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Original Research

Pulp Regeneration with Stem Cells

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Abstract:

Introduction: The immature root with a necrotic pulp and apical periodontitis presents multiple challenges to successful treatment. These challenges are overcome by using a disinfection protocol that does include minimal root canal instrumentation, stimulating the formation of a hard tissue barrier or providing an artificial apical barrier to allow for optimal filling of the canal, and reinforcing the weakened root against fracture during and after an apical stop is provided.

Materials and Methods: The present pilot clinical study was undertaken to evaluate the efficacy of revascularization in 25 cases of infected, immature teeth. Endodontic treatment was initiated, and after infection control, revascularization was performed. The access cavity was sealed with composite resin. The cases were followed up at regular intervals of 3 months and 6 months.

Results: Overall, the response to revascularization procedure could be rated as very satisfactory.

Conclusion: Although current treatment modalities offer a high rate of success, an ideal form of therapy should aim at regenerating the diseased pulp tissue rather than devitalizing it. Stem cells are considered most valuable for regeneration. A multidisciplinary approach is required for making this treatment modality a success.

Key Words: Pulp regeneration, stem cells, tissue engineering

Introduction

Dental pulp has multiple functions in the homeostasis of teeth, and maintenance of the function of pulp tissue is critical for the longevity of teeth. The ideal approaches for endodontic treatment are conservation of healthy tooth structure, prevention of microleakage from the pulp cavity, and maintenance of the properties and mechanical strength of the tooth structure. Stem cell therapy with pulp stem/progenitor cells is a useful strategy to regenerate the dentin-pulp complex. Innervation and vasculature of the dental pulp are intimately associated with pulp homeostasis, and restoration of blood supply and nerve supply both are essential for pulp regeneration.[1]

By definition, the pluripotency is the capacity of cells to produce several discrete genetic responses whereas multipotency means the capacity to make different types of cell fates. Recent advances in the tissue culturing have led the researchers to test the possibility of tooth production and regeneration.[2]

In view of the increasing demand for maintaining pulp vitality and the high cost of endodontic treatments being performed every day, there has been increasing interest in investigating new methods for tissue replacement. With the expanding knowledge of developmental biological processes, and how they are mimicked during dental tissue repair, strategies to regenerate lost or diseased dental tissue will soon enter into clinical practice.[3]

Tissue engineering is a science based on the principle of triad that involves the detection of suitable cells, the development of conducive scaffolds, along with unique morphological signals essential for cells to regenerate a specific tissue.[4]

The pulp tissue contains stem/progenitor cells which under specific influence differentiate into odontoblasts. There are two techniques to regenerate dentin. In the first method, specific molecules (bone morphogenetic proteins) are directly applied to the exposed pulp. In the second methodology, the procedure consists of isolation of stem from the pulp tissue, which are induced into odontoblasts and finally transformed to regenerate dentin.[5]

Dental stem cells display high differential potential to give rise to three different types of cell lineages: Odontogenic, adipogenic, and neurogenic.[6]

Among all the techniques of pulp regeneration root canal revascularization technique has been supported with clinical evidence. This view has been supported with 25 case histories which adopted root canal revascularization and regeneration concept.

Materials and Methods

1. Few cases were presented with fractured tooth in the upper front right side teeth region. The tooth didn't respond to

pulp vitality tests. The teeth were diagnosed with non-vital pulp and symptomatic apical periodontitis. The IOPA showed wide canals with open apex.

2. After carrying out the vitality tests,few cases were diagnosed with non-vital pulp and symptomatic apical periodontitis. The IOPA showed wide canals with open apices in few teeth. Few cases had recent history of trauma. In all the cases the root canal revascularization treatment was decided. Informed consent was obtained.

First visit: Under rubber dam isolation and local anesthesia administration, the access cavity was prepared. The canal was instrumented minimally with copious amount of 1.25% sodium hypochlorite and dried with sterile paper points. Intracanal medicament, calcium hydroxide was placed inside the canal and temporization was done. The next visit was scheduled after a week.

Second visit: After a week the patients were asymptomatic. Under rubber dam isolation and local anesthesia, temporary filling was removed, intracanal medicament was removed and irrigated with normal saline. The canal was over instrumented and bleeding was created into the canal. Then MTA was mixed according to manufacturers recommendations and was placed in the canal till CEjn. After 1 h GIC base was given above which tooth was restored with composite restoration.

Follow up visit (after 1 week): The patients were asymptomatic. The teeth were within normal limits regarding percussion and palpation.

Follow up visit (after 3 months): The patients remained asymptomatic. The teeth were within normal limits regarding percussion and palpation.

Follow up visit (after 6 months): The patients remained asymptomatic. The teeth were within normal limits regarding percussion and palpation. Radiographic examination revealed continued apical development and closure, narrowing of the canal space.

Case selection is important in the treatment protocol. The size of the apical opening should be sufficient to allow ingrowth of vital tissue.

Results

The individual details of these cases are summarized in Table 1 and Table 2. The follow-up of the cases ranged between 6 months to 3½ years. One case could be followed up for 3½ years, 3 for 2 years, 2 for 18 months, 5 for 12 months, and 3 for 6 months. The striking finding was complete resolution of clinical signs and symptoms and appreciable healing of periapical lesions. Thickening of lateral dentinal walls could be appreciated and increased root length was observed. None of the cases presented with pain, reinfection, or radiographic enlargement of preexisting apical pathology. Overall, the response to revascularization procedure could be rated as very satisfactory.

