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Comparative evaluation of Calcium Hydroxide, Mineral Trioxide Aggregate, Biodentine, Platelet Rich Fibrin as direct pulp capping agents: An in-vivo study

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ABSTRACT

Aim: The study aimed to compare calcium hydroxide, mineral trioxide aggregate (MTA), biodentine and platelet rich fibrin (PRF) as direct pulp capping agents in permanent mandibular molars.
Materials and methods: 60 permanent mandibular molars with symptoms of reversible pulpitis were divided into 4 groups according to the agent used (n = 15): calcium hydroxide, MTA, Biodentine, PRF according to the direct pulp capping agent used. The patients were recalled after 1 week, 1,3 6 and 12 months for pain and periapical status assessment.
Results: After a follow - up of 12 months PRF showed maximum dentine thickness formation.
Conclusion: PRF can be used as an alternative to MTA for direct pulp capping in teeth with reversible pulpitis.
Keywords: Platelet rich fibrin, direct pulp capping, tertiary dentine, Biodentine.

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INTRODUCTION

The pulp is an innumerable and vascularized connective tissue responsible for dentinogenesis. Vital pulp therapy maintains the vitality of pulp by regeneration of dentine- pulp complex.[1]

Inclusion criteria	***Exclusion criteria***
Class I and II caries approaching pulp without involving it.	Teeth with periapical widening
No periapical pathology present	Patient's systemic diseases, on opioid or steroid therapy.
No history of nocturnal pain or spontaneous pain. On sensitivity to cold stimuli which is reversible.	Teeth having periapical or periodontal lesions

Indirect pulp capping a biocompatible material is placed after pinpoint exposure of pulp resulting in the formation of reparative dentine, maintaining the vitality of pulp. Various materials are being used like zinc oxide eugenol, calcium hydroxide, resin-modified glass ionomer, adhesive systems, etc. [2]

Calcium hydroxide is the gold standard. But it has several disadvantages like, less bonding to dentine, the dentine bridge formed dissolves with time resulting in tunnel defects. To overcome this calcium silicate cements like mineral trioxide aggregate were introduced.[3][4]

Mineral trioxide aggregate, composed of tricalcium silicate, dicalcium silicate, tricalcium aluminate, and tetra-calcium-aluminoferrite and bismuth oxide, results in faster dentine bridge formation, with excellent adhesion to dentine. It also has some disadvantages like dentine discoloration and slow setting time. [5][6]

Biodentine, a dentine substitute shows similar results like MTA. It results in the formation of a dentinal bridge by stimulating the odontoblasts. It has a shorter setting time and better handling properties. The biocompatibility and bioactivity are better when compared to MTA. The setting time is less MTA (9 to 12 minutes).[7]

PRF a 2nd generation platelet concentrate is responsible for regeneration and revascularization of the dental pulp tissue. Various growth factors like Platelet-derived growth factor, vascular endothelial growth factor; insulin-like growth factors are responsible for the regeneration of dentine pulp complex thus maintaining the vitality of pulp. [8]

MATERIALS AND METHOD

A total of 60 patients with symptoms of reversible pulpitis in permanent mature mandibular molars were selected for the study.

Written informed consent was obtained from the patients. Local anesthesia was administered and isolation with rubber dam was achieved. (2% lignocaine/1:80,000 adrenaline)

The caries was removed with a round bur and pulp was exposed. After pulp exposure, the hemorrhage was controlled with a cotton pellet soaked in normal saline for 2 minutes.

After hemorrhage control the mandibular molars were randomly assigned to one of four groups:

Group 1: Calcium hydroxide

Group 2: MTA

Group 3: Biodentine

Group 4: PRF

In group 1 Dycal was placed over the exposed pulp followed by a layer of resin-modified glass ionomer cement and composite. (Fig 1a & b)

In group 2 MTA (ProRoot, Dentsply) was mixed with a powder: liquid ratio (3 parts of powder: 1 part of distilled water) and placed over the exposed pulp. A moist cotton pellet was placed followed by temporary restoration. On the 2nd

day, final restoration was done with composite. (Fig 2a & b)

