REGENERATIVE ENDODONTIC PROCEDURE USING PRFIN HUMAN PERMANENT TEETH WITH PERSISTENT PERIAPICAL PATHOLOGY AFTER CONVENTIONAL ROOT CANAL TREATMENT : ACASE SERIES

Dr. Shelly Sharma\*, Dr. H.D. Adhikari\*\*, Dr. Abhijit Niyogi\*\*\* Dr. Parthasarathi Mondal\*\*\*\*, Dr. Amrita Ghosh\*\*\*\*

# ABSTRACT

Regenerative Endodontic Procedures (REPs) has been described as a 'paradigm shift' in the treatment of necrotic immature teeth, since it fosters continued root maturation. REPs have also been used to successfully treat human mature permanent teeth with necrotic pulps and apical periodontitis. However, there is no consensus in using REPs in endodontically treated permanent teeth with persistent periapical periodontitis instead of non-surgical retreatment.

AIM:- The aim of this case series was to describe REPs performed in five endodontically treated permanent teeth with persistent periapical pathology using Platelet Rich Fibrin (PRF) as a scaffold, with the objective to eliminate the clinical signs and symptoms and to achieve complete resolution of periapical pathology along with regaining positive response to pulp sensibility testing after REPs.

RESULTS:-All cases were found asymptomatic at 3,6,9 and 12 months follow up visits. Radiographic examination revealed complete resolution or remarkable reduction in the size of the periapical lesions in all five teeth along with apical closure of open apices of two teeth. Formation of calcific bridge was noted in one tooth.

CONCLUSION:- REP can be a viable treatment option for nonsurgical retreatment of nonvital permanent teeth.

### **KEY WORDS**

#### **REP, PRF, Retreatment**

#### **ABOUT THE AUTHORS**

\*Final Year Postgraduate student, \*\*Professor & Head \*\*\*Professor, \*\*\*\*Associate Professor, \*\*\*\*\*Clinical Tutor Dept. of Conservative Dentistry and Endodontics Dr. R. Ahmed Dental College & Hospital Kolkata, West Bengal

### **CORRESPONDING AUTHOR**

Dr. Shelly Sharma Final Year Postgraduate student, Dept. of Conservative Dentistry and Endodontics, RADCH e-mail address:-shellyamaze95@gmail.com Contact number:- 7650025023

### INTRODUCTION

Regenerative endodontic procedures (REPs) can be defined as biologically based procedures designed to physiologically replace damaged tooth structures, including dentin and root structures, as well as the pulp-dentin complex<sup>1</sup>. Successful REP results in elimination of clinical signs and symptoms, resolution of apical periodontitis, thickening of the canal walls and/ continued root development with or without apical closure. Since REPs restore the vitality of the tooth, it restores the immune defense mechanisms to protect the tooth from foreign invaders<sup>2,3</sup>. It is a 'paradigm shift' in the treatment of non-vital immature teeth. Also, it is being used to successfully treat human mature permanent teeth with necrotic pulps<sup>4</sup>. However, reports on using REPs in endodontically treated permanent teeth with persistent periapical pathology are very limited<sup>5,6</sup>.

Keeping this in view, the present study was conducted with five such cases using Platelet Rich Fibrin (PRF) as a scaffold and follow up was done for 12 months.

# MATERIALS AND METHODS

The patients of the present case series reported to the Department of Conservative Dentistry and Endodontics of Dr. R. Ahmed Dental College and Hospital. Different treatment options were explained to them and they agreed on performing REP. Informed consent was obtained. Institutional ethics committee clearance was also taken.

Scaffold plays a key role in REP. In all cases, autologous PRF as a scaffold, MTA (Angelus) as a plugging material, Cavit (3M ESPE, Germany) as a temporary filling material and composite resin (Ivoclar Vivadent, Switzerland) as final filling material were used. Patients were recalled after 3,6,9 and 12 months.

# **CASE REPORTS**

### CASE:-1

A 16 years old female patient complained of pain and swelling for last 2-3 months and gave history of



FIGURE 1:- A. Pre-op view B. Poorly obturated 11 with periapical radiolucency C. GP removed D. WL estimation. E. Calcium hydroxide placed inside the canal (erroneously some amount has been pushed beyond apex). F. Blood being drawn from antecubital vein. G&H. Blood transferred to a test tube to be placed in the Remi R 8C centrifugation machine. I. PRF obtained (middle layer). J(i). PRF separated from platelet poor plasma and RBC (ii) Compressed under sterile gauze. K. PRF inserted into the canal. L&M. 3mm of MTA placed over PRF below CEJ N. Restored with composite resin O. Immediate post-op. P. 6 months post-op. Q. 9months post-op. R. 12months follow up showing remarkable reduction in peri-apical radiolucency and closure of the apex (inset)

trauma causing fracture to 11 six years back for which she underwent conventional root canal treatment. The tooth (Fig 1-A) was sensitive to percussion and palpation. IOPAR revealed poorly obturated 11 with open apex, improper coronal restoration and a large periapical lesion involving 11 & 12 (Fig 1-B). Pulp sensibility test for both teeth were performed. Non-Surgical Endodontic Therapy (NSET) in 12 and REP in 11 was planned.

