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REVIEW ARTICLE

REGENERATIVE ENDODONTICS: AN INSIGHT

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ABSTRACT:
Endodontic treatment involves salvaging the structure and function of a tooth at the expense of the pulp that is sacrificed in the beginning. Regenerative endodontic have been thought to overcome this short coming by replacement of pathologic pulpal tissue with vital tissue. Literature quotes studies which show that hematopoietic and neural stem cells show increase in number of multipotent clones in hypoxic conditions as compared to normoxic cultures. At same time, hypoxic environment also enhances cell survival and increases the proliferation of multipotent precursors. This review highlights some of the interesting aspects of regenerative endodontics.
Key words: Regenerative Endodontics, Revascularization

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INTRODUCTION

With the advances in the field of science and technology, all the field of human life, including dental care has drastically prospered. Reality has crossed the level of imaginations in terms of the word 'Regeneration' in medical field. Repair of teeth and regeneration of lost teeth is one the promising area which regenerative therapy focuses on. The main focus of ongoing researches in regenerative endodontic is its different practical aspects and feasibility in different fields.[1]

The conflicting view in this subject is that pulp loss also does not compromise the structural and functional integrity of the tooth. Pulp treatment in case of immature permanent teeth is particularly important because it ensures complete root development and closure of apical foramen. Over the years, apexification by calcium hydroxide has been successful and main line of treatment for root formation in immature teeth.[2] Although apexification induces root completion; vitality of the pulp cannot be restored.[3] Regenerative endodontic have been thought to overcome this short coming by replacement of pathologic pulpal tissue with vital tissue. [4]

HISTORICAL ASPECT

G.L.Feldman was the first talk on regeneration of tooth in 1932. After that, regeneration of cementum and dentin was experimentally demonstrated in animals by Gavrilov in 1957.[5]

In 1961, Ostby postulated that pulpal regeneration formed the key for successful root canal procedures.[6] Further research in the field of regeneration was carried out by Rule et al, Ostby et al. and Hjortdal et al.[7,8] Further breakthrough in this field was the concept of 'revascularization' Iwaya *et al* in 2001 that led to thickening of walls of root canal and continuation of development of incomplete root portion.[9] The turning point in the field of regenerative endodontics is often considered by the works of Banchs and Trope who established protocols for revascularization clinically.[10]

RESEARCH IN THE FIELD OF REGENERATIVE ENDODONTICS MAINLY FOCUSES ON FOLLOWING AREAS: [11]

ADULT STEM CELLS

Stem cells are the cell of origin for all the tissue of the body. By definition, a stem cell refers to the cells with capacity if continuous division for the purpose

of self replication or for production of highly differentiated, more specialized cells or tissues.[12]

Due to minimal adverse effects, cells which fulfil all the requirements and stand up to the mark for pulpal regeneration are the autologous postnatal stem cells. They are found in almost all tissues of the body and principally, four dental stem cells of humans have been isolated, namely; Dental pulp stem cells, Stem cells from Human exfoliated deciduous teeth, Stem cells from apical papillae and periodontal ligament stem cells.[13-16]

One of the terminally differentiated cells of dental origin is the Odontoblasts that cannot proliferate to replace permanently damaged odontoblasts. Phenomenon of reparative dentinogenesis gives clue for occurrence of distinct small population of competent progenitor pulp stem cells inside the pulpal tissue. For the development of regenerative endodontics, studies must focus on the pathway be which these cells detect and respond to tooth injury. Animal products as usually chosen as media for growing stem cell lines.[11, 17] Literature quotes studies which show that hematopoietic and neural stem cells show increase in number of multipotent clones in hypoxic conditions as compared to normoxic cultures. At same time, hypoxic environment also enhances cell survival and increases the proliferation of multipotent precursors.[18]

GROWTH FACTORS

Growth factors are cellular proliferation and differentiation inducing proteins. While one hand, some of these growth factors are quite versatile, others are more cells specific. Recombination of various types of Bone morphogenic proteins (BMPs) mostly 2,4 and 7 in vitro induced formation of reparative dentin.[19] By promoting by adhesion, supporting cellular proliferation and by inducing migration of human mesenchymal stem cells, MTA induces useful cellular response to achieve suitable tissue wound healing. Mesenchymal stem cells are usually involved in tissue and bone remodeling, and local environment is thought to play an important role in the commitment and differentiation of mesenchymal derived stem cells. [20]

