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A COMPARATIVE EVALUATION OF REVASCULARIZATION IN NON-VITAL IMMATURE ANTERIOR TEETH WITH AND WITHOUT PLATELET-RICH FIBRIN IN PEDIATRIC PATIENTS: AN IN-VIVO STUDY

Dental Science

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ABSTRACT

Trauma to the young permanent teeth leads to necrosis, open apices and blunderbuss canals. These tooth are very challenging to treat and maintain in the oral cavity for a longer period of time. Revascularization is the method of choice for these teeth. Our aim was to study two different methods of revascularization with platelet-rich fibrin (PRF) and with blood clot (BCR) and compare their efficacy both clinically and radiographically in pediatric dental patients. 44 patients with immature necrotic anterior teeth without periapical radiolucency equally divided into two groups were included. The cases were followed up at 1, 3, 6 and 12 months of intervals. Clinically, all cases were asymptomatic of signs and symptoms. Radiographically, insignificant difference was seen in terms dentinal wall thickness, apical closure and root lengthening between the groups. Significant difference was found between the groups in terms of pulp sensibility with Electric Pulp Test (EPT). It was concluded that revascularization done either by using platelet- rich fibrin or by blood clot gave about similar results in terms of clinical and radiographic success.

KEYWORDS

revascularization, platelet-rich fibrin, young permanent tooth.

INTRODUCTION

Treatment of the immature teeth with open apices and blunderbuss canals are very challenging and pose variety of problems to the clinicians. The cleaning and shaping of the canal is difficult, thin fragile wall can fracture during filing and moreover, the obturation is also difficult. Endodontic management of such teeth includes surgery and retrograde sealing, calcium hydroxide–induced apical closure (apexification), and, more recently, placement of an apical plug of mineral trioxide aggregate (MTA) and gutta-percha obturation. A novel concept for the treatment of immature nonvital teeth was introduced which is known as revascularization. The concept of revascularization was introduced far back in 1961 by Ostby.[1]

The development of regenerative endodontics has been in doubt since the dental pulp has no role in form, function and esthetics. Hence, conventional root canal treatment is the most reasonable one. But, there is always a potential risk of reinfection, tooth discoloration due to endodontic filling materials and sealers and reduction in fracture resistance of root dentine due to long-term use of calcium hydroxide. Moreover, there is higher incident of tooth loss after removal of pulp as compared to teeth with normal tissues, despite increased tooth survival after root canal treatment. The main purpose of revascularization is to regenerate pulp-like tissue, ideally, the pulp-dentin complex and to regenerate resorbed root, cervical or apical dentin.

According to **American Association of Endodontists' (AAE)** clinical considerations for a regenerative procedure, the principal goal is to eradicate clinical symptoms or signs and to resolve apical periodontitis and the secondary goal is to achieve thickening of the canal walls and/or continued root maturation.[2] Platelet-rich fibrin (PRF), a second-generation platelet concentrate, was first developed by **Choukroun et al.**[3] PRF is a non-thrombonized autologous fibrin mesh that serves as a reservoir for slow continuous release of growth factors over a period of 7–14 days. In contrast, PRP shows sudden release of growth factors in 7–14 hours of placement approximately.[4] After that, the release of growth factors from PRP intensely reduces, in contrast, PRF continue to release the growth factors. The biological effect of platelet-rich fibrin (PRF) on human dental pulp cells (DPC) was studied by **Fu-Mei Huang et al**.[5] and found that PRF did not interfere with cell viability and also increase DPC proliferation.

The purpose of the present study was to compare different methods of revascularization (with platelet-rich fibrin (PRF) and with blood clot)in pediatric dental patients and to compare their efficacy in terms of clinical and radiological outcome.

MATERIALS AND METHODS

A cross-sectional study was conducted on the patients aged between 9-13 years having immature non-vital anterior teeth. Patients were randomly categorized into 2 groups – Group I was blood clot revascularization and Group II with PRF revascularization.

The conducted study had following inclusion and exclusion criteria:

Inclusion Criteria:

- Patients with non-vital, immature permanent anterior teeth without periapical radiolucency were included in the study.
- Children in the age group of 9 to 13 year-old.

Exclusion Criteria:

- Physically and mentally challenged children.
- All those not willing to participate in the study.

Sampling:

It was confirmed from the literature review that the expected Mean ± Standard deviation of revascularization of Group I and Group II are 0.14 ± 0.03 and 0.11 ± 0.04 respectively and mean difference of two groups for the variables is 0.03 at 95% confidence interval and precision 5%, the sample size comes to be 44, to be equally divided in two groups of 22 each.

