ORIGINAL RESEARCH PAPER

Paediatrics

REGENERATIVE ENDODONTICS , FUTURE IN PEDIATRIC DENTISTRY

KEY WORDS: Regeneration , Pulp Therapy , Stem cells

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ABSTRACT

Regenerative endodontic treatment may encourage continued root development and thus, is a suggested alternative technique for management of traumatized immature permanent teeth with pulp necrosis. On the other hand, ideal treatment method for necrotic immature premolar teeth has not yet been determined. The main advantages of revascularization technique over the traditional apexification or artificial barrier technique in endodontic treatment of immature necrotic teeth include continuation of root development and strengthening the root structure.

INTRODUCTION

Regenerative endodontics is the creation and delivery of tissues to replace diseased, missing, and traumatized pulp. Regenerative Endodontics originated as part of research that is aimed at unlocking the therapeutic potential of stem cells, growth factors, molecular biology and the human genome. Regenerative endodontic procedures can be defined as biologically based procedures designed to replace damaged structures, including dentin and root structures, as well as cells of the pulp-dentin complex.

The potential approaches include root-canal revascularization, postnatal (adult) stem cell therapy, pulp implant, and scaffold implant, three- dimensional cell printing, injectable scaffolds, and gene therapy. These regenerative endodontic techniques will possibly involve some combination of disinfection or debridement of infected root canal systems with apical enlargement to permit revascularization and use of adult stem cells, scaffolds, and growth factors.[1]

It is recommend that, during the revascularization therapy, infected root canals should be treated as conservatively as possible. In the standard protocol, a root canal is irrigated with 2.5-5.25% NaOCl, and no instrumentation is applied. After canal disinfection, medicament is inserted into the root canal and is removed after 3-4 weeks. Although, previous studies have reported successful use of a triple antibiotic paste to eliminate infection in root canals of open apices teeth with apical periodontitis, the antibiotic paste is not commonly used due to esthetic concerns, as the paste causes minocycline induced tooth discoloration.[2]

Tissue Engineering: The aim of gene-enhanced tissue engineering is to regenerate lost tissue by the local delivery of cells that have been genetically-enhanced to deliver physiologic levels of specific growth factors. The basis for this approach lies in the presence of a population of progenitor cells that can be induced, under the influence of these growth factors, to differentiate into the specific cells required for tissue regeneration, with guidance from local cues in the wound environment.[3] The overall goal of tissue engineering is the functional restoration of tissue structures as well as the maintenance of the natural environment, and thus the viability and function of the damaged tissue due to disease or trauma.

Potential Application: Potential applications for gene-based tissue engineering therapies in the oral and maxillofacial complex include:

1. The delivery of growth factors for periodontal regeneration
2. Pulp capping/dentin regeneration,
3. Treatment of malignant neoplasm of the head and neck,
4. Regeneration for bone grafting of large osseous defects in dental and craniofacial reconstruction (e.g. Bone augmentation prior to prosthetic reconstruction, fracture repair, and repair of facial bone defects secondary to trauma, tumor resection, or congenital deformities),
5. Articular cartilage repair.[4]

Conventional techniques for inducing pulpal repair: Calcium hydroxide has long been the "gold standard" for pulp capping. Its effectiveness at promoting dentinal bridge formation over small pulpal exposure sites is believed to be related to a combination of antimicrobial activity (attributed to high pH) and its ability to stimulate tertiary dentin formation (attributed to the release of calcium ions). Recently, mineral trioxide aggregate (MTA) has been proposed as an alternative to calcium hydroxide for pulp capping. In vitro and in vivo studies suggest that MTA may be more effective at inducing dental hard tissue formation than calcium hydroxide, possibly via a physicochemical reaction in which released calcium ions react with tissue phosphates to form hydroxyapatite.[5]

Potential applicability of any dental hard tissue regenerative protocol could include the regeneration of an entire missing tooth or the regeneration of specific components of an otherwise viable tooth (e.g. a decayed tooth with early pulpal involvement). The lack of any enamel forming cells in the enamel of fully developed erupted teeth precludes the potential for cell-based approaches for enamel regeneration.

