



SHORT TERM SUCCESS OF INFLAMED MATURE SINGLE ROOTED TEETH WITH SYMPTOMATIC APICAL PERIODONTITIS FOLLOWING SINGLE VISIT REGENERATIVE TREATMENT PROTOCOLS (A RANDOMIZED CLINICAL TRIAL)

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Abstract

Objective: to clinically and radiographically evaluate the short term success of inflamed mature single rooted teeth with symptomatic apical periodontitis after using conventional blood technique in comparison to platelet rich fibrin technique in single visit pulp revascularization.

Methods: Regenerative procedures was performed in (40) mature permanent inflamed single rooted teeth with symptomatic apical periodontitis which were randomly allocated to two equal groups (n=20). In the intervention group, platelet rich fibrin was used as a scaffold (PRF), while in the control group, blood clot technique was used as a scaffold (BC). Chi-square test and Fisher's Exact test were used for comparisons between the two groups regarding qualitative data.

Results: The overall success of the groups was 55% and 60% in the PRF group and BC group respectively with no clinical significance between the two groups, but there was a significant decrease in the overall success within each group at 6 and 12 months in comparison to the baseline and at 1 and 3 months.

Conclusions: Single visit regenerative endodontics using PRF or blood clot as scaffolds showed some evidence of successful clinical and radiographic outcomes when used to treat mature single rooted teeth with symptomatic apical periodontitis and might applied as an alternative to conventional root canal treatment in the future..

Trial Registration: This study has been registered on clinicaltrials.gov with identification number: NCT03725514, under the title of Short Term Success of Inflamed Mature Single Rooted Teeth with Symptomatic Apical Periodontitis Following Single Visit Regenerative Treatment Protocols. It was registered on 28th of October 2018.

Keywords: Regenerative endodontics, pulp revascularization, scaffolds, single visit, success and failure, pulpitis, apical periodontitis, mature teeth.



Background

For decades preserving the natural dentition through was done using artificial filling materials. But, root canal therapy had several limitations, starting with different iatrogenic errors during endodontic procedures, jeopardizing the remaining tooth structure which affects the tooth survival and requires further restorative intervention. Consequently, pulp regeneration as a therapeutic strategy that makes use of the body's capacity for regeneration was unveiled. Due to challenges with its traditional root canal therapy, immature apex was accordingly treated with pulp revascularization [1].

The American Dental Association recognized pulp regeneration and tissue engineering in 2009. The main goal of regeneration was to save the restorability of teeth by completing the formation of immature necrotic roots. Blood clot was the first to be used and gained a great popularity, as it acted as a scaffold for the migration of stem cells and morphogens to allow regeneration [2].

Based on its success, a great portion of dentists started shifting the traditional treatment of mature necrotic permanent teeth to pulp regeneration as in immature teeth. However, the small apical foramen possessed a serious limitation as it might not allow the passage of stem cells and growth factors, which are two cornerstones for the success of pulp regeneration [3].

Stem cells and growth factors are abundant in platelet concentrates, including platelet rich plasma (PRP) and platelet rich fibrin (PRF). Other platelet sources have developed as a result. Choukroun's platelet rich fibrin (PRF) was superior than PRP because it is completely autologous, simple to make, doesn't require anticoagulant material, and releases growth factors for a longer period of time. Also, the presence of cytokines, leukocytes and few lymphocytes inhibit infection and inflammation [3].

Teeth with incomplete apices are the focus of the majority of papers in the literature that discuss the use of tissue engineering in the field of root canal therapy. Only four publications addressing the treatment of teeth with developed apices were found following a comprehensive, methodical search [2, 4-6]. All four of these studies are case studies. A randomised clinical trial has not been conducted for any of these research. The gold standard for interventional investigations is the randomised clinical trial, which produces the best evidence that effectively supports clinical decision-making. Therefore, in order to achieve the best potential therapeutic results, such study must be carried out.

In order to prolong the survival of the affected tooth, prevent the development of periapical lesions, and restore pulp sensibility, this study compared the short-term overall success of inflamed mature single-rooted teeth with symptomatic apical periodontitis following conventional blood technique to the Platelet Rich Fibrin technique in single visit pulp revascularisation.