In group 3 Biodentine (Septodont) was mixed with a powder: liquid ratio (1 capsule of powder: 5 drops of liquid) and placed over the exposed pulp. The entire cavity was filled with biodentine as a temporary restoration. Biodentine was reduced as a base followed by composite restoration on the 2nd day. (Fig 3a & b)

In group 4 PRF was prepared with the patient's blood. 10 ml blood was drawn from the patient and immediately centrifuged at 3000 rpm for 10 minutes (without anticoagulant). A thin membrane of PRF was placed on the exposed pulp followed by biodentine which was used as a temporary restorative material. Biodentine was reduced as a base followed by composite restoration on the 2nd day. (Fig 4a & b)

The pain was evaluated using the Visual Analog scale. The radiographic analysis was carried out using a grid and Digora software (Sorodex digora software). Two blind folded examiners were selected to carry out the radiographic analysis at 1, 3,6,12 months.

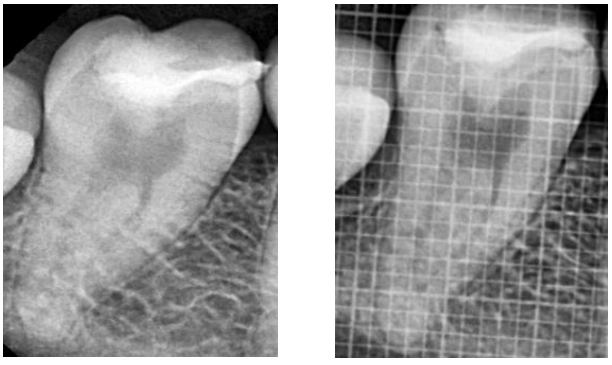

Figure 1 a & b: Calcium hydroxide (group 1) with 12 months follows up.

A -Calcium hydroxide was placed as a direct pulp capping agent followed by resin modified GIC and composite as final restoration. B- After 12 months follow up.

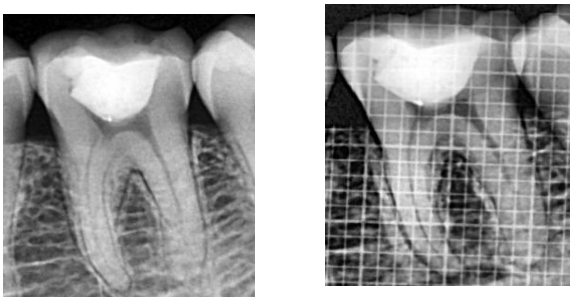

Figure 2 a & b: Mineral trioxide aggregate (group 2) with 12 months follows up.

A –Mineral trioxide aggregate was placed as a direct pulp capping agent followed by resin modified GIC and composite as final restoration. B- After 12 months follow up.

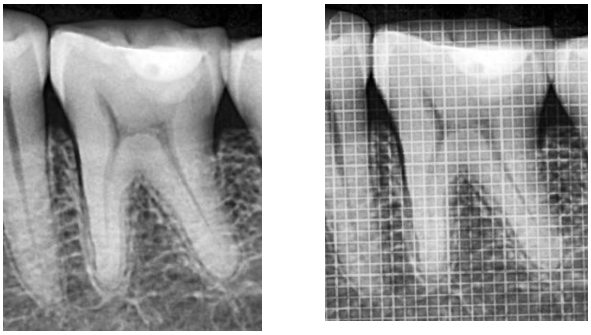

Figure 3 a & b: Biodentine (group 3) with 12 months follows up.

A –Biodentine was placed as a direct pulp capping agent followed by as final restoration. B- After 12 months follow up.

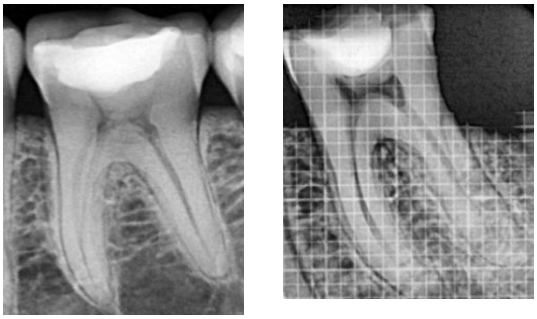

Figure 4 a & b: Platelet rich fibrin (group 4) with 12 months follows up.