METHODOLOGY

The study was approved by the Institutional Ethical Committee of the Faculty of Medicine. Informed consent was obtained from all the parents after explaining the detailed treatment protocol. On the first appointment, after infilteration anesthesia, rubber dam (Hygenic Dental Dam, Coltene) (Fig.1) was placed and tooth was accessed with a round diamond bur. Minimum mechanical instrumentation was performed and working-length was established with ISO #80 K-file (Dentsply Maillefer) and copious gentle irrigation was done with 1.5% sodium hypochlorite (Septodont, India) for 5 minutes followed by normal saline. Lastly, irrigated with 20ml of 17% EDTA for 5 minutes. The canal was dried with paper points and an inter-appointment calcium hydroxide (Dentpro, India) medicament was placed for 3 weeks and cavity was sealed temporarily with zinc-oxide eugenol restoration. This procedure was same for both the groups.

On the second appointment, the tooth was assessed for any signs/symptoms of persistent infection before proceeding to the next step. Revascularization was performed as follows: local infilteration anesthesia without adrenaline was given, rubber dam was placed and cavity was accessed. Calcium hydroxide medicament was removed

with copious and gentle irrigation with 20ml of 17% EDTA for 5 minutes followed by normal saline and the canal was dried with paper point. For Group-I (blood clot) bleeding was induced into the canal by over-instrumenting canal 2mm beyond the determined working length by a sterile precurved K-file. Sharp fine strokes were given past the apex into the periapical tissue. After frank bleeding was evident at the cervical portion of the root canal 3-4 mm from cemento-enamel junction, a 3-mm-thick layer of White MTA (ProRoot; Dentsply) was placed directly over the clot (Fig. 2) and the cavity was sealed with resin-modified glass ionomer cement. For Group-II (PRF revascularization), 8ml sample of whole venous blood was taken out from the patient's forearm and was transferred into a test tube without anticoagulant and centrifuged using a centrifuge at 3000 revolutions/minute for 10 minutes. After centrifugation, the formed PRF was transferred to a sterile tray and was fragmented. The freshly prepared PRF was placed incrementally into the canal with an endodontic plugger below the level of cemento-enamel junction. Directly over the PRF matrix, a 3-mm-thick layer of White MTA was placed (Fig. 3) and the access cavity was restored with resin-modified glass ionomer cement. The patients were followed-up and assessed for the clinical and radiographical outcomes at 1 month, 3 months, 6 months and 1 year recall post-operatively. Cases of Group I and Group-II are shown in Fig. 4-8.

Figures

Fig. 1 Shows The Instruments, Materials And Centrifuge Machine Used In The Study.

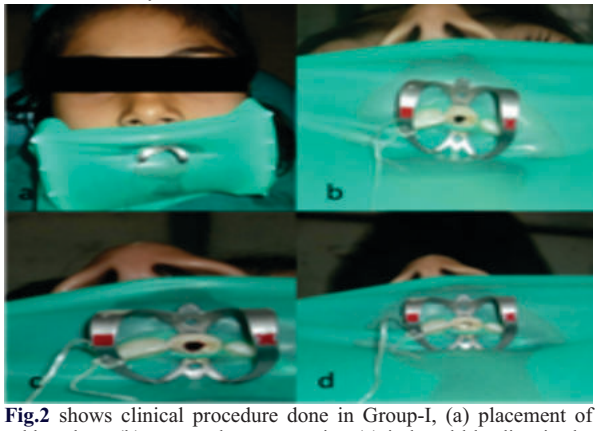

Fig.2 shows clinical procedure done in Group-I, (a) placement of rubber dam, (b) prepared access cavity, (c) induced bleeding in the canal and (d) placement of MTA over blood clot.

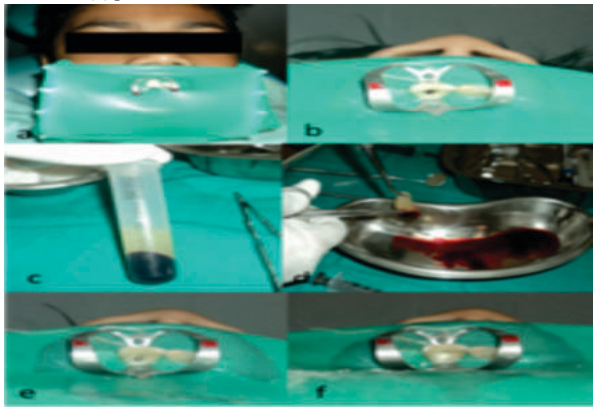

Fig. 3 shows clinical procedure done in Group-II, (a) placement of rubber dam, (b) prepared access cavity, (c) freshly prepared PRF, (d) sectioning of PRF, (e) placement of PRF in the root canal and (f) MTA placed over PRF.