Subjects and Methods:

The protocol for this prospective, parallel, double-blind, randomised clinical trial with a 1:1 allocation ratio was authorised by Cairo University's Faculty of Dentistry Research Ethics Committee (reference no. 18/10/50).

Sample size determination:

G*Power Version 3.1.9.2 was used to determine the sample size. Vitality response was the main result of this power study. The findings of Shivashankar et al. [7] were used to compute the effect sizes $w_1 = (0.7)$ and $w_2 = (0.734)$. With a power of 80%, or a beta (β) level of 20% and an alpha (α) level of 5%, the minimum predicted sample size was 32 participants. To account for a 25% dropout rate, the sample size was expanded to 40 patients overall (20 subjects each group).

Study setting

- This study included 40 patients from the endodontic department outpatient clinic at Cairo University's Faculty of Dentistry who had 40 inflammatory, adult, single-rooted teeth with symptoms of apical periodontitis.
- The principal investigator performed the operations on each patient.

Eligibility criteria

Criteria for inclusion

They were between the ages of 16 and 25.

medically devoid of any chronic illnesses

Mature adult single-rooted teeth with a single canal that exhibit apical periodontitis symptoms and pulpitis clinically.

Positive patient/guardian compliance with study participation and agreement to sign a consent form committing to a 12-month follow-up

Criteria for exclusion

Any adverse events or drug sensitivity that could compromise the trial's successful conclusion.

The treated tooth's non-restorable coronal portion.

Open-apiced, traumatised, multiple-canalled, or non-vital teeth.

Evidence of internal or exterior root resorption in teeth.

Preoperative protocol

- The European Society of Endodontology's checklist for revitalisation operations was followed in gathering personal, medical, dental, and clinical assessment data [8].



- A digitalised periapical radiograph was taken prior to intervention.
- The patient received thorough explanations of the procedures, risks, and advantages, and the participants gave their informed consent.
- In order to establish a baseline for follow-up records, candidates were referred for CBCT.

Randomization and allocation concealment

Using a straightforward randomisation process and computer software, the 40 permanent, adult teeth were divided into two equal groups: Intervention group (PRF): Twenty teeth received platelet-rich fibrin treatment, and the control group (BC): Each patient selected a card at random on the day of intervention from a sealed opaque envelope carrying a number, which was used to allocate the 20 teeth treated with the blood clot procedure. The assistant supervisor took this action.

Blinding

- The study hypothesis on which intervention was thought to be superior was concealed from the participants.
- The statistician and the outcome assessors who gathered the data were blind to the patient's specific intervention.

Intraoperative procedures

All processes used in the treatment of the chosen teeth were identical, with the exception of the scaffold type, which was chosen at random, in accordance with the American Association of Endodontics' [9] clinical criteria for regeneration procedures.

A rubber dam was used to isolate each tooth after 1.8 ml of 3% mepivacaine without a vasoconstrictor was used to anaesthetise it. An electronic apex locator (EAL) was used to establish the working length, and a digital periapical radiograph was used to check the results of the traditional access cavity procedure. Using a modified step-back technique, cleaning and shaping were carried out up to ISO #60 K files as a master file. After that, the flared to #3 gates were glidden with the irrigation of 3 ml 1.5% NaOCl in between each subsequent file, delivering a total of 20 ml 1.5% NaOCl. Finally, using side-vented needles, 20 ml 17%EDTA was irrigated for 5 minutes. After using paper points that matched the master file to dry the canals, patients were split into intervention and control groups.



PRF application and preparation in accordance with Narang et al. [10]:

A red-capped glass tube containing 10 ml of each participant's own venous blood was filled with an anticoagulant and centrifuged for 12 minutes at 3000 rpm. The middle PRF layer was then placed in a sterile cup and allowed to release its serum for 10 minutes. The PRF clot was then broken up and gradually packed into the canals using hand pluggers until it reached the CEJ. A collagen plug was then placed over the PRF, followed by Biodentin and the final restoration.

According to Samra et al. [11], blood clot induction is achieved by purposefully overinstrumenting a precurved K-file #30 2 mm past the apical foramen. This involves two or three slow clockwise rotations followed by an anticlockwise rotation during file extraction, which causes apical bleeding until the blood reaches the CEJ level. A collagen plug was inserted, followed by a 3 mm layer of Biodentin and the final filling after a dry cotton pellet was held in position with tweezers to remove any remaining blood from the pulp chamber and enable the formation of a blood clot, as evidenced by the colour shift.