RECOMMENDATIONS FOR REGENERATIVE ENDODONTIC TREATMENT

For the benefit of the patients and for favorable treatment outcome, guidelines are necessary to ensure that regenerative endodontic procedures are used on teeth. In cases where there are chances of failure of the regeneration technique, it should be not used to avoid patient sufferings. In 1996, to collect regenerative endodontic cases, the American Association of Endodontists (AAE) established a database in which more than 100 cases have been collected to date, but the AAE has not yet established guidelines from the database. The American Dental Association (ADA) in 2010 provided the first treatment codes for regenerative endodontic procedures; for apexification/recalcification, codes are D3351–D3354. Following are the terminologies used more often to describe regenerative endodontic procedures; direct pulp capping, revascularization, apexogenesis, apexification etc.[21, 22]

SCAFFOLDS

Microstructure and chemical composition required for normal cell growth and function forms the ideal requirements of materials which are required for the construction of matrices to engineer tissue in-vivo. In case of regeneration of bone tissue, the materials should have similar physical, chemical and mechanical properties since all these features will influence normal bone cell growth and function.[23]

Purposes of most of craniomaxillofacial reconstructive procedures are done construct missing or damaged skeletal structures and restore their functions. Distant donor site is required from which bone or soft tissue can be harvested to complete operations. Outcomes of such operations from donor sites are greater morbidity than the primary reconstructive procedure and there are chances that there may not be adequate quantities of bone available for harvesting in children. Also, the remodeling process results in bone graft loss, the amount of which varies. Initially, the tissue engineering utilizes harvesting of progenitor or stem cells, expanding and then, differentiating them into cells that have potential to form new tissue (e.g. bone) or organ (e.g. tooth). Scaffolds are used to seed the harvested cells. Fabrication of construction of these scaffolds is fabricated in the laboratory to resemble the structure of the desired tissue or organ to be replaced.[24]

POSSIBLE MECHANISMS OF REVASCULARIZATION[25]

There is a possibility that at the apical end of the root canal, there may remain a few vital pulp cells which may at some point of time proliferate into the newly formed matrix and can, under the organizing influence of cells of Hertwig's epithelial root sheath, further differentiate into odontoblasts, which are quite resistant to destruction and inflammatory processes.[26] Multipotent dental pulp stem cells in the immature permanent teeth represent another possible mechanism of continuing root development.[27] Stem cells in the periodontal ligament also represent another mechanism which can proliferate, grow and deposit hard tissue at the walls of the root portion.[28, 29] Survived stem cells from the apical papilla can also lead to root development .[29]

LIMITATIONS

In cases of permanent tooth which are fully formed, it is difficult to achieve regeneration completely.

Consequences which might occur in such procedures like discoloration of the crown portion, staining of the tooth due to bacterial products, adverse affects of solutions used as medicaments in the canal space. There are chances of re-infection of the tissue which can further lead to necrosis and treatment failure. For successful treatment to occur, the concentration of stem cells in the fibrin clot has to be uniform. Any biasness in this can lead to treatment failure.[28]

FUTURE PROSPECT OF REGENERATIVE ENDODONTICS

Ongoing researches on regenerative endodontic strategies are continuously being added to knowledge and practice of dentistry. American Association of Endodontists Foundation awarded more than one and half a million grants for evaluation of the effectiveness of two regenerative approaches compared with the conventional MTA apexification. One such clinical trial on pulpal regeneration has been started by Misako Nakashima (Japan). Also, recently, platelet-rich fibrin box has been announced to produce homogenously thickened hydrated exudates rich in platelets, vitronectin, leukocytes, and fibronectin expressed from the fibrin clots that have improved the issues regarding the handling of the - platelet-rich fibrin clot.[29- 31]

CONCLUSIONS:

Researchers are going on in the field of regenerative endodontic which have created new horizons for creation of restorative biomaterials, tissue engineering, tissue grafting, molecular biology etc. All these are techniques are taking dentistry to a whole new level. For the development of complete regenerative endodontic pulpal therapies, understanding of the basic knowledge of molecular science, stem cells, and tissue engineering is required.

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