On first appointment, Local anesthesia was given using 2% lidocaine with 1:100000 epinephrine. Rubber dam (Coltene Whaledent, Germany) was placed. Root canal filling material i.e GP was accessed and removed from 11 using H-file (Fig 1-C), without using any solvent. The working length was determined using apex locator (Dentsply Propex Pixi) and was confirmed by IOPAR (Fig 1-D). Minimal instrumentation was done accompanied by copious irrigation with 20ml of 1.5% sodium hypochlorite solution for 5 minutes. Then, the canal was dried with paper points and calcium hydroxide (Ultracal XS of Ultradent, USA) was placed inside the canal (Fig 1-E) and the access cavity was sealed with Cavit (3M ESPE, Germany). 12 was also accessed and NSET was performed on it. Patient was scheduled for second appointment after 2 weeks.

On second visit, the patient was asymptomatic with no pain or swelling. Rubber dam was placed. Cavit was removed from both the teeth followed by flushing of calcium hydroxide by copious irrigation with saline and 20ml of 17% EDTA (Desmear, Anabond, India) for 5 minutes. Final irrigation was done with saline.

10ml blood was drawn from the patient's antecubital vein (Fig 1-F) and transferred to a test tube (Fig 1-G) and immediately placed in the Remi R 8C centrifuge (Remi laboratories, Mumbai (Fig 1-H) and spinned at 2110 rpm (400g, radius of centrifuge as 8 cm) for 10 minutes. PRF membrane thus obtained (Fig 1-I, J) was placed within the canal (Fig 1-K) followed by placement of collagen plug (CollaCote; Integra Life Sciences). MTA (Angelus) of 3mm thickness was packed below the CEJ (Fig 1-L,M). On verifying its setting after 15-20 min, composite resin restoration was done (Fig 1-N,O). Patient was recalled for follow up at 3, 6, 9 and 12 months.



FIGURE 2:- A. Poorly obturated 11 and 21 with periapical radiolucency. B. GP removed C. 3mm of MTA placed over PRF below CEJ. D. Immediate post-op. E&F. 9 months follow up G. 12 months follow up showing resolution of peri-apical radiolucency.

The tooth was found to be asymptomatic and functional at all follow up visits. Radiographic evaluation showed gradual reduction in the periapical pathology (Fig 1-P,Q) with apical closure after 12 months (Fig 1-R). However, pulp sensibility tests-cold and EPT were non-responsive.

### CASE:-2

A 54 years old female patient presented with mild to moderate pain in 11 and 21. The teeth were sensitive to percussion and palpation. Radiographic examination showed poorly obturated canals along with periapical lesions (Fig 2-A). REP was performed on 11 and 21 as it was done for Case 1. IOPAR on GP removal (Fig 2-B), on placing 3mm of MTA(Fig 2-C) and immediately after REP (Fig 2-D) were recorded.

Both the teeth were found to be asymptomatic and functional at all follow up visits, but the teeth were not responding to pulp sensibility tests. Reduction in periapical radiolucencies were observed at 9 month follow up visit (Fig 2-E,F). 12 months follow up IOPAR showed complete resolution of periapical radiolucency wrt 11 and remarkable reduction wrt 21. (Fig 2-G).

#### CASE:-3

A 15 years old female patient reported for the treatment of 11 as she had pain and discomfort for quite sometimes. She gave a history of trauma to

central incisors 2 years back for which root canal treatment had been done in both the teeth. 11 was sensitive to percussion and palpation. IOPAR (Fig 3-A) revealed over-obturated 11 with periapical radiolucency. 21 was seen to be restored with post-core and though there was a gap between post-end and GP, it was left undisturbed as the patient did not want any treatment of 21. PFM crown was placed on it subsequently. REP was performed on 11 as described earlier. All the relevant IOPAR after GP removal (Fig 3-B) and placement of scaffold, MTA and composite resin (Fig 3-C) were recorded.

The tooth was found to be asymptomatic and functional at all follow up visits. Radiographic evaluation (Fig 3- D, E, F) showed gradual reduction in the periapical radiolucencies. Calcific bridge formation and apical closure was achieved at 12 months (Fig 3-F). However the tooth didn't respond to pulp sensibility tests at any of the follow up visits

#### CASE:-4

A 30 years old male presented with pain in 11. The tooth was sensitive to percussion and palpation. He gave a history of dental caries and severe pain. Endodontic treatment was done on 11 two years back. IOPAR revealed poorly cleaned, shaped and obturated 11 with periapical radiolucency (Fig 4-A). REP was performed as had been done in previous cases (Fig 4-B, C)



FIGURE 3:- A. Overobturated 11 with periapical radiolucency. B. GP removed (arrow showing open apex). C. Immediate post-op showing placement of 3mm of MTA and composite resin restoration D, E. 6 and 9 months follow up. F. 12 months follow up IOPAR showing closure of apex (arrow) and calcific bridge formation (circle) along with remarkable reduction in peri-apical radiolucency

FIGURE 4:- A. Poorly cleaned, shaped and obturated 11 with periapical radiolucency B. GP removed C. Immediate post-op. D, E & F. 6, 9 and 12 months follow up respectively, showing reduction in peri-apical radiolucency



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The tooth was found to be asymptomatic and functional at all follow up visits. Radiographic evaluation (Fig 4-D,E,F) showed remarkable reduction in the periapical pathology. However, the tooth didn't respond to pulp sensibility tests.