A –Platelet rich fibrin was placed as a direct pulp capping agent followed by Biodentine and composite as final restoration. B- After 12 months follow up.

RESULTS

All collected data were entered into MS Excel and analyzed. The statistical software SPSS 16.0 for windows (SPSS Inc, Chicago, IL, USA, 2001) was used for the analysis of data. One-way ANOVA followed by the Tukey HSD test was used to compare the dentine thickness between the groups (p<0.01). After statistical analysis, it was found that PRF showed increased dentine thickness followed by biodentine, Mineral Trioxide Aggregate, calcium hydroxide. (Table 1/Fig 5) The amount of pain experienced in all the groups were statistically non-significant (p>0.05) (Table 2/ Fig 6). The intra-group comparison showed significant increase in dentine thickness with 3 months as baseline (p< 0.05) (Fig 7,8,9,10)

Table 1: Platelet rich fibrin showed maximum dentine thickness using Tukey HSD test. The results were highly significant (p< 0.01)

**** Significant p<0.05, ** Highly significant p<0.01, ^{NS} Not significant p>0.05***

Dependent Variable	*(I) Group*	*(J) Group*	*Mean Difference (I-J)*	*Std. Error*	*P value*	*95% Confidence Interval*	
						Lower Bound	*Upper Bound*
Dentine Thickness 3Month	CALCIUM HYDROXIDE vs	MTA	-.09467	.01108	<0.001**	-.1240	-.0653
	CALCIUM HYDROXIDE vs	BIODENTINE	-.16467	.01108	.<0.001**	-.1940	-.1353
	CALCIUM HYDROXIDE vs	PRF	-.28733	.01108	.<0.001**	-.3167	-.2580
	MTA vs	BIODENTINE	-.07000	.01108	.<0.001**	-.0993	-.0407
	MTA vs	PRF	-.19267	.01108	.<0.001**	-.2220	-.1633
	BIODENTINE vs	PRF	-.12267	.01108	.<0.001**	-.1520	-.0933
Dentine Thickness Month6	CALCIUM HYDROXIDE vs	MTA	-.2100	.0119	.<0.001**	-.241	-.179
	CALCIUM HYDROXIDE vs	BIODENTINE	-.3033	.0119	.<0.001**	-.335	-.272
	CALCIUM HYDROXIDE vs	PRF	-.4060	.0119	.<0.001**	-.437	-.375
	MTA vs	BIODENTINE	-.0933	.0119	.<0.001**	-.125	-.062
	MTA vs	PRF	-.1960	.0119	.<0.001**	-.227	-.165
	BIODENTINE vs	PRF	-.1027	.0119	.<0.001**	-.134	-.071
Dentine Thickness Month12	CALCIUM HYDROXIDE vs	MTA	-.23467	.00943	.<0.001**	-.2596	-.2097
	CALCIUM HYDROXIDE vs	BIODENTINE	-.25800	.00943	.<0.001**	-.2830	-.2330
	CALCIUM HYDROXIDE vs	PRF	-.35067	.00943	.<0.001**	-.3756	-.3257
	MTA vs	BIODENTINE	-.02333	.00943	.075^{NS}	-.0483	.0016
	MTA vs	PRF	-.11600	.00943	.<0.001**	-.1410	-.0910
	BIODENTINE vs	PRF	-.09267	.00943	.<0.001**	-.1176	-.0677

