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Tissue Engineering- A New Aspect in Periodontal Regeneration

Sakshi Malhotra[1]

1 *MDS, Department of Periodontics, Post Graduate Institute of Dental Sciences, Rohtak, Haryana, India*

Abstract

The goal behind periodontal treatment is to accomplish regeneration of tissues affected by periodontal disease. Periodontal regeneration is the restoration of original architecture and function of periodontal tissue. Tissue engineering is a way to repair or restore human tissue. It may provide a promising approach to regenerate complex periodontal tissue. Strategies to tissue engineering are conductive approach, inductive approach and cell transplantation approach. The main aim of this review is to explain the available tissue engineering products, their importance and their advantages in terms of periodontal regeneration reported in the literature. Furthermore, we emphasize on recent advances in tissue engineering, gene therapy and nanotechnology.

Keywords: Mesenchymal stem cells, Regenerative medicine, Tissue engineering.

INTRODUCTION

Tissue engineering constitutes principle of biology and engineering that lead to formation of functional substitute for damaged tissue. For tissue regeneration in the field of periodontics, Langer in 1993 proposed tissue engineering. Strategies to tissue engineering are conductive approach, inductive approach and cell transplantation approach. Conductive approach facilitates regenerative capacity of existing tissue. It utilises biomaterial in a passive manner. Inductive approach utilises scaffold as a vehicle to deliver growth factor or genes. Cell transplantation approach transplant cells and partial tissue to host site. Key components of tissue engineered construct are cells, instructive messages, scaffold, and blood supply.

CELLS FOR TISSUE ENGINEERING

Cells harvested for tissue engineering may be autologous, allogenic or heterologous. Undifferentiated progenitor or stem cells are ideal for periodontal tissue engineering. Stems cells are characterised by their self-renewal potential and are pluripotent whereas undifferentiated progenitor cells are descendant of stem cells with more committed differentiation status. An animal study by Lang et al 1998, showed that cultured autologous periodontal ligament cells may favour regeneration *in vivo* [1]. A human clinical case report by Yamada et al., showed that bone marrow mesenchymal stem cells along with platelet rich plasma resulted in reduction in intrabony defect depth [2].

Cell sheet technology has been introduced by Matsurra et al [3]. This technology harvests complete sheet of cellular material and extracellular matrix and cell-cell junction remains intact. It utilises temperature sensitive polymer biomaterial in a cell culturing process unlike traditional enzymatic approach.

SCAFFOLD

Scaffolds are classified as natural and synthetic scaffold. According to Bartold et al, it serve as framework, which maintain shape of the defect and serve as a 3D substrate for cell migration, proliferation and production of extracellular matrix [4].

Multiphase scaffold has also been utilized. These are characterised by the different pore organisation and chemical composition. Lee et al. utilises polycaprolactone-hydroxyapatite scaffold [5]. It has 3 phases- 100micron channels in phase A- for cementum interface, 600 micron channels in phase B - for periodontal ligament, 300 micron channels in phase C- for alveolar bone. Factors delivered in different phases were human amelogenin, bone morphogenic protein-2 and connective tissue growth factor.

***Corresponding author:**
Dr. Sakshi Malhotra
MDS, Department of Periodontics, Post Graduate Institute of Dental Sciences, Rohtak, Haryana, India
Email: sakshi1828@gmail.com

Upon 4 weeks in vitro incubation resulted in formation of distinctive tissue phenotypes in each compartment.

BIOLOGIC MEDIATORS

- Platelet derived growth factor (PDGF)

It is consist of 2 peptide chains termed as A and B chains. It binds to two cell membrane tyrosine kinase receptors and exerts its biologic effect. Lynch and coworkers 1991 first discovered in an animal study that it promote regeneration of periodontal tissue [6]. Nevins et al 2003 reported regeneration in intraosseous defects using PDGF and demineralized free dried bone allograft [7]. It is chemotactic and mitogenic for periodontal ligament cells, mesenchymal cells in cell culture, and osteoprogenitor cells. It stimulates synthesis of gingival fibroblast hyaluronate, which is essential for formation of proteoglycans. It promote angiogenesis, complement the action of vascular endothelial growth factor. Commercially available as GEM 21S.

