EXPLORING THE FRONTIERS OF REGENERATIVE ENDODONTICS

Abstract

Root canal treatment is one of the most common dental procedures, however it does not restore the vitality of the tooth. As the technology and scientific research in the dental field is booming, newer dental procedures to replace conventional root canal treatment are emerging, one of them being regeneration of the pulpal tissue. Techniques like pulp autotransplantation and cell homing technique have also been attempted to regenerate lost vital pulpal tissue.

This chapter briefly discusses scaffolds, stem cells, clinical considerations for regenerative endodontic treatment and its histological aspects.

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I. INTRODUCTION

The most popular method of treating pulp necrosis is root canal treatment (RCT). However, it neither restores the vitality nor the neovascularity of the pulpal tissue. Therefore, with the advancement of tissue engineering, regenerative endodontic therapy (RET) has garnered more interest [1]. RET uses tissue engineering to revascularize, innervate, and restore the odontoblastic layers and fills the cleansed canals with vital tissue as opposed to biocompatible, nonvital foreign substance eg. gutta percha being used in root canal therapy [2,3].

II. DEFINITION

Revascularization - The engraftment of regenerated pulpal tissue to host vasculature in root canals or invagination of undifferentiated periodontal cells from the apical region in immature teeth [4].

Regeneration - The replacement of damaged tissue by cells identical to the lost tissue, leading to the complete reestablishment of biological function that is, both revascularization and revitalization, including dentin, root structure and pulp-dentin complex [5].

Regenerative Endodontics (according to the American Association of Endodontists) - biologically based procedures designed to replace damaged structures, including dentin and root structures, as well as cells of the pulp–dentin complex [6].

1. **Scaffolds:** Scaffolds are essential to regenerative endodontic therapy because they create an environment that encourages the stem cell population to migrate, proliferate and undergo differentiation [7]. Blood clot revascularization is the most commonly used technique in which a K or H file is inserted beyond the apical foramen, thus inducing a periapical bleed resulting in a blood clot capable of serving as a scaffold [8].

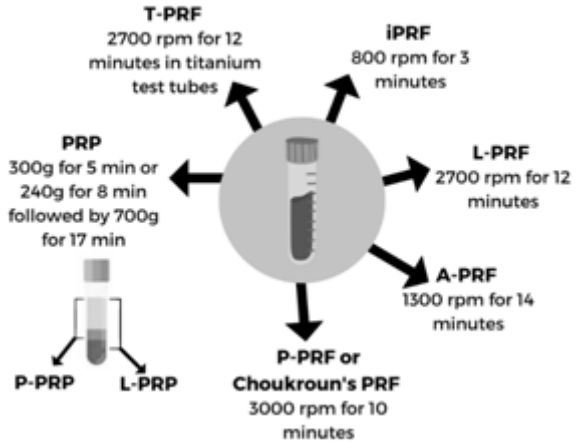

Figure 1: Various platelet products

Platelet products are commonly being used now because concentrated autologous platelets and growth factors can be extracted from the plasma and they replicate the final

stage of the coagulation cascade. The inclusion of leukocytes was done for their immunological and antimicrobial capabilities, role in the healing of wounds by control of regional factors, release of growth factors and promoting cell division [9]. Variable centrifugal time periods and rate, chemical alterations, and choice of supernatants and precipitates have led to the synthesis of several formulations of fibrin network configurations, white blood cell content and cytokines, resulting in different physical and physiological properties of platelet products and its applications [10

2. **Stem Cells :** Stem cells are an intriguing biological foundation for regenerative therapies due to their capacity for self-renewal. Mesenchymal populations are assumed to be the source of dental stem cells. The most prevalent dental stem cells are: Dental pulp stem cells (DPSC), stem cells from exfoliated deciduous teeth (SHED), stem cells from apical papilla (SCAP) and those from periodontal ligament. From the standpoint of endodontic regeneration, DPSC are multipotent cells that can transform into osteoblasts, adipocytes, and neural cells [11]. Its applications are supported by their inherent role in the generation of odontoblasts that produce reparative dentin. Transplantation of DPSC acquired from teeth with irreversible pulpitis necessitating root canal therapy is another method to achieve effective pulp regeneration in the clinical outlook. The simplicity with which DPSCs may be obtained from extracted or discarded teeth [FIGURE 2] makes them an exciting source of autologous cells, while their resemblance to cells of the bone marrow suggests that they may even have uses in musculoskeletal regenerative medicine [12].