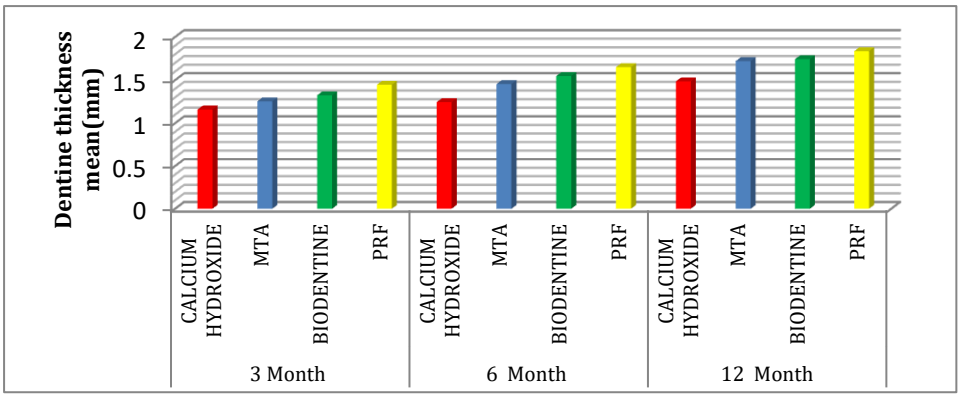

Fig 5: PRF showed maximum dentine thickness at all time intervals. The yellow bar shows PRF which is maximum at 3 months, 6 months, 12 months. Green is biodentine, blue is mineral trioxide aggregate. Red is calcium hydroxide.

Table 2: There is no significant difference in the pain scores at any intervals between all the groups. The p value for pain in all groups at different time intervals was nonsignificant.

	Pain 1Week	*Pain 1Month*	*Pain 3Month*	*Pain 6Month*	*Pain 12Month*
Chi-Square	2.155	4.136	3.293	1.416	.477
Df	3	3	3	3	3
P-value	.541 NS	.247 NS	.349 NS	.702 NS	.924 NS

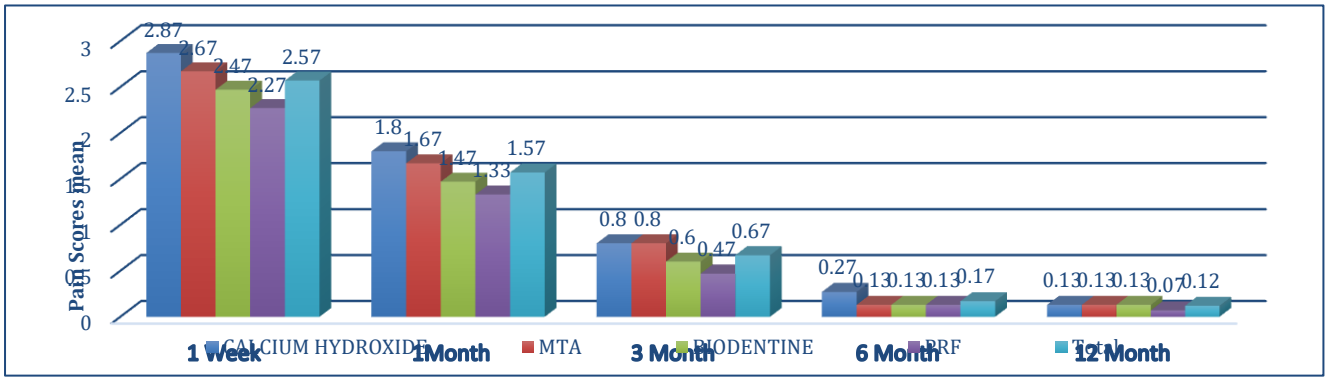

Fig 6: The amount of pain experienced was statistically non-significant in all the groups.

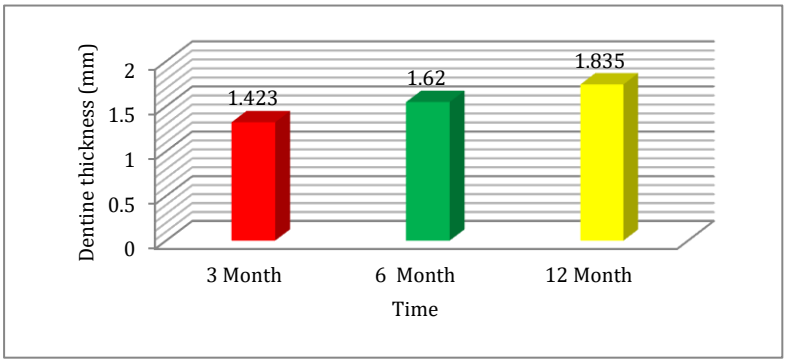

Fig 7: Distribution of means of dentine thickness of the PRF group at different time intervals. There was significant increase in dentine thickness

