Introduction

The most popular method of treating pulp necrosis is root canal treatment (RCT). However, standard therapy does not restore the vitality of injured pulp or restore the neovascularity. 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].

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].

Scaffolds

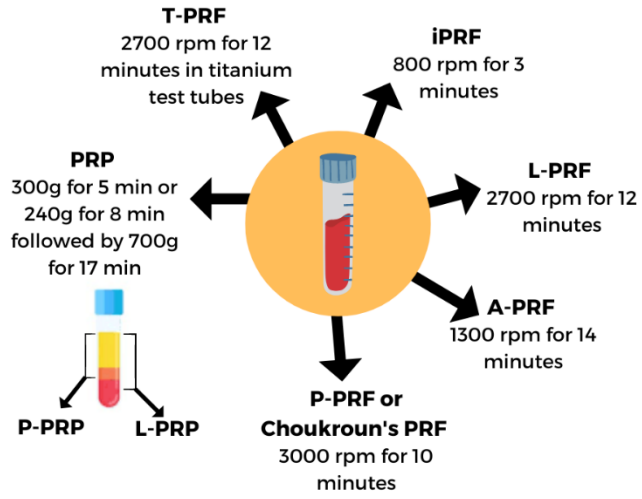

Figure 1: Various platelet products

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]. The most widely used revascularization technique is blood clot revascularization in which an endodontic file is inserted into the root canal beyond the apical foramen, inducing bleeding from the periapical tissue resulting in a blood clot that can act as a scaffold [8].

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]. Various preparations with different fibrin network structures, leukocyte content, and growth factors have been produced based on differences in centrifugation speeds and times, the addition of chemicals, and the

selection of supernatants and precipitates, resulting in different physical and physiological properties of platelet products and its applications [10] [FIGURE 1].

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. Dental pulp stem cells (DPSC), stem cells from exfoliated primary teeth, stem cells from apical papilla and periodontal ligament are some of the most prevalent dental stem cells. From the standpoint of endodontic regeneration, DPSC are multipotent cells that can transform into osteoblasts, adipocytes, and neural cells [11].

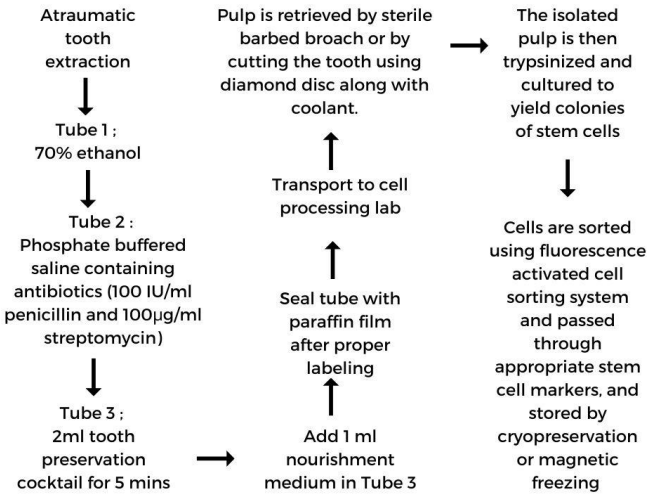

Figure 2:Steps to obtain DPSC

Its applications are supported by their inherent role in the generation of odontoblasts that produce reparative dentin. Transplantation of dental pulp stem cells obtained 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].

Clinical considerations for regenerative endodontics –

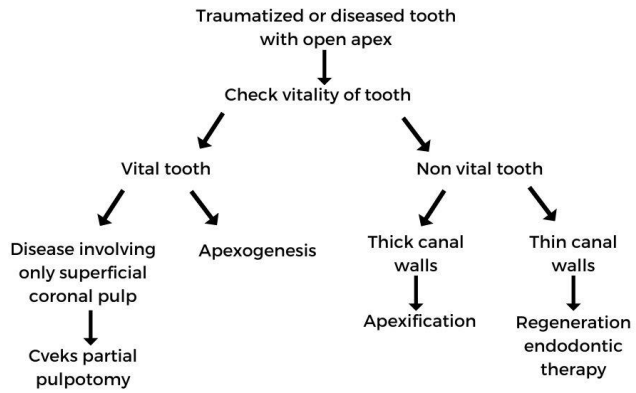

Figure 3: Case selection

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 were effectively disinfected (using triple antibiotic paste, double antibiotic paste, calcium hydroxide or formocresol) and the coronal access was 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 mature apex)