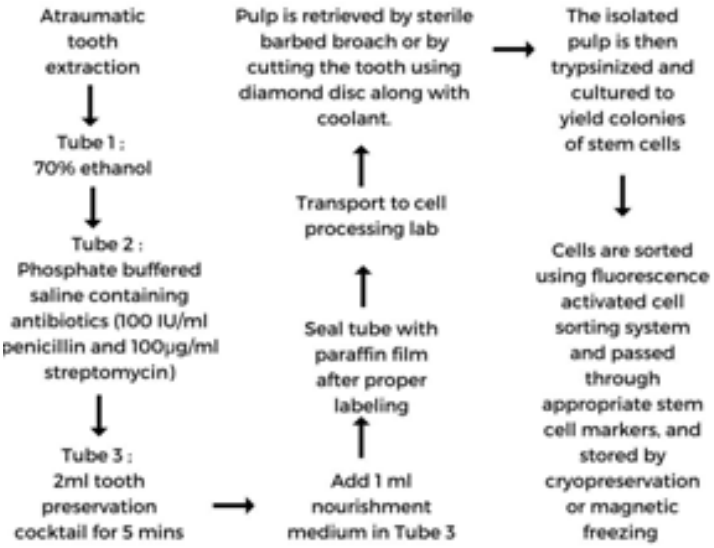

Figure 2: Steps to obtain DPSC

III. CLINICAL CONSIDERATIONS FOR REGENERATIVE ENDODONTICS –

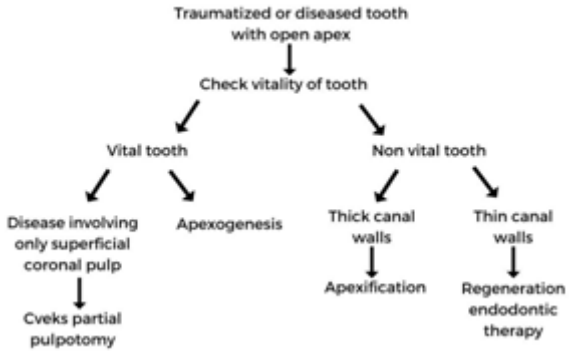

Figure 3: Case selection

Case selection is crucial when selecting treatment procedure for a specific pulpal disease [Figure 3].

Criteria for RET:

1. **Degree of Infection in the Canal -** If the canals are effectively disinfected (using triple antibiotic paste (TAP), double antibiotic paste (DAP), calcium hydroxide or formocresol) and the coronal access is effectively sealed, regenerative endodontic treatment should occur.
2. **Apex Diameter -** 1.1 mm or larger (Now a days, RET is also being performed on teeth with a mature apex)
3. **Patients age – 8 to 16 years** [13] [Figure 4]: Specific disinfection and irrigation protocols are required in order to entirely eliminate tissue remnants and bacteria in the root canal. [14].

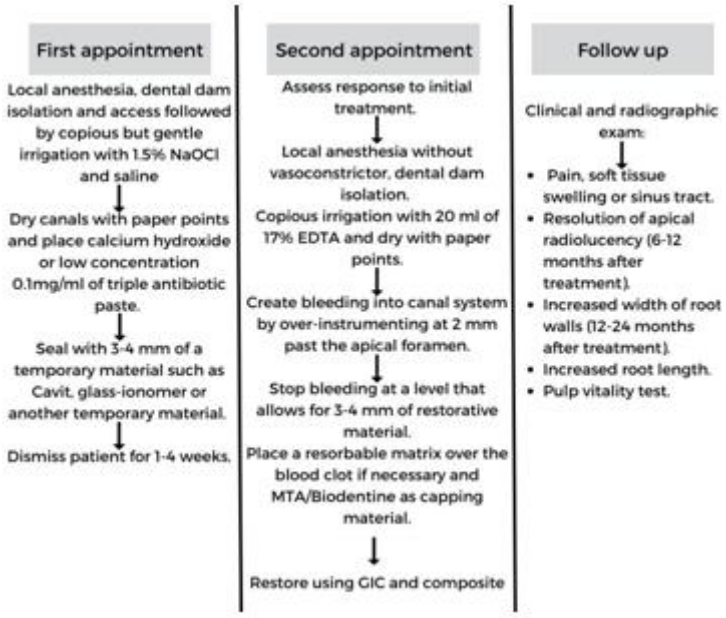

Figure 4: Standard protocol for RET according to American Association of Endodontics

