

BRIEF REPORT

Autologous Stem Cell Application in Periodontal Regeneration Technique (SAI-PRT) Using PDLSCs Directly From an Extracted Tooth...An Insight

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Periodontal regeneration represents the ultimate goal of periodontal therapy. The current regenerative techniques have limited success rates especially in advanced periodontal defects. Currently the research is focused on novel cell-based approaches for periodontal regeneration to overcome the limitations of existing treatment. The human clinical trial on stem cells based periodontal regeneration is promising. The plethora of animal studies provide sound evidence to support the belief that periodontal ligament stem cells (PDLSCs) can be used for periodontal regeneration. The direct application of autologous periodontal stem cells in treatment of intrabony defects is attempted for the first time in periodontal literature. Stem cell Application in Periodontal Regeneration Technique (SAI-PRT) using direct PDLSCs has overcome the limitations and concerns of ex- vivo stem cell culture methods like high cost, technique sensitivity, loss of stemness during cell passage, genetic manipulation and tumorigenic potential. Clinical feasibility, success and cost effectiveness over currently available techniques are encouraging. The clinical utility of this novel idea is recommended.

Keywords: Periodontal ligament progenitors, Regeneration, Periodontitis

Introduction

Periodontitis is an inflammatory disease and is the most common cause of tooth loss in adults. World Health Organization (WHO) has reported that 10~15% of the world populations suffer from severe periodontitis (1) moreover 50% of Indian population suffers from periodontitis (2). Periodontitis manifests clinically as loss of supporting structures including periodontal ligament and

alveolar bone. Following cause-related therapy, periodontal regeneration represents the ultimate goal of periodontal therapy which aims at re-formation of all components of the periodontium: gingival connective tissue, periodontal ligament, cementum and alveolar bone lost during the disease process.

Periodontal tissue regeneration and Stem cell therapy

Periodontal regeneration is especially challenging, as it requires predictable regeneration of three quite diverse and unique tissues (e.g., cementum, periodontal ligament, and bone) and a triphasic interface between these different tissues to guarantee the restoration of their complex structure (3, 4). The current regenerative techniques have limited success rates especially in advanced periodontal defects. In the view of this, current research is focused on novel cell-based approaches for periodontal regeneration

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to overcome the limitations of existing treatments.

Langer in 1993 proposed tissue engineering as a possible technique for regenerating lost periodontal tissues (5). This field consolidates materials science and biocompatibility, and integrates cells, natural or synthetic scaffolds, and specific signals to create new tissues. Tissue engineering represents one of the most sensational advances in regenerative medicine. However, there is scarcity of literature dealing application of tissue engineering for regeneration of periodontal tissues.

Biomaterial assisted direct application of autologous periodontal ligament stem cells in intrabony defects

The human periodontal ligament (PDL) encloses sub-population of stem cells which responsible for maintaining and regenerating periodontal tissue structure and function. These cells exhibit multipotency, as demonstrated by their ability to differentiate into osteoblasts, fibroblasts and tooth cementoblasts and to form cementum- and PDL-like tissues, and are generally termed periodontal ligament stem cells (PDLSCs.) They were first isolated from the PDL tissue of extracted human third molar teeth (6). In addition to the periodontal ligament of the root surface following tooth extraction, the PDL remaining on the alveolar bone surface of the extraction sockets has also been used to isolate PDLSCs (7).

The human clinical trial on stem cells based periodontal regeneration is promising. The plethora of animal studies provide sound evidence to support the belief that PDLSCs can be used for periodontal regeneration (8). The implantation of cells into the periodontal defect is done via either biomaterial-free or biomaterial-based approaches (9) also these host derived cells can either be subjected isolation, ex-vivo expansion (stem cell culture) and re-implantation of these cells into periodontal wound /defect or injected directly as a suspension or delivered by biomaterial scaffolds or cell carriers (10).

Primary cultures using ex vivo methods PDLSCs yielded small cell numbers (an average of 1,250 cells) (11) which is less periodontal regeneration (at least 4×10^6 cells). Thus, PDLSCs must proliferate at least 12 population doublings before application (12).