The overall success/failure of both groups was done after 12 months based on the survival, sensibility and radiographic evaluation of the treatment.

Statistical analysis:

Qualitative data were presented as frequencies and percentages. Chi-square test and Fisher's Exact test were used for comparisons between the two groups regarding qualitative data. Numerical data were explored for normality by checking the distribution of data and using tests of normality (Kolmogorov-Smirnov and Shapiro-Wilk tests). Age data showed normal (parametric) distribution while bone density measurements showed non-parametric distribution. Numerical data were presented as median, range, mean and standard deviation (SD) values. For parametric data, Student's t-test was used to compare between mean age values in the two groups. For non-parametric data, Mann-Whitney U test was used to compare between the two groups. Friedman's test was used to study the changes by time in each group. Dunn's test was used for pair-wise comparisons when Friedman's test is significant. The significance level was set at $P \leq 0.05$.

RESULTS

During the follow up period, three cases (15%) dropped out from the PRF group, while two cases (10%) dropped out of the blood clot group and were excluded from the data analysis throughout the follow up period. A total of 35 cases completed the 12months study period.



Regarding the overall success/failure between both groups, there was no significant difference (P-value=1) at all follow up periods, as seen in table 1.

Table (1) : Descriptive statistics and results of Fisher’s Exact test for comparison between overall success/failure in the two groups

Time	Outcome	PRF (n = 20)		Blood clot (n = 20)		P-value	Effect size (v)
		n	%	n	%		
1 month	Success	18	90	18	90	1	0
	Failure	0	0	0	0		
	Drop-out	2	10	2	10		
3 months	Success	18	90	18	90	1	0
	Failure	0	0	0	0		
	Drop-out	2	10	2	10		
6 months	Success	11	55	12	60	1	0.078
	Failure	6	30	6	30		
	Drop-out	3	15	2	10		
9 months	Success	11	55	12	60	1	0.078
	Failure	6	30	6	30		
	Drop-out	3	15	2	10		
12 months	Success	11	55	12	60	1	0.078
	Failure	6	30	6	30		
	Drop-out	3	15	2	10		

*: Significant at $P \leq 0.05$

Within each group, there was a significant decrease in both groups at the 6 months evaluation period, where the PRF group success rate decreased to 55% and the blood clot group success rate decreased to 60% due to the development of periapical lesions in the CBCTs regardless that the teeth were clinically surviving intraorally, as shown in fig. 1 and table 2.

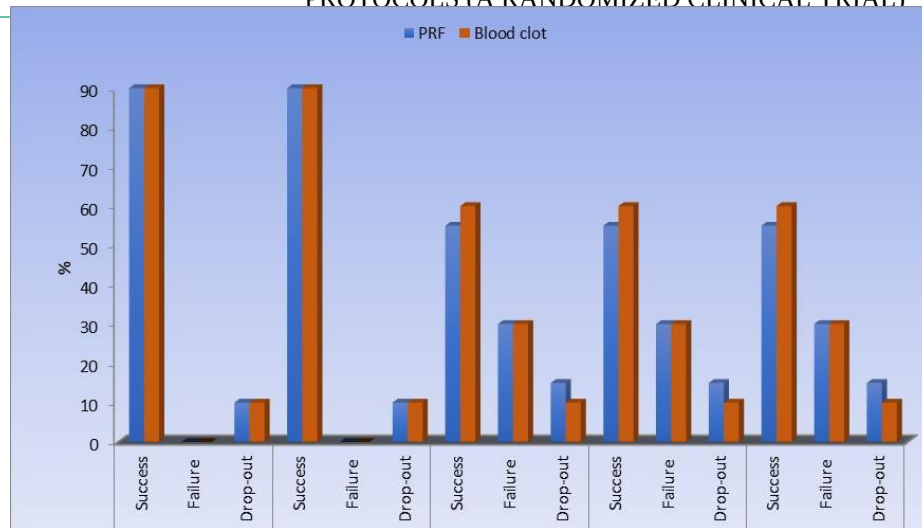


Figure (1) : Bar chart representing overall success/failure in the two groups

Table (2) : Descriptive statistics and results of Freidman's test for the changes in overall success/failure within each group

