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Regenerative therapy on a traumatized adult tooth with periapical lesion: A case report

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Abstract
Revitalization or regenerative therapy in teeth with incomplete root formation and pulp necrosis have become part of the curative endodontic spectrum and should be regarded as an alternative to regular apexification.
Revascularization may be considered because the stem cells present inside canal may help in closure of open apex by differentiating into cells required for root formation.
This report describes a case report of a 44-year-old male patient with an immature non vital 11 with grade 2 mobility and apical pathology which was treated via revascularization using 3% NaOCl and 17% ethylene diamine tetraacetic acid as irrigants; triple antibiotic paste as intracanal medicament and platelet-rich fibrin (PRF) as scaffold.
After 3 months the clinical examination revealed reduction in mobility to physiologic level, negative responses to percussion and palpation tests. 1-year radiographic examination revealed regression of the periapical lesion.

Keywords: pulp regeneration, open apex, triple antibiotic paste, PRF

1. Introduction
The final goal of the endodontic therapy is either to limit the development of apical periodontitis or, in cases where the infection is already existing, to create satisfactory conditions for periradicular tissue healing.
The cause of dental traumatic injuries is the position of maxillary teeth in upper jaw which makes them vulnerable to trauma. In many situations, such trauma leads to the cessation of root growth.
Immature teeth with poor crown root ratio have large root canals, wide apical foramina and thin, fracture-prone dentine walls, which make root canal preparation and predictably sealing the tooth three-dimensionally difficult [1].
For treatment of such teeth, traditionally calcium hydroxide and now mineral trioxide aggregate (MTA) or Biodentine apexification is being done so far. Nevertheless, the remaining thin dentinal walls predispose the tooth to shatter while functioning.
Hence, regeneration came into being as the recent mode of treatment. Regenerative strategies is based on the concept that vital tissue can be developed inside canal of non-vital tooth with revasularization method which will allow continued growth of root length and thickness [2].
Stem cells, scaffolds and growth factors are three important requirements for the success of this procedure. The stem cells involved in the process are those of apical papilla, periodontal ligament (PDL), pulp, and bone marrow. Growth factors or nutrients are furnished by the scaffold which helps in stem cell proliferation and differentiation heading to improved and faster tissue development [3].
Pioneer studies on regeneration used blood clot, collagen, and platelet-rich plasma (PRP) as a scaffold [4]
The traditional mode of revitalization method was done by producing bleeding into the pulp canal by mechanically provoking the periapical tissues.
In necrotic teeth with open apices, little quantity of pulp tissue with Hertwigs Epithelial Root Sheath survive apically and can proliferate once the inflammatory condition are reversed and the canal becomes disinfected. The generated blood clot acts as a matrix for the ingrowth of new tissues into the pulp canal. However, this method will cause discomfort for the patient [5] and clinically, it is a challenge controlling the speed and volume of bleeding to attain the aspired level [6]
Use of biomaterials for regenerative therapies is not a new concept. Almost two decades have passed since the utilization of platelet concentrates for repair and regeneration of the oral [7]
Platelet concentrates are autologous, reasonably simple to make in a dental environment, and contain great concentrations of growth factors including transforming growth factor-beta (TGF-beta), vascular endothelial growth factor (VEGF), and platelet-derived growth factor (PDGF [6]
Platelet-rich fibrin (PRF), a second-generation platelet concentrate, have several benefits over first generation platelet rich plasma (PRP). Firstly, the preparation of PRF does not need the addition of exogenous factors, such as thrombin. Secondly, PRF forms an ordered fibrin mesh in which platelets and leukocytes are trapped which serve as a pool of multiple growth factors for long-term release [6]
The foundation of platelet-rich fibrin (PRF) as an autologous biomaterial has established motion an interesting and assuring era in the advancement of tissue healing and regeneration.

2. Case report
A 44-year-old male patient reported with a chief complaint of a mobile discoloured anterior teeth, patient has noticed the discolouration long time ago did not seek dental treatment. Over the years, the teeth remained asymptomatic and more recently, presented with mobility and intermittent pain. Patient had a history of trauma during his childhood.
The medical history of the patient was noncontributory. Intraoral examination of his teeth revealed the presence of

grayish discoloured tooth (FIG 1) and was of grade 2 mobility. The adjacent and contralateral teeth were healthy. Tooth was tender to percussion. The periodontal examination of all teeth showed probing depths within normal limits. There was no response to cold test or electric pulp test. Further radiographic examination of the tooth revealed a wide-open apex along with thin dentinal walls that appeared prone to fracture associated with periapical radiolucency. (FIG 2)

Symptomatic apical periodontitis with necrotic pulp was the diagnosis. Although age wise this case is not indicated for regenerative procedures a clinical decision of performing treatment using Choukroun's Platelet Rich Fibrin was made as the only other option was extraction. A written informed consent was obtained from the patient.