## DISCUSSION

Apical periodontitis after root canal therapy is primarily caused by persistent root canal infection or root canal reinfection<sup>7.8</sup>. Microbial flora in teeth undergoing secondary root canal treatment is single species of the predominantly gram-positive organism Enterococcus faecalis<sup>9</sup>, which is resistant to almost all intracanal medicaments including calcium hydroxide and irrigation systems. But it might not be resistant to immune defense mechanisms of regenerated vital tissue after REP<sup>10</sup>.

The idea of revascularizing failed endodontically treated tooth is novel. The present case series describes the successful REPs of five previously treated permanent teeth with persistent periapical pathology using PRF as a scaffold with follow up upto 12 months.

Absence of pain, swelling or any other discomfort and bringing the teeth back to function with resolution or reduction of persistent apical periodontitis, closure of open apex (Case 1 and 3) are the signs of successful REP. Calcific bridge formation in Case-3 may have taken place by the influence of bio-material- MTA. It's effect on REP may be discernable in subsequent follow up visits.

Maintaining balance between bacterial elimination and stem cell survival through proper irrigation protocol and intracanal medication is one of the key factors to successful REP. The recommended 20ml of 1.5% NaOCl was used for 5 minutes. Though Triple Antibiotic Paste (TAP) exhibit wide spectrum of antibacterial effect, the concentration (1-5mg/ml) at which it provides adequate anti-bacterial effect without hampering the stem cell survival is difficult to achieve clinically<sup>11</sup>. On the other hand, calciumhydroxide though less effective against some intracanal bacterial species, but it's use at any concentration is associated with lower cytotoxicity to stem cells<sup>12</sup>. Moreover, it can be easily removed (approximately 80%) from the canals, unlike TAP of which greater than 80% remains within the canal  $(>350\mu$  within the dentinal tubules)<sup>13</sup>.

Blood clot is used as one of the scaffolds. It is though associated with ease of operation and minimum armamentarium, it's difficult to induce bleeding up to the level of CEJ<sup>14</sup> and placement of MTA over the blood clot is also challenging thus hampering the coronal seal.

Platelet Rich Plasma (PRP) and PRF are another two commonly used scaffold in REP.

PRP produces a very high-concentration gradient of platelets whose granules are rich in

Platelet-Derived Growth Factor (PDGF), Transforming Growth Factor (TGF- $\beta$ ), Epidermal Growth Factor (EGF), and Vascular Endothelial Growth Factor (VEGF), which are important for angiogenesis and improve tissue vascularization<sup>14</sup>. However, it's use is associated with the development of life-threatening coagulopathies due to the use of bovine thrombin for it's preparation<sup>14</sup>. Also, the effect of PRP on bone and dentine regeneration is limited as it releases 81% of total TGF- $\beta$ 1 and PDGF within 1st day with remarkable reduction at 3, 7, and 14 days such that maximum release occurs before actual cell ingrowth<sup>14</sup>.

PRF, which was used in this study, releases growth factors from its elastic fibrin mesh of unique nature in a sustained manner with the peak reaching at 14 days14 which is the time of cell growth. Growth factors important for regeneration like VEGF, TGF- $\beta$ 1, PDGF, EGF, etc which are known to promote cell migration, adhesion, proliferation and differentiation of periapical stem cells are enmeshed in PRF. This results in periapical bone regeneration, root maturation through development of pulp-dentin complex<sup>15</sup>. Since, there is no bovine thrombin administration, it is more physiologic and free of adverse reactions<sup>14</sup>.

Chemical solvents were not used for removing the previous root canal filling material to avoid associated cytotoxicity. Chloroform and other guttapercha solvents have been shown to be highly toxic in several ex vivo studies<sup>16</sup>.

The biomaterial-MTA, recommended as the plugging material by AAE<sup>17</sup> has been used in the present study. MTA (Angelus) is easy to handle and sets within the clinically acceptable time period.

No tooth in the present case series responded positively to pulp sensibility testing which may be due to the presence of thick MTA in the coronal aspect of the root<sup>18</sup>. Moreover, dentin sensitivity is related to the hydrodynamic activity of dentinal tubules in association with A- $\beta$  sensory fibers. However, histopathological study<sup>19</sup> has revealed that newly regenerated tissue does not have well-organized dentinal tubules to exhibit the same sensitivity as natural tissue.

# CONCLUSION

Under the constraints and limitations of the present study and based on the results obtained upto 12 months follow up period, it may be concluded that REP can be a viable treatment option for nonsurgical retreatment of permanent teeth.

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