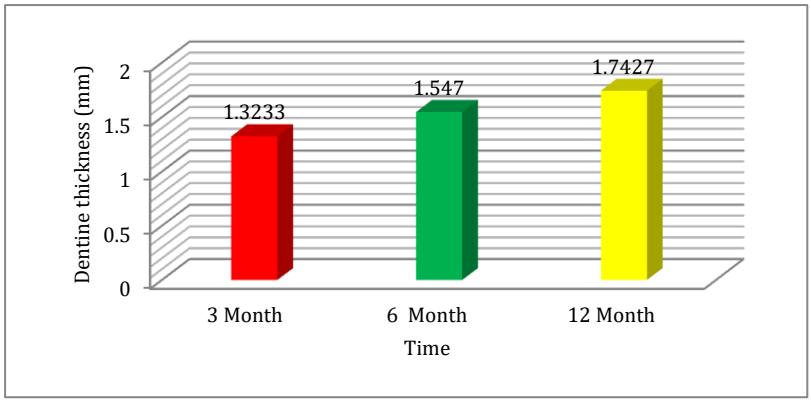

Fig 8: Distribution of means of dentine thickness of the Biodentine group at different time intervals. There was significant increase in dentine thickness.

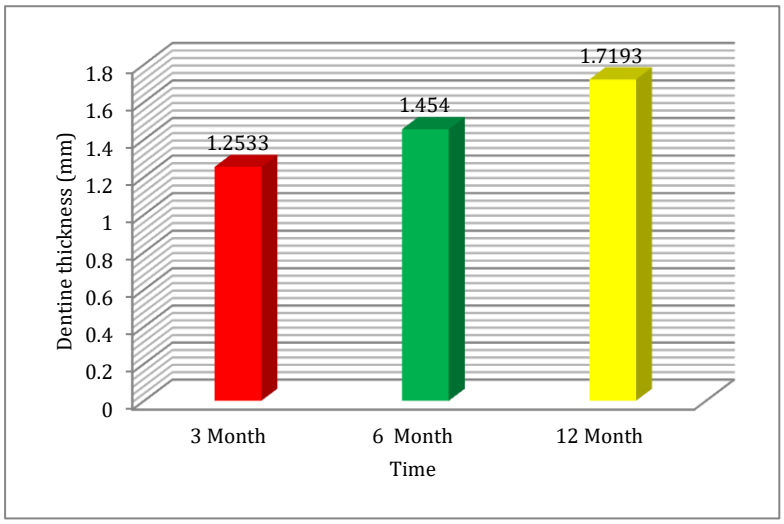

Fig 9: Distribution of means of dentine thickness of the Mineral trioxide aggregate group at different time intervals. There was significant increase in dentine thickness

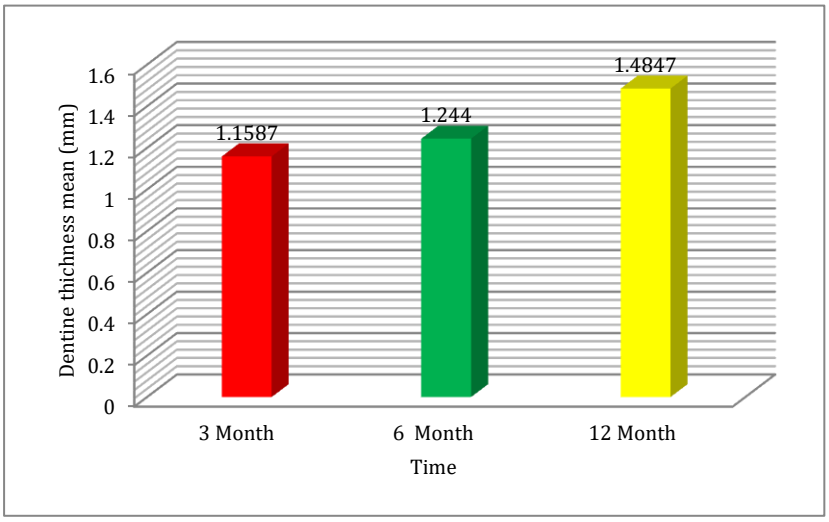

Fig 10: Distribution of means of dentine thickness of the Calcium hydroxide group at different time intervals. There was significant increase in dentine thickness