- Bone morphogenetic protein (BMP)

Multifunctional polypeptide belong to transforming growth factor-B superfamily of proteins. First extracted from bovine bone by Marshall Urist. It binds to type I and type II receptors that function as serine threonine kinase to bring their biologic effect. Bower et al 1991, tested osteogenin in human periodontal defects reported enhance osseous regeneration [8]. It helps in differentiation of undifferentiated pluripotent cells into bone forming cell. Along with basic-fibroblast growth factor it stimulates angiogenesis and alkaline phosphatase activity. Commercially available as INFUSE (rh-BMP-2 on an absorbable collagen sponge).

- P-15

15- amino acid peptide is analogous to cell binding of alpha chain of type 1 collagen. Yukna et al used bio-oss in combination with P-15, showed enhance bone regeneration results [9]. It enhances rate of attachment and migration of periodontal ligament cells on root surface. Commercially available as PEPGEN-15.

- Enamel matrix derivatives

Purified enamel matrix proteins retrieved from porcine developing enamel have been used for periodontal tissue engineering. Rationale behind using enamel matrix proteins is that amelogenins secreted by hertwigs epithelial root sheath induces acellular cementum formation during tooth development. Heijl and coworker compared use of enamel matrix derivatives and placebo in 1 and 2 walled defect, reported that use of enamel matrix derivatives resulted in better clinical attachment level gain [10]. It is osteopromotive not osteoinductive because it stimulates bone formation when combined with demineralized freeze dried bone allograft. It stimulates proliferation of immature progenitor cells and differentiation of mature bone cells. Commercially available as Emdogain.

- Platelet concentrates

First generation platelet concentrate includes platelet rich plasma (PRP) and second generation is platelet rich fibrin (PRF). Whitman berry in 1997 first promoted the use of platelet rich plasma in oral surgery with the purpose to activate vascularisation of graft. It improves soft tissue healing and bone regeneration. Furthermore, it reduce postoperative morbidity. PRP combined with grafts for treatment of intrabony defects yielded contradictory results [11-13]. Disadvantages of first generation platelet concentrates are preparation protocol is expensive, complicated and need for animal thrombin as a coagulant raises legal issues. Platelet rich fibrin was investigated to overcome the disadvantage of PRP. Introduced by Choukroun and coworker in 2001. Components of PRF include 1. Highest concentration of platelets-platelet cytoplasm contain several granules, which contain cytokines, serotonin, von willebrand factor stimulate cell migration and proliferation into fibrin matrix at time of activation 2. Highest concentration of growth factor (PDGF, VEGF, TGF)-initiate wound healing by activating macrophage, fibroblast and endothelial cells. 3. A representative concentration of fibrin, fibronectin- form a biochemical structure with trimolecular junction and favours the entrapment of cytokines and glycosaminoglycans. 4. Approximately 65% of leukocytes-first cells to start neoangiogenesis, mesenchymal stem cells [14].

RECENT ADVANCES IN TISSUE ENGINEERING

- GENE THERAPY

According to Kinane et al 2015, it is the genetic modification of cells for therapeutic purpose. Genetic information to the target cells is transferred, to enable protein synthesis. To overcome the issue related to growth factors delivery at site (short half – life) and to ensure sustained release , gene therapy has been introduced. Jin et al reported, gene transfer of PDGF-B stimulates tissue regeneration at periodontal defect *in vivo* [15]. transceschi et al investigated gene transfer of rh-BMP-2 for bone formation [16].

- NANOTECHNOLOGY

Introduced by Norio taniguchi and popularised by Eric Drexler. There are four generations of nanotechnology -1st is passive nanostructure, 2nd generation active nanostructure, 3rd Robotics and 4th Molecular nanosystem. Properties of nano materials are components less than 100 nm in at least one direction, significant size effect and surface effect. It has an important property of self -assembly.

Applications of nanotechnology in tissue engineering are nanofibers - commonly used as tissue engineered scaffold, it provides larger surface area per unit mass. Chen et al utilise nanotechnology for dental enamel formation (biomimicry) [17].

LIMITATIONS OF TISSUE ENGINEERING

It is expensive. Furthermore, role of inflammation, existing cytokines and growth factors must be considered when evaluating tissue engineering methods. Having correct factor at appropriate time, at effective concentration and proper duration are other issues related to this.

CONCLUSION

The ultimate goal behind treating periodontal defects is to restore the original architecture and function of the tissue. Different biologic mediators are available now a days. Thorough search of literature revealed their applicability in field of periodontics. Clinical practitioners should be aware of ongoing researches and they should implement this knowledge to provide best treatment possible to the patients.

Conflict of Interest

None declared.

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