Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 3448-3452 | ISSN:2251-6727

Guided Tissue Regeneration in Periodontics- A recent update

Poonam Rai[1], Muzzammil Mukadam[2], Kanchan Deshmukh[3], Satpreet Singh[4], Suparno Banerjee[5] and Isha Suri[6]
[1,2,3,4,5,6] Department of Periodontics and Oral Implantology, DY Patil School of Dentistry, Navi Mumbai -400614, India.
[1]Poonam Rai (Professor MDS), [2]Muzzammil Mukadam (1st MDS), [3]Kanchan Deshmukh (1st MDS), [4]Satpreet Singh (3rd MDS), [5]Suparno Banerjee (3rd MDS), [6]Isha Suri (MDS)

(Received: 07 January 2024 Revised: 12 February 2024 Accepted: 06 March 2024)

KEYWORDS
GTR; growth factors; periodontal; regeneration; ePTFE; PDGF; Tissue regeneration; 3D printing; Stem cells; PRF

Abstract
The three major goals of periodontal treatment are to eliminate the underlying reasons, regenerate or restore the damaged attachment mechanism, and avoid further periodontal damage. Periodontic regeneration refers to the tooth-supporting tissues regeneration such as cementum, alveolar bone, and periodontal ligament. Among various techniques, GTR (guided tissue regeneration) has been proved to be an effective approach for acquiring periodontal regeneration. GTR is a dental technique that has lately been used to address maxillomandibular abnormalities, oral surgery, periodontal surgery, and implant dentistry. Membranes of many sorts are crucial in GTR operations. This article discusses the bioproperties of a resorbable barrier membrane carrying a growth factor that is now available to GTR.

INTRODUCTION

Periodontal diseases occurrence is more frequent in this current era as the population aging rapidly.[1] Rapid growth of periodontal pathogens with destructive potential increases need for prevention and treatment of periodontal tissues.[2] The utmost goal of periodontal therapy comprises of disease eradication, prevention from recurrence, periodontium regeneration that was lost due to periodontal disease.[3] Periodontal Regeneration refers to reconstruction of lost periodontal tissues, including viable periodontal ligament, cementum as well as bone.[4]

World Workshop in Periodontics, 1996 states that, "GTR techniques through differential tissue responses aims to regenerate lost periodontal tissues. Barriers are used for excluding gingival corium as well as epithelium from the root surface as they might obstruct regeneration process.

REQUIRED DESIGN CRITERIA FOR GUIDED TISSUE REGENERATION MEMBRANES[5]:

1. Tissue integration: It should provide an open microstructure while limiting epithelial migration and establishing a firm location for wound healing**.**

2. Cell occlusivity: It should be able to differentiate all cell types for the chosen cells to repopulate the faulty location.

3. Clinical manageability: It should be simple to cut and shape to achieve specific periodontal abnormalities.

4. Space provision: It should maintain appropriate space throughout the healing phase by resisting break down from the surrounding tissue pressure**.**

5. Biocompatibility: It should be non-antigenic, non-toxic, and causes only mild inflammatory reaction in the host.

6. Membrane stability: It should provide a sufficient amount of time for progenitor cells to repopulate the defect region without any hindrance caused by gingival connective tissue or epithelium.

7. Membrane resorption: After cell selection is complete, the membrane should be destroyed, replaced, or resorbed into the healing flap.

Additional criteria must be met for bioresorbable and biodegradable membranes.[2] These include-

• Tissue reactions caused by membrane resorption should be very mild;
• Reactions should be reversible
• Reactions should not interfere with the desired tissues regeneration.

Indications of GTR include

1. Involvement of the class II molar furcation and a two or three walled infrabony defect.
2. Miller's Class II & III Gingival Recession
3. Alveolar Ridge Expansion
4. Palato -Gingival Grooves
5. Alveolar Bone Augmentation around the implants
6. Fenestration defects /Dehiscence defects

Contraindications for GTR Therapy

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 3448-3452 | ISSN:2251-6727

- Class II furcations on the mesial and distal side of maxillary molars
- Class III & IV furcations
- Premolar furcations
- Horizontal bone loss
- One-walled infra bony defects
- Circumferential /Moat type defects

GOTTLOW (1993) CLASSIFIED THE MEMBRANE INTO THREE DIFFERENT GROUPS

1. First generation (Non-resorbable)

1. Rubber Dam
2. Nucleopore membrane
3. Expanded poly tetrafluoroethylene membrane (ePTFE)(Goretex)

4-. Millipore filter

2.Second generation (Resorbable)

1. Collagen
2. Vicyl mesh (polyglactin 910)
3. Polylactic acid membrane (Guidor)
4. Oxidised Cellulose
5. Cargile membrane