DISCUSSION

Reversible pulpitis is mild to moderate direct pulpal aggravation brought about by a boost where the pulp returns to its unique uninflamed state after the expulsion of improvement. [9] The side effects for reversible pulpitis are affectability to hot, cold or sweet upgrade. The tooth is not delicate to percussion, palpation, with no periapical pathology. [10]

The principle point of indispensable pulp treatment is to keep up pulp vitality. The recovery of the pulp dentine complex is by the arrangement of tertiary dentine. Indirect pulp capping a biocompatible material is put over the exposed vital pulp tissue securing it and keeping up the imperativeness of pulp. Pfaff, in 1756 was the first to utilize gold foil for direct pulp capping treatment. [10] Direct pulp capping aides in recuperating of reversibly harmed pulpal tissue, the arrangement of dentinal connect reestablishing the structure and capacity of pulp dentine complex. [9]

Calcium-hydroxide was utilized as an immediate pulp capping operator in 1962, and the main clinical examination directed in 1963 had a triumph pace of 85%. [11] In the 1990s, Torabinejad and White presented, mineral trioxide aggregate (MTA), which discharges calcium hydroxide gradually while setting. Following this Biodentine was acquainted with conquering the burdens of MTA. [12] Recently the utilization of PRF is additionally supported. PRF is fibrin work comprising of development factors, progenitor cells, cytokines inducing dentinal bridge formation.

Under rubber dam isolation, ordinary saline was utilized as a hemostatic specialist. Hemostasis was accomplished by applying pressure with cotton absorbed saline for 2 minutes. Sodium hypochlorite is a decent hemostatic specialist, yet since the pH is 12, antacid in nature, it might separate development factors from the dividers of dentine similarly as Calcium hydroxide. Consequently, ordinary saline was utilized as a hemostatic operator. [13] Four direct pulp capping materials were utilized Calcium hydroxide, Mineral Trioxide Aggregate, Biodentine, and Platelet Rich Fibrin.

The dentine thickness in PRF group ($p < 0.01$) at all interims (3 months, a half year and a year) is essentially higher than others, trailed by Biodentine group, MTA group and least in Calcium Hydroxide group (Table 1/Fig 5)

The purpose behind the accomplishment of PRF is because of the cells living in aroused pulp having undifferentiated cell multiplication capacity like the solid pulp. These immature microorganisms are invigorated by the development factors discharged from PRF. PRF is a fibrin meshwork of platelets, development factors and undeveloped cells liable for a regenerative limit of platelet rich fibrin. [14]

PRF discharges cytokines like IL-1 upgrading the recuperating capability of pulp. It likewise inhibits the arrival of prostaglandins and other provocative go-betweens balancing the aggravation and causing recovery of pulp dentine complex. [15] The PRF is centrifuged in test tubes without anticoagulants. The absence of an anticoagulant enacts the platelets in a couple of moment's minutes bringing about coagulating of blood. The accomplishment of this relies upon the speed of blood assortment and move to the axis. The prompt application improves the achievement of PRF. On the off chance that the centrifugation is postponed, the fibrin will polymerize into a cross-connected meshwork decreasing the viability of PRF. This outcome is disappointment and a little coagulation of poor consistency is acquired. [14]

The aftereffects of our examination were as per an investigation by Sneha S Vanaki et al who looked at the clinical and radiographical results of pulpotomy utilizing biodentine and Platelet

rich fibrin for a half year. Platelet rich fibrin was better than biodentine. [16] Dou L et al likewise concluded that PRF as a potential pulp capping operator controlling the moderate irritation, expanded cell expansion liable for recovery of the pulp tissue. [17] An expansion in the thickness of dentine connect was seen between 2 interims because of ordinary juxtaposition and testimony of tertiary dentine. (Fig 7). This is because of the moderate and supported arrival of development factors, expanding the dentine thickness with time.