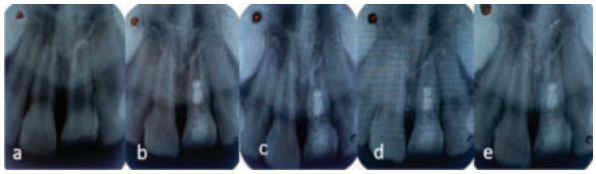

Fig. 4 shows case of revascularization with blood clot (Group-I) in tooth 11, (a) pre-operative radiograph, (b) post-op radiograph, (c) radiograph at 3 months follow-up, (d) radiograph at 6 months follow-up and (e)radiograph at 12 months follow-up.

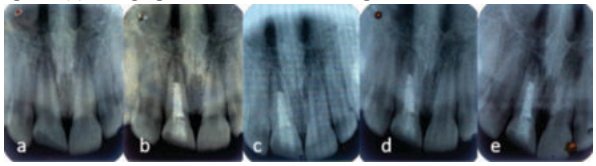

Fig. 5 shows case of revascularization with blood clot (Group-I) in tooth 21, (a) pre-operative radiograph, (b) post-op radiograph, (c) radiograph at 3 months follow-up, (d) radiograph at 6 months follow-up and (e)radiograph at 12 months follow-up.

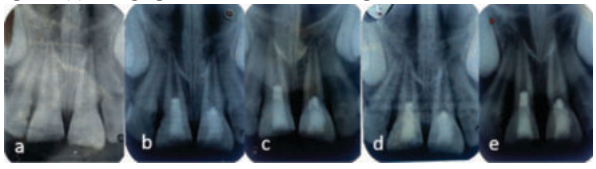

Fig. 6 shows case of revascularization with blood clot(Group-I) in tooth 21(left side) and with PRF(Group-II) in tooth 11(right side), (a) pre-operative radiograph, (b) post-op radiograph, (c) radiograph at 3 months follow-up, (d) radiograph at 6 months follow-up and (e)radiograph at 12 months follow-up.

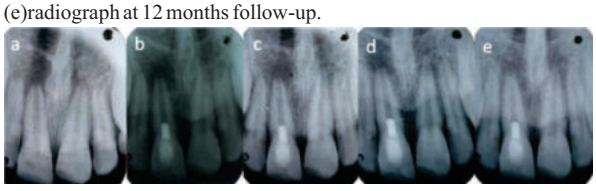

Fig. 7 shows case of revascularization with PRF(Group-II) in tooth 21, (a) pre-operative radiograph, (b) post-op radiograph, (c) radiograph at 3 months follow-up, (d) radiograph at 6 months follow-up and (e)radiograph at 12 months follow-up.

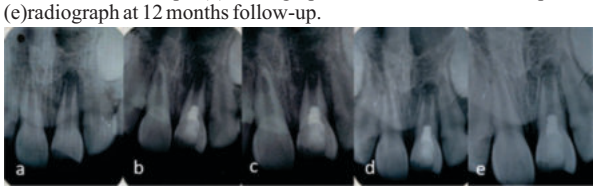

Fig. 8 shows case of revascularization with PRF(Group-II) in tooth 11, (a) pre-operative radiograph, (b) post-op radiograph, (c) radiograph at 3 months follow-up, (d) radiograph at 6 months follow-up and (e)radiograph at 12 months follow-up.

Statistical Analysis:

All the data was collected and analyzed. The statistical software SPSS 16.0 is used for analysis of data. The significance between the parameters for qualitative data is tested by Pearson's Chi square test and Fisher's exact test. The 95% Confidence interval and 5% level of significance was used for analysis of data. *Significant $p<0.05$ and ^{NS} not significant $p>0.05$ was considered.

RESULTS

Clinically, all the cases were asymptomatic at follow-up visits. For radiographic assessment, the intraoral periapical radiographs were analysed by two observers who were not involved in the main study. Standardization and validation of the observers was done before the conduct of the study. X-rays were scored as (0) No change, (+) Fair, (++) Good or (+++) Very good. The details of the observations were given in Tables 1-5.

