ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Tissue Engineering in Periodontal Regeneration.

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ABSTRACT

Periodontal diseases occur due to various factors which includes plaque, calculus and it is characterized by inflammation of the periodontal tissues, loss of attachment. Periodontal regeneration refers to the complete recovery of the periodontal tissues. Periodontal healing is the most complex process because it occurs in a contaminated area, under bacterial load and the occlusal forces on the teeth affects the healing process. Many techniques have been used for regeneration of the periodontal tissues like bone grafts and tissue membranes. Natural healing can lead to tissue scarring. Tissue engineering is the new emerging field of science for fabrication of new tissues in replacement based on principles of cells. In tissue engineering, the extracellular matrix, stem cells, and molecular signals are the three important factor to be considered.
Keywords: Periodontitis, regeneration, tissue engineering.

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ISSN: 0975-8585

INTRODUCTION

Periodontitis is a common inflammatory disease leading to loss of teeth. It is characterized by progressive destruction of the bone supporting apparatus, including gingiva, alveolar bone, periodontal ligament and root cementum, if left untreated it can lead to loosening and subsequent loss of teeth [1,2]. The successful treatment starts with establishing excellent oral hygiene followed by the removal of bacterial plaque and calculus to control inflammation and stop progressive bone loss. Regeneration of periodontal tissues is a complex phenomenon required interplay between various processes in a timely manner. Tissue engineering was proposed as a possible technique for regenerating lost periodontal tissues by Langer and colleagues in 1993 [3].

Tissue engineering

Tissue engineering is defined as the science of fabrication of new tissues for replacement and regeneration of lost or destroyed tissues. It is an inter-disciplinary field that applies principles and methods of engineering and life sciences towards the development of biological substitutes that restore, maintain, and improve the function of damaged tissues and organs [4]. To manage the periodontal defects the regenerative medicine has developed tissue engineering which could overcome the limitations of the available methods [5-10] like bone grafts. Tissue engineering has involved the combination of cells, engineering materials and suitable biochemical and physiochemical factors to improve or replace biological functions [5-7,11]. Tissue engineering approach to bone and periodontal regeneration combines three key elements to enhance regeneration are conductive scaffolds, signalling molecules and stem/progenitor cells [12]. The main goal of the this approach is to bring the capacity of the periodontal tissues to be active functionally and physiologically to respond the mechanic cues. Regeneration occurs through recapitulation of key events which includes cellular migration, proliferation/apoptosis, differentiation, inductive/inhibitory interaction and periodontal tissues morphogenesis [14,11,13]. The three key elements is necessary to reproduce this developmental sequence of events [figure 1].

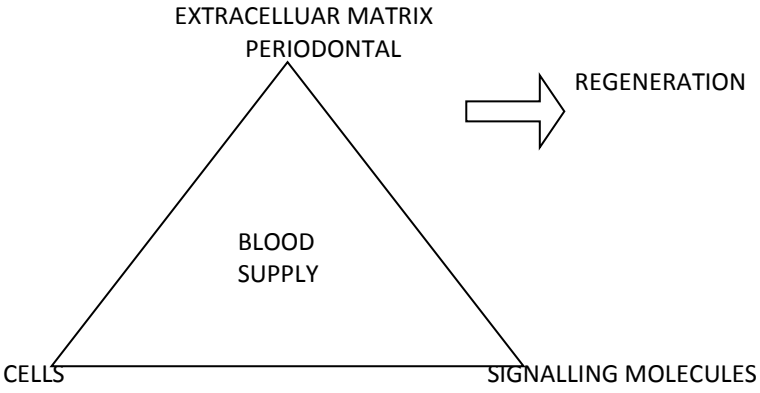

Figure 1: The Tissue Engineering Triad

Extracellular matrix

The scaffold provides a complex 3D environment in which cells can reside, proliferate, differentiate and form a functional tissue with a desired shape. The synthesis and deposition of extracellular matrix largely occur in response to growth factor, cytokines, and mechanical signals mediated via cell surface receptors.

Scaffolds are porous, degradable structures fabricated from either natural materials like collagen [14-18] fibrin[19,20] or synthetic polymers like polyglycolide, polylactide and polylactide coglycolide [20,21]. They can be sponge like sheets, gels or highly complex structures with intricate networks of pores and channels fabricated using new material processing technologies. Enamel matrix proteins are commercially available as Emdogain.

