REVIEW

LIGAPLANTS – HOW FAR ARE WE FROM IT

[1]Swaminathan Nivethaprashanthi, [2]Sivaramalingam Senthilnathan, [3]Haritheertham Gayathri, [4]Sankaralingam Thirumalai, [5]Elumalai Ahila, [6]P Hema

[1]Postgraduate student, Department of Periodontology, Sri Venkateshwaraa Dental College, Ariyur, Puducherry
[2]Professor and Head, Department of Periodontology, Sri Venkateshwaraa Dental College, Ariyur, Puducherry
[3,4,5]Reader, Department of Periodontology, Sri Venkateshwaraa Dental College, Ariyur, Puducherry
[6]Senior Lecturer, Department of Periodontology, Sri Venkateshwaraa Dental College, Ariyur, Puducherry

Correspondence:
Dr. S. Nivethaprashanthi
Post Graduate Student, Department of Periodontology, Sri Venkateshwaraa Dental College, Ariyur, Puducherry
Email: drnivethaswaminathan@gmail.com

Abstract

Periodontitis is a chronic inflammatory multifactorial disease that causes destruction to periodontium. Periodontal therapy plays a vital role in restoring lost periodontal structure. Lack of periodontal treatment ultimately leads to progression of periodontal destruction; thus, tooth mobility and loss of tooth occurs. Replacement of missing teeth by dental implant is considered as gold standard treatment method over the past decades. At present, Osseointegrated implants are the most widely used with various short comings. To overcome this, development of tissue engineered periodontal ligament cells surrounding the implant (Ligaplants) has now become the new therapeutic and promising tool in field of implant dentistry. Ligaplants improves the biological performance and increase the life of dental prosthesis, hence considered as new dimension in the field of implant dentistry. This review article highlights the existing and scientific literature available on ligaplants.

Keywords: Dental Implants, Dental Prosthesis, Ligaplants, Periodontal ligament, Osseointegration, Tissue Engineering

Introduction

Periodontitis is a chronic inflammatory disease, multifactorial by origin, initiated by microbes and characterized by loss of periodontal ligament and supporting alveolar bone. The purpose of periodontal therapy is to regenerate the lost supporting structures, but it is compromised in cases of severe destruction. Hence early diagnosis is a key to success for periodontal therapy. If left untreated, there is more destruction which will eventually lead to tooth loss. The periodontal ligament cells are also lost once the tooth is extracted.(1)
Replacement of missing teeth includes fixed and removable partial denture. Among these, replacement with dental implants gained popularity amidst the population. At present, the most widely used implant are the osseointegrated implants.(2) In conventional osseointegrated implants, there exist a direct contact of bone and implant with no periodontal ligament support. The tissue surrounding the implant are called peri implant tissue. According to the literature, the survival rate of dental implant is of 90%. Many times, inflammation around the implants do occur causing severe bone loss when compared to bone loss occurring in natural tooth, thus leading to implant failure.(3) Localized bone loss surrounding the implant possess a serious clinical challenge.(4) These shortcomings can be resolved by developing the implant with PDL cells.(5) Most often, inflammation around the implants do occur. This causes severe bone loss when compared to bone loss occurring in natural tooth, thus leading to implant failure

Periodontal ligament is a highly vascular and rich fibrous connective tissue, present between roots of teeth and alveolar bone socket.(3) It contains several cells like fibroblasts, cementoblasts, cementoclasts, osteoclasts, osteoblasts and undifferentiated mesenchymal stem cells. They play an important role in regulation of tooth supporting structures and bone. It also consists of different types of progenitor cells which plays an important role in homeostasis of periodontium i.e., alveolar bone formation and remodeling.(2,5) Periodontal ligament has regenerative potential, thus restores the tissue strength.(3)

In recent times, the new concept of replacement of missing teeth with the help of cultured periodontal ligament cells on the surface of implant resembling the natural tooth, “Ligaplants” (6) is being extensively studied. The present article reviews the clinical and existing scientific literature.

Hypothesis

In contrast to conventional implants (concept of osseointegration), the periodontal ligament formed in ligaplants act as a shock absorber and facilitate micromovements. The primary advantage of ligaplants on abutments and implant supported prosthesis is that they provide beneficial effect on quality of force distribution. As these imitate the form and function of natural tooth, the lifespan of the prosthesis can be increased.(2)

Tissue Engineering: Principle of Ligaplants

Tissue engineering was proposed by Langer et al 1993. This is the concept of reconstruction of lost natural tissue by the process of regeneration. This can be done by both in vivo and ex vivo technique. The main elements responsible for tissue engineering is

i) Matrix or scaffold
ii) Signaling molecules
iii) Cells

In ex vivo/ in vitro technique, preparation of tissue is carried out in laboratory. The cells are cultured in a scaffold or matrix which is made up of bio-degradable polymers enriched with growth-factors. The cultured tissue is then transferred into the body. The scaffold will function as a three-dimensional structure which facilitates cell migration and proliferation.
In vivo technique, the cultured cells undergo physiological healing process when placed in tissue defect thus leads to regeneration. The second approach is inducing inherent healing process at the tissue defect with the use of these 3 elements. Both these techniques can be used to culture Ligaplants (2,6) (Figure 1).