Time	Outcome	PRF (n = 20)		Blood clot (n = 20)	
		n	%	n	%
1 month	Success	18	90	18	90
	Failure	0	0	0	0
	Drop-out	2	10	2	10
3 months	Success	18	90	18	90
	Failure	0	0	0	0
	Drop-out	2	10	2	10
6 months	Success	11	55	12	60
	Failure	6	30	6	30
	Drop-out	3	15	2	10
9 months	Success	11	55	12	60
	Failure	6	30	6	30
	Drop-out	3	15	2	10
12 months	Success	11	55	12	60
	Failure	6	30	6	30
	Drop-out	3	15	2	10
P-value		<0.001*		<0.001*	
Effect size (w)		0.350		0.300	

*: Significant at $P \leq 0.05$



DISCUSSION

For a number of years, regeneration has been a breakthrough in the treatment of necrotic juvenile apices. Later, it was expanded to be employed in necrotic adult teeth. In contrast to the traditional root canal therapy, its excellent success rate in resolving apical periodontitis in both mature and immature cases demonstrated its potential for use in cases with inflamed pulp with symptomatic apical periodontitis [11, 12, 13].

Since scaffolds offer a place for stem cells to be located and encourage cell-biomaterial interactions, cell adhesion, and extracellular matrix deposition, they were compared in this experiment as one of the fundamentals of the triad of regeneration [14]. The most well-known scaffold, blood clots, were used as a control because they stabilise, stimulate the innate and adaptive immune systems, provide platelet-derived growth factors, mesenchymal stem cells, and stem cells from apical papillae, which produce odontoblast-like cells even when there are menstrual infections [12, 15, 16]. Because PRF is a better platelet concentrate than PRP and can overcome the limitations of the blood clot as a scaffold, it was selected as an intervention. PRF produces 1050% higher platelet concentration than blood clot, guarantees sustained cytokine and growth factor release for up to 28 days, and eliminates the requirement for anticoagulants like PRP [16].

Since tissue ingrowth and favourable clinical outcomes are possible when the apical size diameters fall between 0.5 and 1.0 mm, the apical diameter was taken into consideration as one of the important parameters influencing the regenerative endodontic treatment [17]. To obtain the benefits of tissue ingrowth, efficient cleaning, and deeper irrigant penetration, the root canal apical diameter was increased to size #60 K-file in this study [18].

Because of its biocompatibility, capacity to encourage biomineralisation, reparative dentin synthesis, quick setting time, high push-out bond strength, and improved aesthetics by preventing crown discolouration, biodentin, a calcium silicate-based substance, was selected to seal the canal orifice [19, 20].

The obvious finding is the significant drop of the overall success rate from 90% in both groups at 1 and 3 months to 55% in the PRF group and 60% in the blood clot group as shown in table 4 and fig.4. There was no significant difference between both groups, but the significance was within each group after 6, 9 and 12 months in comparison to 1 and 3 months. Both groups showed a 30% failure ,not in terms of survivability as the teeth were intact and functioning, but because of the development of periapical lesions which was discovered at 6 months radiographic evaluation. This



came in accordance with Samra et al, Arslan et al, Kateb and Fata and Nassar et al. [11,18,21,22]. This failure rate had several possible explanations, where according to Lee and Song [23], they claimed that the persistent infection contributes to this failure, especially with the dilemma of achieving complete disinfection when low concentration irrigants are used. Another explanation was stated by Arslan et al. [21], which might be due to the persistence of inflammatory mediators associated with apical periodontitis, which decreases the release of stem cells specially in mature teeth. A third explanation concerning the dissolving capacity of sodium hypochlorite was stated by Stojicic et al.[24], where they stated that the optimum concentration for dissolving organic tissues is 5.25%, while the concentration used in our study was 1.25%, which according to their study lowering the concentration lowers the dissolving effect and might contribute to the failure of regenerative procedures.

The following conclusions can be drawn within the constraints of the current investigation. In treating mature single-rooted teeth with apical periodontitis, single visit regenerative endodontics showed some evidence of success. However, more research is necessary to compare the long-term results to traditional root canal therapy. Both PRF and the blood column may be utilised as scaffolds to treat inflamed pulp in patients with apical periodontitis symptoms.



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