Table 1: Root canal revascularisation in children aged between 8-15 yrs group for single canal teeth

Sl no	Patient age	Tooth number	Treatment	Disinfection
1.	9 yrs	21	Root canal revascularisation	Calcium hydroxide disinfection for two weeks
2.	9.5yrs	22	RCR	Same as above
3.	10 yrs	21,22	RCR	Same as above
4.	10.5 yrs	11	RCR	Same as above
5.	11 yrs	11	RCR	Same as above
6.	9 yrs	13	RCR	Same as above
7.	10.5 yrs	31	RCR	Same as above
8.	13 yrs	34	RCR	Same as above
9.	16 yrs	35	RCR	Same as above
10.	10 yrs	21	RCR	Same as above
11.	8 yrs	21	RCR	Same as above
12.	14.5 yrs	11	RCR	Same as above
13.	11 yrs	21,11	RCR	Same as above
14.	11 yrs	12	RCR	Same as above
15.	12.5 yrs	11,12	RCR	Same as above
16.	13 yrs	22	RCR	Same as above
17.	12.5 yrs	12	RCR	Same as above
18.	11 yrs	11,21	RCR	Same as above
19.	8.5 yrs	12	RCR	Same as above
20.	10.5 yrs	13	RCR	Same as above
21.	9.5 yrs	44	RCR	Same as above
22.	14 yrs	35	RCR	Same as above
23.	15 yrs	21	RCR	Same as above
24.	14.5 yrs	11	RCR	Same as above
25.	11	12	RCR	Same as above

RCR: Root canal revascularisation

Discussion

Stem cells have the ability to continuously self-replicate or to produce specialized cells of different lineage thus showing multilineage differentiation. These are considered to be most essential for regenerative procedures.[7]

Dental stem cells obtained from different parts of the teeth. The first stem cells isolated from adult human dental pulp were termed dental pulp stem cells (DPSCs). They are isolated from permanent third molars and exhibited high proliferative rate. Stem cells isolated from exfoliated deciduous teeth stem cells from human exfoliated deciduous may induce bone formation. Stem cells from the apical part of the papilla are a type of stem cells present at the root apex. Periodontal ligament (PDL)-derived stem cells are derived from PDL and have differentiation prospective similar to connective tissue stem cells and DPSC. Dental follicle progenitor cell can be isolated and grown under specific tissue culture conditions to form precursor bone cells.[8]

Tooth engineering – approaches

Dental cell/tissue re-associations - In these types of experiments, cells/tissues of dental origin are dissociated and subsequently

Table 2: Root canal revascularisation for a period ranging from 24 h to 6 months

Intracanal plug	Permanent restoration	Follow up after 24 hours	Follow up after 3 months	Follow up after 6 months
3 mm of MTA plug at CEjn	GIC base followed by composte resin restoration	Clinically asymptomatic, responses within normal limits to percussion	Clinically asymptomatic, responses within normal limits to percussion, radiographic features showing continued development of root apex	Clinically asymptomatic, responses within normal limits to percussion, radiographic features showing continued development of root apex and flecks of radioopacitiesthrough out the canal at different levels
3 mm of MTA plug at CEjn	GIC base followed by composte resin restoration	Clinically asymptomatic,responses within normal limits to percussion	Clinically asymptomatic,responses within normal limits to percussion,radiographic features showing continued development of root apex	Clinically asymptomatic,responses within normal limits to percussion,radiographic features showing continued development of root apex and flecks of radioopacitiesthrough out the canal at different levels
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MTA: Mineral trioxide aggregate, CEJN: Cementoenamel junction, GIC: Glass ionomer cement, DPSL: Dental pulp stem cells, PDL: Periodontal loigament, IOPA: Intraoral periapical radiograph

re-associated to demonstrate the ability of dissociated cells to re-unite and reform the tooth.[9]

Recombination of inducing dental tissues/cells with inducible progenitor cells. The concept of using dental tissues to induce stem cells has proved that the engineered tooth might be formed with contribution of different stem cells.[9]

Induction of odontogenic potential by molecular and other factors instead of using cells, the induction of odontogenic properties may also be achieved by different stimuli like molecular factors. The influence of distinct molecular players has already been studied in the odontogenic differentiation.[9]

Several systems for tooth tissues engineering have been developed.

Scaffolds for DPSCs

Cells require interactions with their microenvironment to survive, proliferate, and function. In living tissue, extracellular matrix proteins perform this function. In tissue culture, biodegradable and biocompatible scaffolds are used.

They provide an appropriate environment for differentiation of these cells. Eventually, the host cells begin to secrete and shape their own microenvironment. Thus, scaffolds are a significant component of tissue engineering.[2]

Role of vascular supply in tooth tissue regeneration

Vasculogenesis is defined as *de novo* formation of blood vessels. Angiogenesis is the progression of new blood vessel formation from pre-existing vasculature. While vasculogenesis plays an important role in embryonic development, angiogenesis is critical in postnatal physiological responses.

In the perspective of the dental pulp, it is well-known that conventional pulp treatments like direct pulp capping activate wound healing events that are supported by an elegantly regulated angiogenic response. In the dental pulp, endothelial cell injury is resolved by recruitment of odontoblast-like cells.[2]

Conclusion

Stem cell-based dental tissue regeneration is a new field that has the potential to change the way that we practice dentistry.[10,11] The field of stem cell-based regenerative dentistry is an upcoming venture, which will change the future of dental practice. Only by good cooperation and coordination between various experts and advancement toward the aim of developing biological approaches to regenerate dental histological tissues can be fulfilled.

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