MTA and biodentine then again were nearly at a similar level. This could be because of the comparable arrangement of the two materials. Tricalcium silicate responds with tissue liquids framing calcium hydroxide liable for hard tissue mineralization and tissue recovery.

Although measurably not huge, biodentine has preferred properties over MTA. The treatment of Biodentine is better than MTA with a short setting time (9-12 min). MTA requires 3-4 hrs to harden. It brings about dentine staining because of the nearness of bismuth oxide (radiopacifier). Biodentine has zirconium oxide as a radiopacifier which doesn't cause staining. The ingestion of calcium and silicon particles is more noticeable in biodentine than MTA, shaping miniaturized scale labels in dentine. [18] Biodentine infiltrates into the dentinal tubules bringing about smaller scale mechanical holding answerable for better fixing capacity and minimal flexibility. Be that as it may, MTA doesn't cover all the dentinal tubules liable for microleakage and bacterial infiltration. [19] MTA because of its high pH and moderate release of calcium particles actuates hard tissue development taking after hydroxyapatite in an arrangement. MTA's prosperity is likely because of the way that it fills in as a repository for calcium.

Katge et al conducted a split-mouth study contrasting Biodentine and MTA and presumed that both the materials demonstrated a 100% achievement rate at 6 and a year development. When contrasted and MTA, biodentine was anything but difficult to deal with a shorter setting time. (9-12 minutes). [20]

Swaroop Hegde et al indicated a triumph pace of 91.7% and 83.3% for biodentine and MTA separately as immediate pulp capping operators in carious teeth. The purpose behind the accomplishment of biodentine was its capacity to type of dentin connect, antibacterial property, and brilliant sealing capacity. [21]

In any case, the consequences of certain investigations were not in agreement with our examination. Claudia Brizuela et al looked at calcium hydroxide, MTA and biodentine with follow up interims at multi-week, 3 months, a half year and 1 year. No factually huge contrast was found among the three gatherings, however, biodentine and MTA offered favorable circumstances over calcium hydroxide. [22]

The thickness of dentine connect between 2 interims was measurably critical for both MTA and biodentine (Fig 8,9). This is because of the arrival of odontoblastic markers for the pulpal cells answerable for mineralization. Biodentine and MTA advance cell multiplication and upregulation of development factors and bone proteins. These outcomes in a constant statement of tertiary dentine. [23]

Calcium hydroxide demonstrated the least dentine bridge formation in the range of a year. Even though calcium hydroxide was considered as the best quality level for fundamental pulp treatment. Calcium hydroxide due to its high pH (12.5) irritates the exposed area. This zone advances division and relocation of forerunner cells on the substrate surface. These cells separate into odontoblasts answerable for dentine connect arrangement. The dentine connect

framed is permeable and less sorted out. Because of the soluble pH of calcium hydroxide, it removes development factors from dentine walls resulting in tunnel defects. [24]

In an examination led by Leye Benoist et al., which compared Ca (OH)2 and MTA on indirect pulp capping, no factually noteworthy distinction in the dentin thickness and achievement rate toward the finish of a half year was accounted for; notwithstanding, MTA was more fruitful than Ca (OH)2. [25]

Tran et al assessed the homogeneity of dentine bridge formed comparing Biodentine and Calcium hydroxide. It was presumed that the reparative structures incited by biodentine were homogenous and incongruity with reparative dentine. Interestingly, the reparative tissue incited by Ca(OH)2 had a permeable association. [26]

There is a continuous arrangement of dentine connect that is statistically significant between interims

(Fig 10). The measure of pain experienced by all the four groups were statistically non-significant ($p > 0.05$) (Table 2/Fig 6)

CONCLUSION

In the current examination, PRF demonstrated the most extreme dentine thickness with no post-operative pain and force when contrasted with biodentine and mineral trioxide aggregate and calcium hydroxide. Further examinations are required to completely comprehend the properties and advantages of PRF as a direct pulp capping agent.

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