3. Patients age – 8 to 16 years [13] [FIGURE 4]

In order to completely remove the leftover tissues from the root canal area and be able to get rid of the germs, specific disinfection and irrigation techniques are needed [14].

A triple antibiotic paste (TAP) consisting of ciprofloxacin, metronidazole, and minocycline was suggested by Hoshino et al. in 1996 to disinfect the canal; this medication can be used successfully in regenerative endodontic treatment [15]. On the other hand, Chueh et al. demonstrated that calcium hydroxide alone can completely cleanse the canal and promote regeneration [16]. Bose et al. conducted a global analysis of RET cases in 2009. When compared to the control group, RET with the triple antibiotic paste, calcium hydroxide, and formocresol significantly increased root length and width. Nevertheless, there were no appreciable variations in root length across the three groups of medications. In comparison to the other two medication groups, the triple antibiotic paste considerably increased dentin wall thickness without altering root width [17].

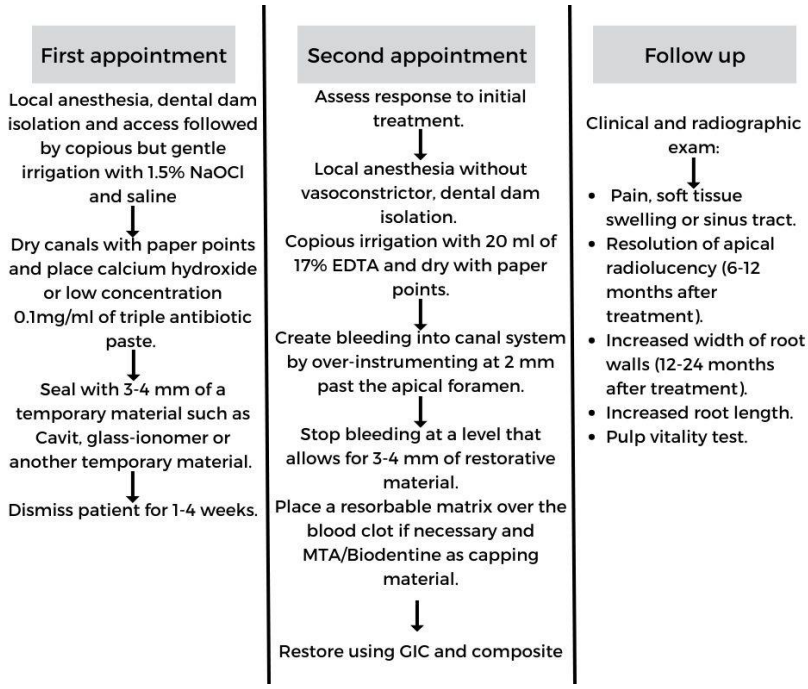

Figure 4: Standard protocol for RET according to American Association of Endodontics

Drawbacks of TAP:

According to Ding et al., two patients experienced pain following the administration of the triple antibiotic paste; as a result, they were not included in the study. As reported by Jung et al., utilising triple antibiotic paste led to the establishment of a chronic sinus tract. The intracanal medication was switched out for calcium hydroxide, and the patient's problems subsided [18,19]. Minocycline, one of the ingredients in the triple antibiotic paste, 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 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].

Other methods of regenerative endodontics -

- **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].

- **Cell homing technique -**

The cell homing method is based on the physiological 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 tissue engineering are present in the blood clots that follow, filling the pulp space, as well as a biological structure supporting cellular activity [23].

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].

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