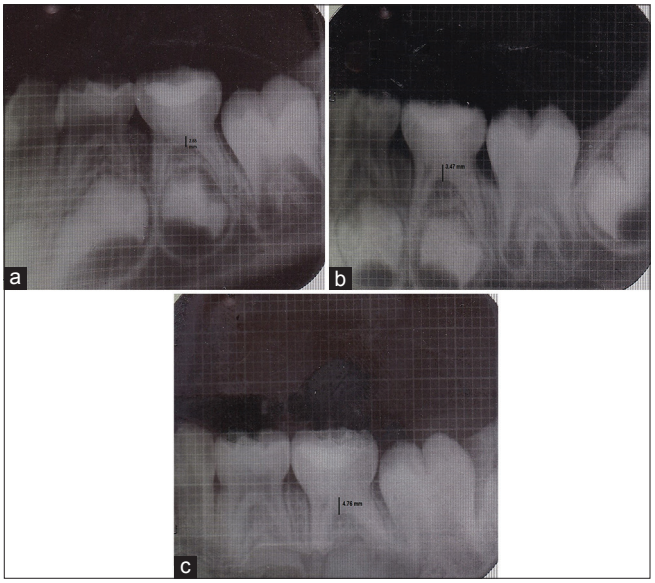

Figure 3: Postoperative measurements. Baseline (a). Six months follow-up (b). Twelve-month follow-up (c) showing increase in dentin thickness

Table 3: Intergroup comparison of change in distance from reference Point-A to Point-B

Time interval	Mean±SD (mm)		Intergroup comparison	
	Ca_3SiO_5 – Based dentin substitute, *n*=15 teeth	CH, *n*=15 teeth	*t*	*P*
Baseline to 6 months	0.537±0.245	0.425±0.209	1.835	0.088
Baseline to 12 months	0.910±0.319	0.668±0.259	3.153	0.007*
6-12 months	0.373±0.232	0.243±0.165	1.647	0.122

SD: Standard deviation; CH: Calcium hydroxide; *P<0.05 - significant up to 5% level

Table 4: Intergroup comparison of computed percentage of modified Cvar and Ryge criteria scoring at baseline

Characteristics	Group	Scores (%)			
		A	B	C	D
Color matching	1	85	15	0	0
	2	83.3	16.7	0	0
Marginal discoloration	1	86.7	13.3	0	0
	2	86.7	13.3	0	0
Secondary caries	1	100	0	0	0
	2	100	0	0	0
Anatomic form	1	93.3	6.7	0	0
	2	86.7	13.3	0	0
Surface texture	1	100	0	0	0
	2	100	0	0	0
Marginal integrity	1	96	4	0	0
	2	98	2	0	0
Pulp sensitivity	1	98	2	0	0
	2	98	2	0	0

Table 5: Intergroup comparison of computed percentage of modified Cvar and Ryge criteria scoring at 12 months

Characteristics	Group	Scores (%)			
		A	B	C	D
Color matching	1	73.3	26.7	0	0
	2	70	30	0	0
Marginal discoloration	1	85.6	14.4	0	0
	2	83.3	16.7	0	0
Secondary caries	1	100	0	0	0
	2	100	0	0	0
Anatomic form	1	90.7	9.3	0	0
	2	82	18	0	0
Surface texture	1	81	19	0	0
	2	81	19	0	0
Marginal integrity	1	97	3	0	0
	2	97	3	0	0
Pulp sensitivity	1	98.7	1.3	0	0
	2	98	2	0	0

nanohybrid composite resin or ceramic onlay which were assessed for any evidence of marginal deterioration based on Cvar and Ryge criteria. The restorations were scored for marginal integrity not below Score-B as seen, under ×9 magnification. This was done to ensure no tunnel defects at the restoration and tooth interface which could have affected the success rate of the procedures.

Stainless steel crowns were not given as it would not have made the radiographic assessment of dentin bridge formed by the pulpotomy agent at the pulp tissue interface area possible. Hence, only teeth with one walled defect were selected. The dentin bridge observed radiographically was detected through sequential standardized radiographs where the constant Point-B was kept at bifurcation of roots and changes in thickness were measured through superimposed images using same contrast as the starting point and measuring by digitization of the image using software named Digora.

Since the reliability of history of pain or sensitivity to cold impulses is questionable in children, Ekstrand's criteria no. 4 was taken as a radiographic standard for presence of carious lesion radiolucency in pulpal one-third of dentin. However, the clinical status of the hemorrhage was a final deciding factor to proceed with regenerative pulpotomy procedure. Clinical failure was observed in one case in CH Group-2 and none in Biodentine Group-1.

Tricalcium silicate cement has been shown to induce dental pulp stem cell differentiation.[11] The ability of this material to aid or induce this differentiation and maturation affects its bioactivity and biocompatibility. Tumor necrosis factor-alpha-induced TRAP1 expression in odontoblast cell bodies and processes in carious teeth was significantly reduced in the presence of Ca_3SiO_5.[12] The pulpal and periapical responses of dogs' teeth after pulpotomy and pulp capping with Ca_3SiO_5, when compared with MTA by radiographic, histopathologic and histomicrobiological analyses, showed that mineralized tissue bridge formation was observed in more specimens treated with Ca_3SiO_5 (96.8%) than with MTA (72.2%).[13] Daltoé *et al*. found no significant differences in cell viability between MTA and Ca_3SiO_5. Ca_3SiO_5 stimulated similar mineralization markers as MTA. Thus, Ca_3SiO_5 could be advantageous in the long-term for conservative endodontic treatment.[14]

All the studies and case reports of Ca_3Si0_5-based dentin substitute as a pulpotomy agent since then have documented only the histological evidence of formation of reactive dentin formation in permanent molars. Since, Ca_3SiO_5-based dentin substitute has been launched as advancement over MTA exhibiting bioactive and better physical properties, its ability to form mineralized tissue bridge in pulpotomized primary teeth has limited evidence. Therefore, the present study was undertaken with Ca_3Si0_5 and its *in-vivo* potential for dentin bridge formation was compared with CH which is the gold standard as regenerative pulpotomy agent in primary teeth due to maximum longitudinal *in-vivo* studies in the past.[15]

Conclusion

Based on the clinical and radiographic results of the present study, Ca_3SiO_5-based dentin substitute showed a significant potential as a pulpotomy agent for regenerative pulpotomies in primary molars with the advantage of good sealing ability

and short setting time when compared with CH whose mechanical stability is questionable. Further, longitudinal follow-ups of these cases would add to the results of functional performance and outcome of these teeth over a longer period.

Acknowledgments

The present study was conducted with ethical clearance from the Ethical Committee of the Institute/University before the start of the study vide letter No. BFUHS/2K13/P-Th/8083 dated August 06, 2013.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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