After administration of 2% lignocaine with 1:200000 adrenaline and rubber dam application, access opening was done. The pulp chamber and root canal were mildly irrigated with 20 mL of 3% NaOCl without any mechanical instrumentation. The canal was then dried using sterile paper points. Next, an inter-appointment medication of triple antibiotic paste comprising a mixture of Ciprofloxacin (Cifran 500mg, Ranbaxy Lab, India), Metronidazole (Metrogyl 400mg, J.B. Chemicals and Pharmaceuticals, India), and Minocycline paste (Minoz 50 mg, Ranbaxy Lab, India. (1:1:1)) was prepared into a creamy consistency and introduced into the canal using a lentulospiral. A cotton pellet was placed and the cavity was temporarily sealed with cavit (Dental Products of India, India).

The patient returned after 21 days to the clinic and the teeth were re-accessed thoroughly irrigated with sterile saline solution and dried with paper points. A volume of 5mL of patient's blood was drawn from the patient's cubital vein collected in a glass test tube (FIG 3) and centrifuged under 3000 rpm for 10 minutes in centrifuge machine (REMI) (FIG 4) to obtain the PRF which was jelly like in consistency.

In the test tube PRF was the middle layer with acellular plasma at the top and red blood cell (RBC) at the bottom. (FIG 5). Using sterile tweezers, the fibrin clot was removed (FIG 6) and squeezed between 2 gauze pieces to drive out the fluids trapped in the fibrin matrix, and autologous strong fibrin membrane was obtained

The freshly processed PRF membrane was then placed into the canal opening (FIG 7) then pushed below the level of cementoenamel junction (CEJ) using finger and hand pluggers such that it reached to the apical end. 3 mm of biodentine was placed over the PRF followed by placement of GIC as a permanent restoration.

The 1-year followup showed absence of signs and symptoms and satisfactory resolution of periapical lesion (FIG 8).

3. Discussion

Regenerative endodontic procedures are defined as biologically based procedures designed to replace damaged structures, including dentin and root structures, as well as cells of the pulp-dentin complex [8, 9]

The understanding that reestablishment of vascular system within the root canal after traumatic injuries, is crucial for the completion of root development is a significant contribution that led to the shift in term regeneration to revascularization [1]

However, the term Revascularization is imprecise and takes into account only one perspective of the newly formed tissue. The term, 'revitalization', which appeared in later case reports, represents the overall fact more precisely. After that, it was suggested to use the term 'revascularization' for autotransplanted teeth and the term 'revitalization' for infection-related cases [1]

It has been reported that the remnants of Hertwig's epithelial root sheath or cell rests of Mallasez are resistant to peri-apical infections. Thus, the signaling networks from these remnant cells may stimulate various stem cells like stem cells from apical papilla (SCAP), bone marrow,and multipotent pulp stem cells to form odontoblasts-like cells in non-vital, immature and non-infected teeth. These newly formed odontoblasts-like cells form dentine which helps in normal root maturation [4].

First strategies to regenerate dental pulp date back to the 1960s, when ostby evaluated 'the role of the blood clot in endodontic therapy' [1]

In the past two decades, an increased understanding of the physiological roles of platelets in wound healing has led to the idea of using platelets as therapeutic tools. Platelet-Rich Plasma (PRP) consists of a limited volume of plasma enriched with platelets, which is obtained from the patient. However, the use of bovine thrombin for the activation of Platelet Rich Plasma (PRP) led to the evolution of the second-generation Platelet concentrate known as Choukroun's Platelet Rich Fibrin (PRF)which is an autologous leukocyte- and platelet-rich fibrin (L-PRF) biomaterial [4].

Choukroun's PRF is a fibrin mould where platelet cytokines and cells are wedged. They serve as a resorbable membrane following their release after a certain time [8]

Also, the mechanical properties of PRF might aid in the condensation of overlying biodentine which makes it an optimal bioscaffold for revitalization [6].

All manipulation inside the root canal, such as the use of irrigants and intracanal medicaments, should be considered under the proposition to create the best achievable environment for remnant HERS and apical pappila cells to execute their regenerative potential.

As for standard root canal treatment, removal of necrotic tissue and sufficient disinfection are crucial for regenerative endodontics. However, mechanical cleaning is not advised as it may weaken the thin root canal walls further and remove vital tissue remnants that might still be present in apical parts of the canal.