Properties of Ligaplants

1. Act as a shock absorber
2. Provides proprioception
3. Distribution of occlusal forces
4. Provide osteoconductive property to implant
5. Provide anchorage similar to natural tooth, thus facilitates orthodontic treatment
6. For the growth and development of alveolar bone, it provides an appropriate environment.(2)

Interphase of Implant and Periodontal Ligament

The periodontal ligament fibroblasts have the capacity to transform into the cementoblasts

thus leading to the formation of cementum. The formation of bone surrounding the ligaplants was also noted. The regeneration of periodontal ligament depends on site specific signaling, expressed by homeogene-coded transcription factor. Cell surface and signaling components synthesis are influenced by homeoproteins.

Role of Homeogene Msx2 and asporin (SLRP protein present in extracellular matrix)

- Discriminates mineralized versus non-mineralized bone
- Inhibits mineralization of PDL (3,5,6)

Preparation of Ligaplants

The best method to prepare ligaplants is double PDL stimulation. The donor tooth is extracted and replanted immediately into alveolus. By inducing intentional trauma, proliferation and differentiation of cell occurs which triggers the healing process within the periodontal ligament. This in-vivo cell culture reaches its peak after 14 days. (4,5) After 2 weeks it is transplanted for in vitro culture.

The steps involved in vitro ligaplants preparation are as follows:

- Preparing temperature responsive culture dishes
- Cells and culturing of cells
- Culturing of periodontal ligament cells in bioreactor(4,6)

Preparation of Temperature Responsive Culture Dishes

Polystyrene culture dishes containing N- isopropyl acylaminde monomer and 2- propranolol solution. The dishes are irradiated by exposing them to Area Beam Electron Processing System (ABEPS). The culture plates are rinsed with cold water to remove ungrafted monomer. They are sterilized by ethylene oxide.(4,6)

Cells and Culturing of Cells

After extraction of donor tooth, the cells of periodontal ligament are obtained by scraping from middle third of root using scalpel blade. The cells thus obtained are transferred to culture dishes containing Dulbecco's Modified Eagle's Minimal Essential Medium. This medium is supplemented with 100 units/ ml of penicillin, streptomycin and 10% fetal bovine serum. These cells are cultured in an environment of 5% CO_2 at 37^{o}C for 48 hours, where they get attached to the dishes. The debris are removed by rinsing the dishes and the medium

changed three times a week. The periodontal ligament cells sheet is harvested by inoculating on temperature responsive culture dishes (Diameter- 35 mm) at 37^{o}C at a cell density of 1 X 10^{5}.(3,5) This acts as an osteodifferentiation medium, by supplementing 50 mg/mL ascorbic acid 2-phosphate, 10 nM dexamethasone, and 10 nM β-glycerophosphate.

Culturing of Periodontal Ligament Cells in Bioreactor

Bioreactor consists of titanium pin coated with hydroxyapatite in hollow plastic cylinder. These are positioned such that a space of 3 mm is left between the pin and the cylinder. The culture medium is continuously pumped through the left space. The human periodontal ligament cells are seeded first into the plastic vessel followed by titanium pins for a span of 18 days (3,5,6) (Figure 2).

Precaution while Preparing Ligaplants

- Maintaining a proper sterilization is a must throughout the procedure.
- Optimal culturing protocol and ideal cell growth is essential, to prevent the differentiation of non- periodontal ligament cell types.
- Small mechanical movements/vibration of the growth medium are must for the close integration of implant.
- Optimal time for surface treatment must be done for the successful outcome of the ligaplants.