Scaffolds are intended to degrade slowly after implantation, being replaced by new tissue [22]. It can also be designed to release growth factors that induce cellular differentiation and tissue growth in vitro or cell

migration into the wound site in vivo. Hydrogels are new class of biomaterials that could potentially be injected into the periodontium. These biomaterials are composed of viscous polymer made of synthetic or natural hydrophilic macromolecules [23,24,20].

The extra cellular matrix/ scaffolds should fulfill the following requirements [19,23,20].

- Interconnected micropores for cell migration and in-growth
- Optimal porosity with adequate surface area and mechanical strength and
- Controlled absorption kinetics and degradation.

Signaling molecules

Signaling molecules are proteins that may act locally or systematically to affect the growth and function of cells in various manners. Growth factors and morphogens act by altering the cell phenotype that is by causing the differentiation of stem cells into bone forming cells, a process commonly known as osteoinduction.

Growth factors are biologically active polypeptide hormones that affect immune function as well as differentiation of cells from the epithelium, bone and connective tissues [25]. In periodontal tissue engineering, of particular importance are PDGF, IGFs, FGF, TGF-B and those that regulate the epithelial mesenchymal interactions involved in initial tooth formation. PDGF and IGF-1 enhance regeneration when combined [26-30]. TGF-B is chemotactic for fibroblasts and cementoblasts and promotes fibroblast accumulation and fibrosis in the healing process.

Platelet rich plasma (PRP) presents a new approach in tissue regeneration and a developing area for clinicians and researches. It is a component of autologous whole blood isolated after the centrifugation of the plasma. PRP acts as a source of growth factors including PDGF and TGF-B both of which appear to be critical growth factors involved in periodontal regeneration [33,32,26]. PRP stimulates the proliferation of human osteogenic cells and perodontal ligament cells. The easy application of platelet rich plasma in the clinic and its possible beneficial outcome, including reduction of bleeding, rapid soft tissue healing, and bone regeneration hold promise for new treatment approaches [34,35].

Bone morphogenic proteins (BMP) were originally identified in extracts of bone matrix by their capacity to induce endochondral bone differentiation in heterotopic sites. It is noteworthy that there was morphogenesis of periodontal ligament and a faithful insertion of sharpey's fibres into cementum. These proteins are known to possess the unique ability to induce cartilage and bone formation. They play a role in blood vessel formation. The hallmark property of the BMP is the differentiation factor in which undifferentiated mesenchymal cell differentiate into an osteoblast. Studies provide an important insight that space provision appears critical to draw clinically significant benefits from a construct.

- rhBMP2 has been combined with ACS astellocollagen sponge.
- rhBMP2 has also been used in a DFDBA / fibrin clot barrier.
- rhBMP2 and calcium phosphate cement matrix [36,37].

Cells

Stem cells are immature progenitor cells capable of self renewal and multi-lineage differentiation through a process of asymmetric mitosis that leads to two daughter cells, one identical to the stem cell and one capable of differentiation into more mature/progenitor cells.[38] it can be totipotent, pluripotent, and multipotent. Both tissue specific cells and stems have influence on the success of the tissue engineering

Autologous cells appear the most appropriate for tissue engineering as their activity remains high whereas allogenic and xenogenic cells are immunogenic and would likely require adjunctive immunosuppressive therapy [24,39].

Due to difficulties encountered in isolating specialized cells and the associated morbidity involved, stem cells served as a better alternative. On the basis of their potency to differentiate, stem cells can be classified into embroyonicstem cells and post natal stem cells [40]. During periodontal regenerative procedures the remaining healthy periodontal ligament , PDL derived cells plays a key role in the regeneration of new compartments. The regenerative capacity of the periodontal ligament itself attributed to a few progenitor cells maintaining their proliferation and differentiation potential in the periodontium [6].

The clinical application of autologous PDL derived cells can be challenging due to [41,42]

- Insufficient cell availability
- Difficulties in harvesting
- Time consuming cell culture
- High quality laboratory conditions
- Possible viral infection that may accompany the fetal calf serum, which is most commonly used in cell culture.

CONCLUSION

The older methods of repairing the periodontal tissues were based on infection control. The newer technologies are introduced in the field of regenerative medicine to overcome the limitations of the older methods. Tissue engineering is the new technique for regenerating lost periodontal tissues. It promotes complete healing, tissue's structure and function, more qualitatively, more quickly and less invasive.

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