6, Hydrolyzable polyester

3. Third generation (Resorbable with growth factors)

THIRD GENERATION MEMBRANES

Development of tissue engineering has made the concept of third generation membrane more apparent. At wound site for better adaptation and direct natural wound healing these membranes work as delivery devices to release specific agents such as adhesion factors, antibiotics, growth factors, and various other factors at the wound site on a need basis for achieving better adaptation and direct natural wound healing.[6] They may be further classified as:

i) Barrier membranes with antimicrobial activity- Microbial infection is the major factor contributing to a poor result of the wound regeneration. Some of the elements that may influence GTR result include bacterial count, bacterial type, and bacterial contamination area present on the GTR membrane.[7] Gingival recession is related with a higher membrane bacterial count, while clinical attachment gain is associated with a lower level.[8] It was shown that including amoxicillin or tetracycline onto different GTR membranes can improve periodontal ligament cell attachment in the presence of the bacterial pathogens such as streptococcus mutans and Aggregatibacter actinomycetemcomitans.[9]

A GTR membrane comprises of polyglycolic acid and polylactic acid with 25% doxycycline added seems to help dog's periodontal bone regeneration.[10] When utilized in clinical settings, tetracycline-loaded expanded polytetrafluoroethylene (ePTFE) membranes increased clinical attachment gain while decreasing bacterial contamination.[11] Their recently identified non-bacterial features, which include anti-inflammatory, anti-collagenolytic, osteoclast inhibitory, and fibroblast stimulating capabilities, may further contribute to their proven efficiency. Tetracylines thereby prolonged the time it took for collagen membranes to break down; this property can be employed in therapeutic contexts where maintaining the membrane for a longer amount of time is desired.

Another naturally occurring resorbable membrane with antibacterial qualities is chitosan. It is created by deacetylating chitin and has the ability to heal wounds, be highly biocompatible, and have antimicrobial properties. There are currently no approved commercial medicines for GTR, and the disease is still in the preclinical stage. [12]

ii) Barrier membranes with Bioactive calcium phosphate incorporation -Various invitro studies has been conducted to investigate the influence of nanosized hydroxyapatite (HA) particles in electrospun matrices on regeneration of bone. Liao et al.'s studies on the membrane revealed that the incorporation of nano-carbonated hydroxyapatite (nCHAC) increased the biocompatibility as well as the osteoconductivity of the membrane. This triple-layered membrane featured a porosity side (for cell development) made up of nCHAC/PLGA/ collagen, a non-porous side made up of pure PLGA (to inhibit cell attachment), and a transitional layer made up of PLGA/ nCHAC. The scientists revealed that the addition of nano-apatite had a substantial impact on membrane bioactivity and cell differentiation early.

Gelatin, a naturally resorbable substance, has also been studied in vitro for GTR. Gelatin is generated from collagen and has high biocompatibility, which stimulates osteoblast adhesion and development, making it a suitable biomaterial for GTR.[13]

iii) Barrier membranes with Growth Factor release - The growth factors are crucial for the creation of new tissue and the healing process. They regulate the creation and breakdown of extracellular matrix proteins and have an impact on angiogenesis, chemotaxis, and cell

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 3448-3452 | ISSN:2251-6727

proliferation in addition to tissue repair and illness. Their method of action involves attaching themselves to a target growth factor receptor's extracellular domain, which then triggers the intracellular signal transduction pathways.

Preclinical and clinical investigations have shown that a number of bioactive compounds have potent effects in aiding periodontal wound recovery. These bioactive molecules, which have demonstrated positive results in stimulating periodontal regeneration, include platelet derived growth factor (PDGF), insulin-like growth factor (IGFI), basic fibroblast growth factor (bFGF - 2), transforming growth factor (TGF -1), bone morphogenetic protein (BMP) -2, -4, -7, and -12, and enamel matrix derivative (EMD).[14]

In rat calvarial abnormalities, it was discovered that PDGF-BB loaded poly(L-lactide) acid (PLLA) membrane can possibly improve directed tissue regenerating effectiveness.[15] In beagle dogs, controlled basic fibroblast growth factor (b - FGF) release from a sandwich membrane composed of gelatin microspheres and collagen sponge scaffold for a limited amount of time resulted to the effective periodontal tissues regeneration.[16] Following the construction of a system constituted of a PLLA asymmetric membrane was attached with an alginate film, it was shown that growth factors like TGF- beta may be incorporated into alginate membranes which functioned as vehicle for drug delivery. Critical sized segmental defects were shown to be successfully repaired by a hybrid alginate/nanofiber mesh system along with recombinant bone morphogenetic protein -2 (rhBMP - 2) delivery method.[17]

The delivery method of growth factors and the requisite for various signals to bring about the regeneration process are variables that are restricting the present efforts. Therefore, for promoting comprehensive tissue regeneration, a wide spectrum of biological mediators must be delivered.

