

Research on the current situation of regenerative pulp surgery

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Abstract. Regenerative dental pulp therapy uses the principle of biological tissue engineering to replace the damaged dental pulp tissue with living tissue and repair the complex of dental pulp and dentin, so as to restore the normal function of dental pulp dentin structure. For root canal therapy, it is a new type of alternative therapy. In front of it, the treatment is divided into two types: cellular pulp regeneration therapy and acellular pulp regeneration therapy. Cellular regeneration is based on exogenous stem cell transplantation and acellular regeneration is based on endogenous stem cell homing. This paper reviews the latest progress in the treatment of regenerative dental pulp at home and abroad.

Keywords: regenerative pulpectomy, Cell homing, stem cell transplantation.

1. Introduction

When dental caries gradually change into deep caries over time, resulting in irreversible infection of dental pulp or pulp necrosis, we need to formulate a reasonable treatment plan for patients according to the need to retain the affected teeth, such as root canal therapy, acellular regenerative pulp therapy and dental implant technology. In contrast, pulp regeneration may help to prolong the life of teeth. The treatment of acellular regenerative dental pulp includes cell homing and pulp revascularization. The treatment of cellular regenerative dental pulp includes stem cell transplantation.

2. Pulp revascularization

The traditional treatment of pulpitis and periapical periodontitis is root canal therapy. With the development of Biomedical Engineering, IWAYA et al. First proposed dental pulp revascularization in 2001^[1]. The division and regeneration of tissue cells is still an area of exploration. At present, relevant scholars have defined stem cells as: cells are regenerative and permanent, and their own cells produce more than one kind of progeny cells in the process of differentiation, which has a high degree of differentiation^[2]. These cells exist in many parts of the tooth body: dental pulp, apical mastoid and periodontal ligament^[3]. For dental pulp cells, their potential has multiple differentiation characteristics. They not only have the ability to form mineralized nodules, but also can differentiate into other cell types under the induction of various cytokines, such as liver, muscle, fat, cartilage, vascular endothelium and nerve cells^[4]. Pulp revascularization is to establish the blood flow channel of the root canal system about 1-2cm away from the root in vitro under sterile conditions, so as to promote periapical blood circulation and restoration regeneration and form a biological scaffold. At the same time, periodontal ligament, dental papilla mesenchymal stem cells and dental pulp stem cells should be protected. By inducing differentiation to form cementum cells and dentin cells, the thickness and length of teeth also increase with the development of root compression. Revascularization is a new method for the treatment of pulp necrosis of young permanent teeth. It is intended to replace the inflamed / necrotic pulp tissue with regenerated pulp tissue. The known indications of pulp revascularization: young patients with periapical diseases of permanent teeth, especially for patients with abnormal central cusp and patients with crown fracture and pulp exposure.

3. Advantages of pulp revascularization over root canal therapy

Dental pulp tissue is located in the dental pulp cavity. It has the functions of providing nutrition, protecting teeth from potential danger, generating secondary and tertiary dentin, repairing, defense and protection, absorbing, sensing and forming dentin cells. For young permanent teeth, root canal therapy is a challenge for doctors because the apical foramen are not closed after pulp necrosis. Root canal therapy is to disinfect and expand the root canal after removing the necrotic nerve in the dental pulp, and fill the root canal with special medicinal filler. Generally, after root canal treatment, the affected teeth will be more vulnerable to microbial infection, leading to pulpitis or periapical diseases. When removing the infected tissue around the root canal and periapical, first pay attention to clean up the residue, and then fill the root canal tightly. However, after this series of operations, the dental pulp will lose blood supply and nutritional supply, which can not stimulate the narrowing of the apical hole and the increase of the thickness of the root canal wall, which will lead to the slow metabolism. Therefore, the affected teeth will become extremely fragile or even discolored, prone to tooth cracks and other diseases, resulting in shorter tooth life. What are the advantages of pulp regeneration as an alternative to root canal therapy? The root growth of young permanent teeth is affected by trauma, caries and other factors, resulting in: ① the root stops growing and the apical hole is too large to completely seal the root tip, resulting in the continuous invasion of bacteria into the root tip; ② The root canal wall is fragile, which is prone to root fracture; ③ The tooth root becomes shorter, which is easy to cause tooth loosening and falling off. The purpose of this treatment is to eliminate inflammation, seal the root tip and maintain root growth, so as to retain most of the functions of the teeth. The regeneration of dental pulp in revascularization can restore the function of most dental pulp, retain the anatomical structure of the original teeth, and make the affected teeth close to the level of normal teeth after treatment. It can not only make the teeth grow continuously, but also improve the toughness of the root. The effects of periodontal cells and active tissues were also preserved. Two points should be achieved before the implementation of pulp regeneration: ① effective disinfection of root canal; ② The size of apical hole is appropriate. At present, stem cell transplantation and cell homing technology are used for root canal repair.