DISCUSSION:

To achieve the goals of revascularization, a good disinfection is always the principal thing needed. In this study, disinfection was attained by the use of 1.5% NaOCl as an irrigant.[2] Nageh M et al.[6] and Bakhtiar H

et al.[7] also used 1.5% NaOCl in their study. Nageh M et al.[6] and Bakhtiar H et al.[7] suggested that higher concentration like 5.25% of NaOCl is cytotoxic to the stem cells in the apical tissues and also decreases the odontoblastic differentiation needed for revascularization. After irrigating the canal with NaOCl, the canal was once rinsed with normal saline to remove any remaining toxicity.[2]

But, in contrast, Jadhav G et al.[8] used 2.5 % NaOCl in their study. Apart from this, Adhikari et al.[9] used 3% NaOCl whereas Keswani D et al.[10] used 5.25% NaOCl concentration. Ulusoy AT et al.[11] had used 1.25% NaOCl in their study.

In the present study, irrigation with 17% EDTA solution was done on both the visits after NaOCl irrigation.[2] The chelating effect of EDTA removes the smear layer and promotes the release of dentin derived growth factors that earlier got embedded into dentin during the process of dentinogenesis [6]. The release of growth factors from dentinal walls helps in proliferation and differentiation of stem cells. It also does affect the survivability of Stem Cells of Apical papilla (SCAP)[7].

In our study, we had used $Ca(OH)_2$ as an intracanal medicament for 3 weeks, as $Ca(OH)_2$ is effective in killing microorganism present in the infected root canals of the teeth. The use of $Ca(OH)_2$ was also suggested by AAE [2] and Chen MYH et al.[12] In contrast to the present study, Jadhav G et al.[8] had used triple antibiotic paste(TAP) as an intracanal medicament. However, Thomson A and Kahler B [13] contraindicated the use of $Ca(OH)_2$. According to them, $Ca(OH)_2$ inhibits further root growth and may even kill viable pulp cells, including stem and progenitor cells present in the apical papilla. However, in a recent study by Ruparel NB et al.,[14] showed that higher concentrations of antibiotics in TAP have a detrimental effect on the survival of SCAP, but lower concentrations of TAP and $Ca(OH)_2$ at all tested concentrations are conducive with the survival and proliferation of SCAP. The same was ascertained by Althumiary RI et al.,[15] who found that the TAP or double antibiotic paste usually has a concentration of 1000mg/ml when both are used clinically in a paste consistency. This higher concentration has lethal effect and prevents SCAP survival. They also suggested that $Ca(OH)_2$ promotes SCAP survival and proliferation.

Similar to the present study, all the cases remained asymptomatic clinically in the studies done by Rizk HM et al.[16] and Sharma S et al.[17] In contrast, Torabinejad M et al.[18] reported reinfection of the tooth treated with revascularization. Proper disinfection and a leak-proof coronal seal is considered an important factor for successful revascularization.

The radiographic assessment in the present study was done based on the qualitative scoring of the radiographs same as done by Jadhav G et al.[8] and Chen MYH et al.[12] in their studies. This is because of the unavailability of any digitalize radiographic method in the college where the study was conducted.

Similar to our study, Rizk HM et al.[16] and Sharma S et al.[17] found that in terms of dentinal wall thickness, PRF-group showed better results than blood-clot group but the results were not statistically significant. This could be due to the fact that PRF is a rich source of signalling molecules and cytokines as compared to blood clot in the canal. These signalling molecules are involved in tissue regeneration and cellular differentiation. PRF consist of thrombin which forms equal junctions within the polymerized fibrin, resulting in prolonged release of signalling molecules.[16] In contrast, Narang I et al.[19] showed that in terms of dentinal wall thickness, blood clot showed good results in more number of cases than PRF with no statistically significant difference.

In the present study, in terms of increase in root length, PRF gave better results than blood clot, the results were not statistically significant (p=0.143) at 12 months similarly shown by Rizk HM et al.[16] In contrast, Narang I et al.[19] showed that there is no difference between the blood clot and PRF groups in terms of increase in root length. Also, Sharma S et al.[17] showed that PRF gave less effective results in terms of root lengthening than blood clot.

In the present study, there was no statistically significant difference between both the groups in terms of apical closure at 12 months' follow-up (p=0.166), though PRF showed better results than blood clot. This was in accordance to Sharma S et al.[17] since PRF is strong but has a flexible membrane having rich amounts of growth factors needed for cellular proliferation, differentiation and angiogenesis. Though Rizk HM et al.[16] found that PRF group showed better results than the blood clot group and was statistically significant. This is because PRF functions by stimulating stem cell proliferation and expresses huge amount of osteoprotegrin proteins and alkaline phosphatase. These proteins are stated as odontoblast differentiation markers. However, Narang I et al.[19] suggested no difference in apical closure between PRF and blood clot groups.