Electrospinning (e-spinning) for membrane

Processing membranes for periodontal regeneration has shown to be a highly promising use of the e-spinning technology. Fibrous scaffolds have been investigated by many research groups recently for tissue regeneration. A natural or synthetic polymer that is biocompatible and biodegradable, and that often mimics the structure of the extracellular matrix (ECM), is created using e-spinning. According to Li et al., the nanofiber structure may promote cell attachment and proliferation by cultivating a variety of cells on PCL and PLGA nanofibrous e-spun scaffolds, including cartilage cells, fibroblasts, as well as mesenchymal stem cells.[18] Many comprehensive reviews in tissue engineering are available on the e-spinning procedure and uses of these nanofibers.[19] One of electrospinning's drawbacks is that it might be challenging to create macropores within the scaffold for repair of alveolar bone. Thus, in order to create multilayered periodontal scaffolds, electrospinning has to be coupled along with another technologies (such as 3-dimensional [3D] printing). The quick technique of 3D printing gives exact control over a scaffold's porosity and form. In order to restore the complicated structure of alveolar bone, PDL, and cementum, a biomimetic scaffold for 3D printing was created. To fill the gap between 3D printing and electrospinning, a novel method called melt electrowritten (MEW) was created.[20] Due to a high voltage current at the jet tip, the MEW filaments have a lesser diameter than the fibers which are directly created from fused-deposition modeling. Still in its infancy, 3D printing as well as the implication of a biphasic or triphasic scaffold for regeneration of periodontal tissue have optimistic outcomes. Therefore, in order to develop this topic in the future, in vivo investigations and more sophisticated technology are needed.

Platelet-rich fibrin (PRF)

In France, Choukroun et al. (2006) created the first autologous membrane PRF with its implications in oral and maxillofacial surgery.[21] The protocol for PRF is straightforward: In 10 mL tubes, a blood sample is collected in absence of anticoagulant and promptly centrifuged at 3000 rpm for about 10 minutes. A fibrin clot is created in the centre of the tube, between the red corpuscles at the bottom and at the top the acellular plasma. Platelets are hypothetically abundantly trapped in fibrin meshes. Practitioners will get extraordinarily impervious autologous fibrin membranes by extruding the fluids present in the fibrin matrix. The scientific basis for using these preparations is that platelet granules serve as a reserve for several growth factors (GFs) that play a critical function in hard and soft tissues repair process. According to Gassling et al. (2010), PRF membrane produced better outcomes than collagen when utilized as a scaffold to promote the growth of human periosteal cells.[22] According to a recent analysis, PRGF can facilitate and quicken the healing mechanism. PRGF improves the quality of life of patients by lowering pain,

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 3448-3452 | ISSN:2251-6727

swelling, and the pace at which inflammation occurs. It also speeds up the regeneration of bone and soft tissue.[23]

Stem cells-

Nyman et al.(1982) first showed that it is possible to obtain periodontal regeneration invitro by removing cells of gingival epithelial and fibroblastic lineages from the site and directing the colonization of the periodontal wound healing site by progenitor cells from the periodontal ligament and alveolar bone.[24] Progenitor cells are probably the parental cells of synthetic cells that helps in restoring damaged periodontal tissues, such as cementoblasts, osteoblasts, and fibroblasts.[25] Recent research suggests that subset populations obtained from the periodontal ligament exhibit stem cell properties.[26] Thereby, recent research is focusing on creating cellular-based approaches for periodontal regeneration.

C O N C L U S I O N

The GTR treatment has been and continues to be widely used in periodontal practice, and in periodontal regenerative medicine, it has been recognized as a fundamental approach. Even though indications of GTR membrane in periodontal regeneration are confined to three wall and class II furcation defects, experimental efforts are stretching the boundaries to incorporate more advanced periodontal abnormalities with an anticipated result. Although considerable data is currently missing, it appears likely that combining different methods (such as GTR in conjunction with bone transplants) may increase the odds of a favorable outcome.