4. Process and clinical effect of cell homing

At present, cell homing technology is one of the most commonly used dental pulp revascularization technologies. This technology usually refers to injecting a biological scaffold material with stem cell chemokine into the root canal cavity, using chemokine to promote the transfer of stem cells in periapical tissue to the root canal, so as to separate dentin and dental pulp, so as to achieve the purpose of dental pulp regeneration^[5]. Since there is no need to isolate and process stem cells in vitro, the cell homing strategy is easier to achieve clinically than cell transplantation^[6]. Three clinical steps of cell homing: ① disinfection in root canal and apical expansion; ② Bioactive scaffold implantation and dental restoration using signal molecules; ③ Check the vitality of regenerated dental pulp regularly. The transplanted cells can transfer, proliferate and differentiate through scaffolds. The size of the apical hole should be determined during the operation, and the apical hole should be as small as possible without affecting other operations. At the same time, it is also very necessary to select appropriate scaffolds and combined growth factors. Cell homing can be used as an effective substitute for dentin derived growth factor in scaffold materials, and can induce endogenous cells to produce dental pulp tissue^[7]. Research shows that the tissue growing into the root canal after operation is the tissue containing blood vessels, nerves, periodontal ligament, cementum and alveolar bone, which is not completely pulp regeneration, but tissue regeneration is more accurate. Revascularization is also a kind of autologous stent implantation, which comes from the blood clot of periapical tissue. At present, autologous platelet rich plasma PRP and platelet rich fibrin PRF are used clinically. At present, the safety and effectiveness of synthetic chemokines in human experiments need to be further tested, and there are some difficulties in preclinical research.

5. Process and clinical effect of stem cell transplantation

In the process of dental pulp regeneration, stem cells were isolated and operated in vitro. Then, the cells were loaded on scaffolds bound to signaling molecules and transplanted into the root canals of isolated or in situ teeth. The formation of pulp like tissue (connective tissue with angiogenesis and dentin like tissue deposition) was observed in many experimental studies^[8,9]. Concentrated growth factors (CGF) are the third generation platelet concentrates. CGF uses a special centrifuge to release more growth factors after platelet fragmentation through variable speed centrifugation. The tensile strength and adhesion of fibrin are better than those of previous blood agglutinates, and can form a three-dimensional network structure of fibrin. This porous structure protects the growth factor from hydrolysis, makes the growth factor release slowly and continuously, provides a physical scaffold for cell growth, and promotes cell attachment, migration and differentiation^[6]. At present, CGF has been used in orthopedics, stomatology and other regenerative medicine. CGF can significantly reduce the medullary stage at the operation site and improve the medullary rate.

5.1. Stem cell transplantation steps

① Open the marrow and uncover the roof; ②. When cleaning the root canal and medullary cavity, normal saline and sodium hypochlorite should be used alternately; ③. Triple antibiotic paste (metronidazole + ciprofloxacin + minocycline) should be used when sealing the medullary cavity; ④. The fistula disappeared after about two weeks; ⑤. Puncture bleeding, embedding with MTA and injecting glass ions; ⑦. Follow up every 3 months and 2 years.