Although the ex vivo expansion of stem/ progenitor cells is necessary, these cells typically reduce their ability to self-renew and proliferate during passaging. The major difficulties facing widespread clinical implementation of existing cell delivery strategies for periodontal therapy are the qualification, cost and time required for ex vivo cul-

ture of a patient's autologous cells prior to re-implantation, and the potential risks and availability constraints associated with transplanting allogeneic (foreign) cells (10). In addition to reduced washing out of the implanted cells in an ex vivo cultures, the use of a carrier material enables the introduction of additional biological cues such as the release of angiogenic factors to improve connection to the host vascular network or factors that drive a differentiation process (13, 14). Hence a gelatine sponge owing to its flexibility, biocompatibility, and biodegradability, and potential to be used as a scaffold to support osteoblasts and to promote bone regeneration in defective areas was considered (15).

The human clinical trial on stem cells based periodontal regeneration is promising. In the first experiment in humans using autologous periodontal ligament derived -derived cells, including PDLSCs, to reconstruct the periodontal intra-bony defects in three patients, the periodontal ligament stem cells were cultured (ex-vivo) and then transplanted which induced a significant improvement of periodontal disease, suggesting that PDLSCs transplantation may be an efficacious and safe alternative for the treatment of human periodontitis (12).

Periodontal regeneration is defined histologically as regeneration of the tooth's supporting tissues, including alveolar bone, periodontal ligament, and cementum over a previously diseased root surface (16). PDLSCs are multipotent and have demonstrated their ability to differentiate into osteoblasts, fibroblasts and tooth cementoblasts and to form cementum- and periodontal ligament (PDL)-like tissues (6). Cementum appear to play a critical role in the regeneration of the tooth attachment apparatus. Cementum is the site where soft-tissue attachment has to be re-established, and cementum matrix is a rich source of many growth factors such as IGF, FGF, BMPs and many more which influence the activities of various periodontal cell types (17, 18).

Based on current literature on use of ex vivo culture and associated problems, a humble attempt was made to harvest autologous PDLSCs for direct application using Abgel[®] (gelatin sponge-Shri Gopal Krishna Labs Pvt. Ltd. Mumbai India.) as scaffold in regeneration of intrabony periodontal defect bypassing ex vivo culture. We used periodontal ligament of an extracted impacted wisdom tooth to restore the periodontal defect of another molar of the same patient. The trial was based on tissue engineering triad using PDLSCs from impacted third molar (cells), Abgel[®] (gelatine sponge – scaffold) and cementum scrapings (which consist of variety of signaling molecules e.g. IGF, VEGF etc. resulted in successful clinical and radiographic pa-

rameters such as clinical attachment gain, decreased probing pocket depth and satisfactory defect fill of intrabony defect when evaluated for a period 1 year. (unpublished data). The direct application of autologous periodontal stem cells in treatment of intrabony defects was attempted for the first time in periodontal literature.

The acceleration of a patient's endogenous regenerative mechanisms by recruiting host stem/progenitor cells, for periodontal regeneration has been considered. Although direct application of periodontal ligament stem cell therapy looks promising but it is still in its stage of infancy, more work is needed in this area to validate the results. Stem cell Application in Periodontal Regeneration Technique (SAI-PRT) using direct PDLSCs has overcome the limitations and concerns of ex-vivo stem cell culture methods like high cost, technique sensitivity, loss of stemness during cell passage, genetic manipulation and tumorigenic potential (19).

Conclusion

Although in vitro and pre-clinical animal studies have been pursued with a large and diverse collection of scaffolds, cells and biomolecules, and clinical studies are beginning to emerge, the field of periodontal tissue engineering and regeneration is fragmented to the point that a clear translational roadmap has yet to emerge.

Innovative stem cell therapy by great researchers has been a boon and an interesting development in various treatment modalities. A simple task of PDLSCs procurement and immediate placement are the major advantages of the current concept autologous Stem cell Application in Periodontal Regeneration Technique (SAI-PRT) has emerged a constructive avenue in treatment of periodontal osseous defects. Moreover the clinical feasibility, success and cost effectiveness over currently available techniques are encouraging. The clinical utility of this novel idea is recommended.

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