[1] Persson GR. What has ageing to do with periodontal health and disease?. Int. Dent. J.2006 Aug;56(S4):240-9.
[2] Popova C, Dosseva-Panova V, Panov V. Microbiology of periodontal diseases. A review. Biotechnol Biotechnol Equip. 2013 Jan 1;27(3):3754-9.
[3] Kwon T, Lamster IB, Levin L. Current concepts in the management of periodontitis Int. Dent. J. 2021 Dec 1;71(6):462-76.
[4] Chen FM, Jin Y. Periodontal tissue engineering and regeneration: current approaches and expanding opportunities. Tissue Eng Part B: Reviews. 2010 Apr 1;16(2):219-55.
[5] Gottlow J. Guided tissue regeneration using bioresorbable and non-resorbable devices: initial healing and long-term results. J Periodontol. 1993 Nov;64(11 Suppl):1157-65.
[6] Wang HL, MacNeil RL. Guided tissue regeneration. Absorbable barriers. Dent Clin North Am. 1998 Jul;42(3):505-22
[7] Machtei EE, Dunford RG, Norderyd OM, Zambon JJ, Genco RJ. Guided tissue regeneration and anti-infective therapy in the treatment of class II furcation defects. J Periodontol. 1993 Oct;64(10):968-73.
[8] Selvig KA, Kersten BG, Wikesjö UM. Surgical treatment of intrabony periodontal defects using expanded polytetrafluoroethylene barrier membranes: influence of defect configuration on healing response. J Periodontol. 1993 Aug;64(8):730-3.
[9] Hung SL, Lin YW, Wang YH, Chen YT, Su CY, Ling LJ. Permeability of Streptococcus mutans and Actinobacillus actinomycetemcomitans Through guided tissue regeneration membranes and their effects on attachment of periodontal ligament cells. J Periodontol. 2002 Aug;73(8):843-51.
[10] Chang CY, Yamada S. Evaluation of the regenerative effect of a 25% doxycycline-loaded biodegradable membrane for guided tissue regeneration. J Periodontol. 2000 Jul;71(7):1086-93.
[11] Zarkesh N, Nowzari H, Morrison JL, Slots J. Tetracycline-coated polytetrafluoroethylene barrier membranes in the treatment of intraosseous periodontal lesions. J Periodontol. 1999
[12] Xu C, Lei C, Meng L, et al. Chitosan as a barrier membrane material in periodontal tissue regeneration. J Biomed Mater Res B Appl Biomater 2012;100(5):1435–43.
[13] Liu X, Smith LA, Hu J, et al. Biomimetic nanofibrous gelatin/apatite composite scaffolds for bone tissue engineering. Biomaterials 2009;30(12):2252–8.
[14] Mehta M, Rai P, Shetty D. Concentrated Growth Factor: A Review. Int. J. Dent. Oral Sci. 2020 Aug 31;7:799-803.
[15] Park JB, Lee JY, Park YJ, Rhee SH, Lee SC, Kim TI, Seol YJ, Lee YM, Ku Y, Rhyu IC, Han SB, Chung CP. Enhanced bone regeneration in beagle dogs with bovine bone mineral coated with a synthetic oligopeptide. J Periodontol. 2007 Nov;78(11):2150-5
[16] Nakahara T, Nakamura T, Kobayashi E, Inoue M, Shigeno K, Tabata Y, Eto K, Shimizu Y. Novel approach to regeneration of periodontal tissues based on in situ tissue engineering: effects of controlled release of basic fibroblast growth factor from a sandwich membrane. Tissue Eng. 2003 Feb;9(1):153-62.
[17] Kolambkar YM, Dupont KM, Boerckel JD, Huebsch N, Mooney DJ, Hutmacher DW, Guldberg RE. An alginate-based hybrid system for growth factor delivery in the functional repair of large bone defects. Biomaterials. 2011 Jan;32(1):65-74.
[18] Li WJ, Laurencin CT, Caterson EJ, Tuan RS, Ko FK. Electrospun nanofibrous structure: a novel scaffold for tissue engineering. J Biomed Mater Res. 2002 Jun 15;60(4):613-2
[19] Pham QP, Sharma U, Mikos AG. Electrospinning of polymeric nanofibers for tissue engineering applications: a review. Tissue Eng. 2006 May;12(5):1197-211
[20] Brown TD, Dalton PD, Hutmacher DW. Direct writing by way of melt electrospinning. Adv Mater 2011;23(47):5651–7
[21] Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, Dohan AJ, Mouhyi J, Dohan DM. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part IV: clinical effects on tissue healing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Mar;101(3):e56-60
[22] Gassling V, Douglas T, Warnke PH, Açil Y, Wiltfang J, Becker ST. Platelet-rich fibrin membranes as scaffolds for periosteal tissue engineering. Clin Oral Implants Res. 2010 May;21(5):543-9.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 3448-3452 | ISSN:2251-6727

[23] Solakoglu Ö, Heydecke G, Amiri N, Anitua E. The use of plasma rich in growth factors (PRGF) in guided tissue regeneration and guided bone regeneration. A review of histological

[24] Nyman S, Lindhe J, Karring T, Rylander H. New attachmentfollowing surgical treatment of human periodontal disease.J Clin Periodontol 1982;9:290–296.46.

[25] Karring T, Nyman S, Gottlow J, Laurell L. Development ofthe biological concept of guided tissue regeneration–animaland human studies. Periodontol 2000 1993;1:26–35

[26] Ivanovski S, Gronthos S, Shi S, Bartold PM. Stem cells in theperiodontal ligament. Oral Dis 2006;12:358–363