In contrast, the regeneration of dentin is feasible because dentin is in intimate contact with an underlying highly vascular and innervated pulpal tissue, forming a tightly-regulated "dentin-pulp complex". During primary tooth formation, dentin is produced by odontoblastic cells located within the pulp. Following tooth eruption, the secretory activity of these cells is down-regulated, although they continue to produce secondary dentine at a low level. Pulpal tissue retains a limited potential to repair itself following various insults. These healing stages in the pulp resemble those of other hard tissues. Depending on a number of poorly defined factors, surviving post-mitotic odontoblastic cells can secrete tertiary dentin, a process known as reactionary or reparative dentinogenesis, or, alternatively, perivascular progenitor cells in the pulp can be triggered to differentiate into odontoblastic-like cells under the influence of specific growth factors.[6]

Stem Cells: Stem cell biology is a new field, which is advancing at an incredible pace with new discoveries being reported from all over the globe. Stem Cells are unspecialized cells, can divide and renew themselves for long periods of time and become specific specialized cell types of the body. Pluripotent stem cells from embryos and fetal tissue possess the ability to repair or replace cells or tissues that are damaged or destroyed by many of our most devastating diseases and disabilities.[7]

An adult stem cell is a multipotent cell, still capable of differentiating into only a few specialized cells. Evidence suggests that, given the right environment, some adult stem cells are capable of being "genetically reprogrammed" to generate specialized cells that are characteristic of different tissues. This phenomenon is termed adult stem cell plasticity or trans-differentiation.

Source of Stem cells: The source to procure the stem cell, the amount to be infused, the route of infusion of the cells, the age of the patient at therapy and so also the concentration of stem cells

being used, are all important considerations. How- ever, very little knowledge is available to answer these is- sues. It is presumed that the newborns and more so the infants produce better quality and concentration of stem cells. Embryonic cells and the placental blood from the umbilicus at the time of birth are the best sources, if anticipated in advance or in mothers with high-risk pregnancy.[8]

To achieve higher level of concentration at the site of the target organ, the stem cells need to be either infused through the arterial supply or injected locally. The actual therapy to infuse would vary for various surgical conditions. To direct the stem cells to Liver in infants, we have used hepatic artery (20%) and the portal vein (80%). In cases with spina bifida, we have injected stem cells in the epidural space and also directly in the defective spinal cord during surgical repair of the defect.

ORBO – AIIMS Central facility for storage Facilities for storing of stem cells for future use are one of the important issues at present. In the European countries, apart from the initial storage cost (Euro 10.000/-), the monthly maintenance is around Euro 100/-.[9] The AIIMS has again taken the lead and is presently the third country after South Korea and England, establishing the Stem cell banking facility at the Organ Retrieval and Banking Organization (ORBO) at AIIMS. Samples would be preserved at around minus 186 degree Celsius in liquid nitrogen. Preservation of the embryonal cells for its possible future use is also in pipeline.[10]

Future scope: Future Applications include the exploration of the effects of chromosomal abnormalities in early development. This might include the ability to monitor the development of early childhood tumors, many of which are embryonic in origin. Another future use includes the testing of candidate therapeutic drugs. Stem cells are likely be used to develop specialized liver cells to evaluate drug detoxifying capabilities and represents a new type of early warning system to prevent adverse reactions.

Embryonic stem cells undoubtedly will be the key research tools for understanding fundamental events in embryonic development that may explain the causes of birth defects and approaches to correct or prevent them. An- other important area of research that links developmental biology and stem cell biology is the understanding, the genes and molecules, such as growth factors and nutrients that function during the development of the embryo. So that these can be used to grow stem cells in the laboratory and direct their development into specialized cell types.[11]

During the coming years, embryonic stem cells and adult stem cells will be compared in terms of their ability to proliferate, differentiate, survive and function after transplant, and how can we avoid the immune rejection. The process of research is still ongoing and predicting the future of stem cell application is not possible at this stage. However, current challenges are to direct the differentiation of embryonic stem cells into specialized cell populations and also to devise ways to control their proliferation once placed in patients. Only further research and its wider clinical application will solve many practical and theoretical queries related to the use of stem cells.

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