TAP consisting of ciprofloxacin, metronidazole, and minocycline was suggested by Hoshino et al. in 1996 to decontaminate the canal and can successfully be used in RET [15]. Contrastingly, Chueh et al. demonstrated calcium hydroxide to completely cleanse the canal and promote regeneration [16]. Bose et al. conducted a global analysis of RET cases in 2009 which concluded that RET with the TAP, calcium hydroxide, and formocresol significantly increased root length and width. However, TAP substantially increased dentin wall thickness without altering root width [17].

4. **Drawbacks of TAP:** According to Ding et al., two patients experienced pain following the administration of TAP and thus, were not included in the study. As reported by Jung et al., utilising TAP resulted in a chronic sinus tract and when switched out for calcium hydroxide, and the patient's problems subsided [18,19]. Minocycline, one of the ingredients in TAP, is the main contributor to tooth discolouration, claim Kim et al. Through dentinal tubules, minocycline can enter the tooth and combine with the tooth's crystal structure. Before applying the TAP, the coronal dentin wall can be sealed with flowable composite resin. The other procedure is retrograde antibiotic filling with a 20 gauge needle to reduce contact with the coronal area of the tooth. According to case studies, cefaclor and amoxicillin can be substituted for minocycline. However, amoxicillin can cause allergic reactions as a side effect [20].

Double antibiotic paste is thought to be an efficient medication for removing harmful germs from root canals since it contains both metronidazole and ciprofloxacin. The problem of tooth discolouration brought on by the presence of minocycline in the TAP formulation is currently being addressed in endodontics with DAP [21].

IV. OTHER METHODS OF REGENERATIVE ENDODONTICS

1. **Pulp Autotransplantation:** The ideal "scaffold" for DPSC differentiation in their natural habitat might be produced by transplanting the complete pulp. Additionally, majority of the nerves and vessels are already developed, which facilitates the revascularization of grafted pulp tissue. Overall, this approach modality might be achieved in clinical settings without the necessity for an extension of the in vitro DPSC laboratory [22].

2. **Cell Homing Technique:** Cell homing technique is based upon the biological principles of typical tissue wound healing. Cell recruitment and differentiation are two discrete biological processes that need to take place. Over-instrumentation results in bleeding, which is used to start cell homing therapy. Endogenous cells and growth factors required for RET are present in the blood clots that follow, filling the pulp space, as well as a biological structure supporting cellular activity [23].

V. HISTOLOGICAL ASPECT OF RET

Investigations on animals showed that platelet concentrates do not produce healthy, sound pulp tissue; instead, they generate bone-like tissue in the root canal [24]. Numerous histological investigations regarding regenerative endodontic treatments have demonstrated that the tissues developed in the root canal space were mineralized akin to cementum and bone as well as fibrous connective tissue similar to periodontal ligament [25]. Without histological proof, radiographic thickening of the canal walls and ongoing root maturation of

young permanent teeth with necrotic pulps following regenerative endodontic operations should not be interpreted as the regeneration of dentin-pulp complex [26].

VI. CONCLUSION

The goal of tissue engineering via regenerative endodontics is to re-generate the pulp-dentin complex of immature young permanent teeth thereby resuming root formation. RET has been able to meet the main objectives of root canal therapy that are: to treat apical periodontitis in addition to eradicating the patient's clinical signs, symptoms and indicators. Although further development of the root is unpredictable, RET has the prospective to encourage further root formation as opposed to apexification.

Instead of pulp-like tissue, RET has shown to grow periodontal-like tissues in the canal space. Despite the vitality of the tooth being restored, the biological functions of dental pulp cease to exist. Nevertheless, young permanent teeth with necrotic pulpal tissues can be effectively and consistently treated with RET, resulting in patient-focused results like tooth preservation, symptom-free conditions, and appealing aesthetics.

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