In the present study, in terms of pulp sensibility test, a more positive response to EPT in Group-II was seen which was statistically significant (**p=0.048**). However, a statistically insignificant (p=0.112) results was found in term of thermal test. This was in agreement with Nageh M et al.[6] which showed in their study that 9 out of 15 cases (60%) gave positive response to the sensibility test after 12-month follow-up in cases treated with revascularization using PRF.

According to them, nerve regeneration could have been attributed to various growth factors present in PRF. More precisely, transforming growth factor beta helps in regulation of mitogenic effects of other growth factors i.e. nerve growth factor and brain derived neutrophic factor. It also stimulates neurite outgrowth and regulates differentiation of Schwann cells. Platelet derived growth factor (PDGF) helps in induction of stem cell proliferation, differentiation and myelin formation while vascular endothelial growth factor (VDGF) promotes blood vessel growth, neurogenesis and neuroprotection.[6] In normal healthy teeth, electric current is usually applied on the incisal edge of the teeth for assessment but in revascularization procedure, when the tooth was sealed with MTA and restorative material, the distance between the vital tissues and the coronal region gets increased. So it is better to place the tip in the middle third of the root as done in the present study. In contrast, Rizk HM et al.[16] showed no positive response to the pulp sensibility tests. According to them, positive response to pulp sensibility is a variable phenomenon and this could be due to the presence of layer of MTA or 12-month follow-up time might not be enough for the formation of blood vessels and nerve fibres within the root canal.

In the present study, both the methods of revascularization gave outstanding regenerative results and desirable healing properties which is a necessary requirement in revascularization. Since, PRF is purely autologous and no reagents are needed for its preparation, there is no risk of any hypersensitivity reactions to the patients. It can be freshly prepared by the clinicians at the chair-side and inserted into the canal space. The disadvantage of this procedure is extra time needed in taking out the blood, young uncooperative child patients and the increased cost of treatment. These drawbacks become minimal in comparison to the improved healing and regenerative response of PRF procedure. PRF gave comparable results to blood clot. However, studies showed concerns about the damage to Hertwig's epithelial root sheath (HERS) cells which occurred during intentional overinstrumentation of the canal to induce bleeding during blood clot revascularization (BCR). HERS cells, apart from formation of cementum, also do control the differentiation of stem cells. Thus differentiation of stem cells into odontoblasts/cementoblasts might get prevented due to the damage of HERS cells hampering the continued root formation [20] which can be eliminated with revascularization using PRF.

CONCLUSION:

From the present study, we conclude that platelet- rich fibrin fulfilled all the requirement needed to bring about revascularization in an immature necrotic permanent teeth and can be used as a scaffold in revascularization effortlessly in pediatric dental patients.

Table. 1: Comparison Of Dentinal Wall Thickness Between Group-I (Blood clot) And Group-II (PRF) At 1, 3, 6 And 12 Months' Follow-up Intervals

Dentinal wall thickness	Follow-up (months)	n	Scoring								Pearson Chi-Square [a]	d.f [a]	P value [a]
			No change (0)		Fair (+)		Good (++)		Very good (+++)				
			No.	%	No.	%	No.	%	No.	%			
Group- I (Blood clot)	0	22	22	100	0	0	0	0	0	0	2.360	2	0.307
	1	21*	21	100	0	0	0	0	0	0			

	3	21*	21	100	0	0	0	0	0	0			
	6	20**	0	0	14	70	6	30	0	0			
	12	19***	0	0	12	63.2	7	36.8	0	0			
Group- II (PRF)	0	22	22	100	0	0	0	0	0	0			
	1	22	22	100	0	0	0	0	0	0			
	3	22	22	100	0	0	0	0	0	0			
	6	16**	0	0	12	75	4	25	0	0			
	12	16**	0	0	12	75	3	18.8	1	6.2			

* 1 patient dropped out in Group-I at 1-month recall visit, making a total of 21.
** 1 more patient in Group-I and 6 patients in Group-II dropped out, making a total of 20 and 16 patients in Group-I and Group-II respectively at 6 months recall visit.
*** Another 1 patient dropped out having 19 patients in Group-I and 16 patients in Group-II respectively at 12 month recall visit.
[a]The values were calculated at 12 months follow-up only.