5.2. result

At present, a large number of clinical trials have been carried out on autologous dental pulp stem cell transplantation at home and abroad, and good repair results have been achieved. The results showed that the dental pulp tissue obtained from autologous third molars or deciduous teeth could be cultured in vitro, and then transplanted into the dental pulp cavity, so as to repair the dentin and dentin complex, realize the redistribution of nerve fibers, and restore the sensory function of dental pulp. However, the research on the source of dental pulp stem cells and their biosafety is still facing great challenges, which is far from reaching large-scale clinical application.

6. Case screening

1. Because the stem cells in adolescents have good differentiation ability, most patients have differentiated in adulthood, and it is difficult to differentiate in multiple directions. Therefore, for young permanent teeth aged 9 ~ 18, pulp regeneration is the best choice.

2. systemic diseases such as lupus erythematosus, nephrotic syndrome, or chronic diabetes, long-term use of hormones can damage the immune system.

3. Anesthesia drug allergy, (if the patient has a history of anesthesia allergy, antibiotics are required during root canal disinfection. Pay attention to antibiotic allergy and the selection of antibiotics)

4. Patients with inconvenient treatment (pulp reconstruction requires multiple follow-up observation)

5. Root condition: apical X-ray examination showed that the root was short, the root canal wall was thin, and the apical hole was open. When the diameter of apical foramen > 0.5 mm, the blood supply of dental pulp can be restored, while when the diameter of apical foramen is greater than 1.0 mm, the root still has good growth. Current treatment options should only target immature teeth.

6. Dental pulp condition: it usually refers to permanent teeth with complete pulp necrosis and incomplete apical foramen. Neither living pulp nor residual living pulp can be used for treatment.

7. Periapical condition: the appearance of periapical disease indicates pulp necrosis and large inflammation in root canal. The relationship between periapical lesions and pulp regeneration has not been fully understood. For patients with incomplete apical foramen, the lesions in the apical region will cause changes in the local microenvironment, which will affect the stem cells and cytokines in

the apical region. However, so far, most successful cases are periapical lesions. The correlation between periapical injury and pulp repair needs further clinical and controlled experiments.

8. Periodontal condition: the dental pulp repair treatment effect of patients with periodontal injury may have a certain impact. Therefore, patients without periodontal disease and with appropriate crown root ratio after treatment should be selected.

7. Conclusion

The advantages of regenerative pulp therapy are: 1 All are autologous material transplantation, which reduces the possibility of rejection; 2. Most of dental pulp function was preserved; 3. Continue to develop young permanent teeth and make them closest to normal teeth; 4. Eliminate peripheral inflammation; 5. Prolong the life of permanent teeth. According to clinical data, mesenchymal stem cell therapy is safe and reliable, and there are no obvious adverse reactions to patients. A few patients will have local discomfort, transient low fever and other symptoms. The main indication is pulp necrosis of young permanent teeth. Most of the patients are teenagers or teenagers. The pulp tissue has rich blood vessels, vigorous vitality and strong repair ability. Compared with root canal therapy, it can provide a better life for young people in the future. However, at present, the application of this operation is still not as popular as traditional root canal therapy. It is expensive and time-consuming, and has higher requirements for doctors. It is believed that in the near future, with the development of stem cell engineering, this technology can be widely and skillfully used to reduce the pain of patients. "Clinical considerations of pulp regeneration therapy" was published by the American dental pulp Association in 2012. Its main purpose is to standardize the clinical operation. The article was revised in 2018. Subsequently, the clinical operation specifications on pulp regeneration were issued by the expert committee of the European Association of dental pulp diseases (ESE) in 2016^[10]. With the maturity and recognition of the technology, its clinical application has achieved great success.

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