Pros

- Resembles natural teeth (presence of periodontal ligament)
- Problems like gingival recession and intra-bony defects of missing tooth are minimized.
- Though the ligaplants are not anchored unlike conventional implants, there is establishment of firm integration at tissue -bone interface, without any direct contact or interlocking with bone.
- In periimplantitis, the amount of bone loss is reduced.
- In spite of movements at bone- implant junction, there is continuous remodeling of bone and establishment of good communication between bone and implant surface. (3,4,6)

Cons

- Culture sensitive: should be done with utmost care i.e., relies on the temperature, the time duration used for culturing of cells.
- High cost
- Host acceptance is not predictable.
- Complicated and sensitive procedure. (3,4,6)

Evidence Based Research

1. In the study conducted by Nyman et al (7) in 1982, suggested that cells of periodontal ligament possess the capability to reestablish connective tissue attachment to teeth surface
2. Buser et al (8) in the year 1990 conducted a study on monkeys. They evaluated the healing of titanium dental implants placed in contact with retained root tips. They stated the development of hard tissue on the implant surface from the PDL cells of adjoining tooth.
3. In the year 2000, Byung Ho Choi (11) used Ti screw-type implant with periodontal ligament cells collected from the mid surface of root.
4. Rinaldi et al (9) in the year 2010 evaluated the titanium miniplants placement in twenty-four rats between the buccal roots of mandibular first molar.
5. In 2011, Lin et al (10) conducted a study in which they used dental progenitor cells to form periodontal ligament cells on implants in maxilla rat. The presence of PDL on dental implant surface led to conclusion that dental progenitor cells have the capability to reorganize the periodontium in missing teeth site.

Conclusion

In dentistry, Implants are considered as the novel procedure in replacement of the missing teeth. Introduction of tissue engineered periodontal ligament implants have carried the implant dentistry to higher level. Ligaplants enhances stability for longer tenure with less inconvenience and discomfort. They are introduced to overcome the disadvantages of conventional implants. Positive results were observed in various studies done on animals using implants. However, more human studies with longer follow up period are required to validate the success of ligaplants.

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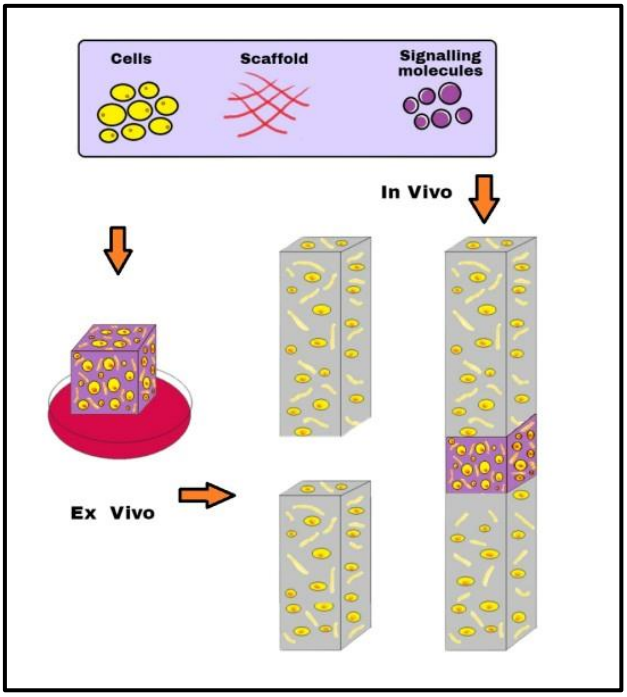

Figure 1: Tissue Engineering

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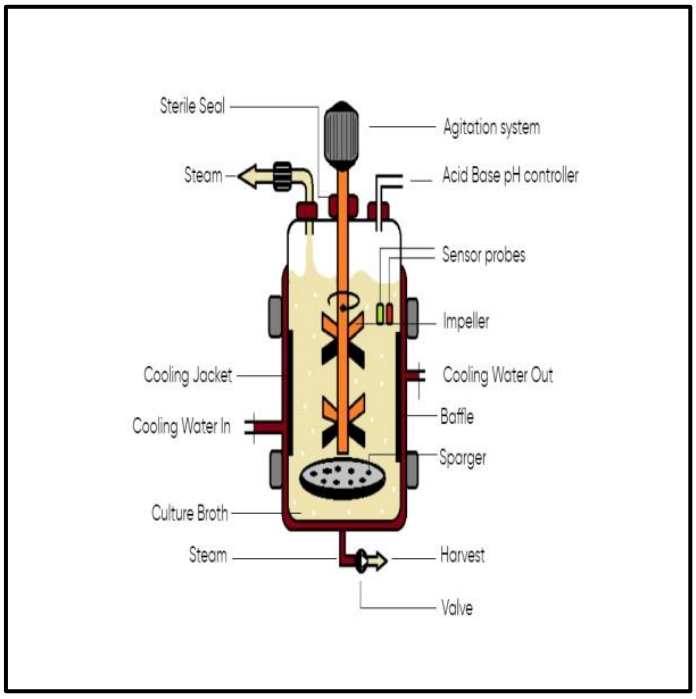

Figure 2: Bioreactor