Recent data show failure of a revitalization procedure due to infection; thus, mechanical debridement was advised in this context as it might enhance the chance of success due to a disruption of the biofilm.[10]This decision might be taken individually, considering the thickness of the dentinal walls, presence of vital or necrotic tissue and the duration of infection [1].

For REP to be successful, it is necessary to receive a bacteria-free canal which can be done only through chemical debridement. it is noted that with increasing concentrations of sodium hypochlorite, there was decreased survival of stem cells. A concentration of 3% was used in this study to accomplish balance between maximum disinfection along with stem cell survival [2].

However, a succeeding rinse with 17% EDTA could nullify the toxic effects of hypochlorite and recover cell viability. EDTA, also release growth factors on the dentine surface, which support cell recruitment, proliferation and

differentiation. Thus, irrigation with sodium hypochlorite followed by EDTA, appears feasible [1]

Hoshino *et al*., demonstrated in vitro and in vivo that a combination of ciprofloxacin, metronidazole and minocycline efficiently eliminated diverse flora commonly found in infected root canal dentine [1]

As the maximum the release of growth factors is within the first hour, promptly following preperation of PRF, it was placed into the RC [2].

The PRF inside the root canal ideally should be 3 mm below the cementoenamel junction (CEJ) and be overlayered by a biocompatible material capable of induction of mineral formation [1].

An adequate coronal seal of the cavity to limit reinfection of the root canal can be achieved with various materials, for example composite restorations in combination with dental adhesives [1]

Predictors of a clinically succesfull regenerative endodontic method involve the absence of signs and symptoms of inflammation, radiographic data of healing periapical lesions, increased root length and canal wall thickness as a sign of continued root growth and positive response to vitality testing. Pre-existing external inflammatory root resorptions have been shown to arrest after revitalization [1]

However, whether true regeneration as regarding formation of dentin is occurring or not can only be ascertained via histology of the formed tissue [3]

The analysis that true regeneration is required to summon a treatment successful or whether repair is satisfactory is still ongoing. To date, more and more clinicians direct to a patient-based outcome evaluation and appreciate the absence of signs and symptoms of inflammation and the formation of an immunocompetent tissue inside the root canal as success [1]

Hargreaves *et al*. proposed that positive responses to pulp vitality tests after tooth revascularization/revitalization indicate the occupation of previously vacant space by innervated tissue. Johns and Vidyanath suggested that thick layers of MTA (3–4 mm) and glass ionomer cement (2 mm) might lead to negative responses to vitality testing [6]

Regenerative endodontic methods have become a viable remedial approach to save or prolong the life of necrotic, immature teeth, as well as to shield the alveolar bone and maintain optimal function in the long term [11].

Fig 1: preoperative clinical view of tooth 11 with greyish discolouration

Fig 2: preoperative radiographic view with large periapical lesion on 11

Fig 3: patients freshly extracted 5ml blood

Fig 4: REMI centrifuging machine with test tubes

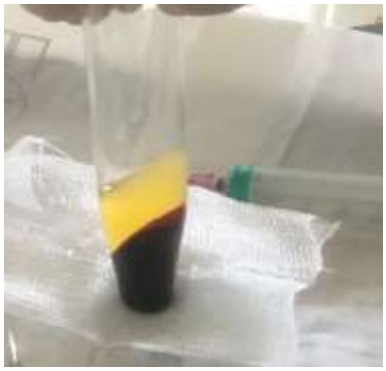

Fig 5: centrifuged blood with plasma at top, PRF in middle and RBC at bottom

Fig 6: PRF placed on a sterile gauze

Fig 7: PRF inserted into canal of 11

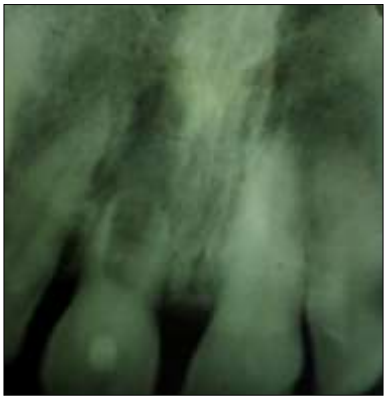

Fig 8: 1-year postoperative radiograph showing healing of periapical lesion

4. Conclusion

On the basis of the results obtained in our case report we conclude that even though there is no evident increase in dentinal wall thickness or apical closure, revitalization procedure can also be undertaken for aged patients as it helps in resolving signs and symptoms of necrotic infected immature tooth under conditions of total canal disinfection and PRF as an ideal biomaterial for pulp-dentin complex regeneration.

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