Table. 2: Comparison Of Root Lengthening Between Group-I (Blood clot) and Group-II (PRF) at 1, 3, 6 And 12 Months' Follow-up Intervals

Root lengthening	Follow-up (months)	n	Scoring								Pearson Chi-Square[a]	d.f [a]	P value [a]
			No change (0)		Fair (+)		Good (++)		Very good (+++)				
			No.	%	No.	%	No.	%	No.	%			
Group- I (Blood clot)	0	22	22	100	0	0	0	0	0	0	3.896	2	0.143
	1	21*	21	100	0	0	0	0	0	0			
	3	21*	21	100	0	0	0	0	0	0			
	6	20**	0	0	20	100	0	0	0	0			
	12	19**	0	0	19	100	0	0	0	0			
Group- II (PRF)	0	22	22	100	0	0	0	0	0	0			
	1	22	22	100	0	0	0	0	0	0			
	3	22	22	100	0	0	0	0	0	0			
	6	16***	0	0	13	81.2	3	18.8	0	0			
	12	16***	0	0	13	81.2	2	12.5	1	6.2			

Table. 3: Comparison Of Apical Closure Between Group-I (Blood clot) And Group-II (PRF) at 1, 3, 6 and 12 Months' Follow-up Intervals

Apical closure	Follow-up (months)	n	Scoring								Pearson Chi-Square [a]	d.f [a]	P value [a]
			No change (0)		Fair (+)		Good (++)		Very good (+++)				
			No.	%	No.	%	No.	%	No.	%			
Group- I (Blood clot)	0	22	22	100	0	0	0	0	0	0	3.587	2	0.166
	1	21*	21	100	0	0	0	0	0	0			
	3	21*	21	100	0	0	0	0	0	0			
	6	20**	0	0	14	70	6	30	0	0			
	12	19**	0	0	12	63.2	7	36.8	0	0			
Group- II (PRF)	0	22	22	100	0	0	0	0	0	0			
	1	22	22	100	0	0	0	0	0	0			
	3	22	22	100	0	0	0	0	0	0			
	6	16***	0	0	13	81.2	3	18.8	0	0			
	12	16***	0	0	13	81.2	2	12.5	1	6.2			

Table. 4: Comparison Of Pulp Sensibility (Electric Pulp test - EPT) between Group-I (Blood clot) and Group-II (PRF) at 1, 3, 6 and 12 months' follow-up intervals

Pulp sensibility (EPT)	Follow-up (months)	n	Scoring				Pearson Chi-Square [a]	d.f [a]	P value [a]
			Absent (-)		Present (+)				
			No.	%	No.	%			
Group- I (Blood clot)	0	22	22	100	0	0	3.896	1	0.048
	1	21*	21	100	0	0			
	3	21*	21	100	0	0			
	6	20**	20	100	0	0			
	12	19**	19	100	0	0			
Group- II (PRF)	0	22	22	100	0	0			
	1	22	22	100	0	0			
	3	22	22	100	0	0			
	6	16***	14	87.5	2	12.5			
	12	16***	13	81.2	3	18.8			

Table. 5: Comparison Of Pulp Sensibility (Thermal Test) between Group-I (Blood clot) and Group-II (PRF) at 1, 3, 6 and 12 Months' Follow-up Intervals

Pulp sensibility (Thermal heat test)	Follow-up (months)	n	Scoring				Pearson Chi-Square [a]	d.f [a]	P value [a]
			Absent (-)		Present (+)				
			No.	%	No.	%			
Group- I (Blood clot)	0	22	22	100	0	0	2.519	1	0.112
	1	21*	21	100	0	0			
	3	21*	21	100	0	0			
	6	20**	20	100	0	0			
	12	19**	19	100	0	0			
Group- II (PRF)	0	22	22	100	0	0			
	1	22	22	100	0	0			
	3	22	22	100	0	0			
	6	16***	16	100	0	0			

	12	16***	14	87.5	2	12.5			

Summary:

The present study which was conducted with an aim to compare the efficacy of platelet-rich fibrin (PRF) with conventional method (blood clot revascularization), hence based on the results it can be deduced that revascularization using PRF was inconsequentially more effective than blood clot revascularization. Platelet-rich fibrin has an advantage of having brilliant regenerative and healing properties. However, the follow-up of 12 months for revascularization is considered short. Therefore, we suggest to conduct more clinical studies with longer follow-ups and with a larger sample size.

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