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REVIEW ARTICLE

GUIDE THE TISSUES FOR PERIODONTAL REGENERATION (GTR): A REVIEW

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ABSTRACT

To restore periodontal tissues that are lost through disease or trauma is the very rationalae of periodontal treatment. Guided Tissue Regeneration (GTR) technique has been applied for treating periodontal defects such as intrabony defects, furcation involvements. Outlook of periodontal regeneration has changed by incorporation of GTR concept and GTR membranes. Membranes are of several types used for regeneration. The concept that the fibroblasts from the periodontal ligament or undifferentiated mesenchymal cells can re-create the original periodontal attachment is well applied here. Clinically this is accomplished by placing a barrier over the defect thereby excluding gingival tissues from the wound during early healing. There are two 2 types of membranes: Non absorbable and Absorbable membranes. There is a necessity to remove non absorbable membranes for which second surgery is needed, so these are occasionally used now. Absorbable membranes need not be removed so are used frequently. This paper reviews briefly about the GTR membranes, its uses for various periodontal defects and the predictability of a successful treatment outcome.

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INTRODUCTION

Periodontitis is an inflammatory condition that leads to destruction of periodontal tissues causing intrabony defects, furcation involvement and gingival recession. Guided tissues regeneration techniques can be used to treat these defects. In 1950 Hurley used barrier membrane to develop a gap between soft and hard tissue and this described GTR (1). In 1980 GTR was launched by Nymann and coworkers to regenerate tissues of periodontium as a therapy for periodontal lesions, by generating new attachment, by stopping migration of cell from connective tissue of gingiva and epithelium into periodontal defect (2). The term Guided Tissue Regeneration was given in 1986 by Gottlow (3). Melsher in 1976 constructed the hypothesis - certain cells in periodontium have the power to create new periodontal apparatus, if they get good chance to crowd the wound (4). Collagen fibres needs to be inserted in the newly formed cementum on one side, and in alveolar bone on other, in order to reinforce the normal function which requires fine co-ordination between these three tissues.

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Karring *et al* experimentally established this hypothesis and verified it histologically (5). They stated that this can be possible when epithelial cells of gingiva and fibroblasts are excluded from the space of the wound and cells of periodontal ligament are allowed to wander and crowd at this space. The requirement for removal of epithelium and cells of connective tissue of gingiva from wound led to creation of material known as membranes used in GTR. In 1996 World Workshop in periodontics, GTR was defined as "procedures attempting to regenerate lost periodontal structures through differential tissue response. Barriers are employed in a hope of excluding epithelium and gingival corium from root surface with a belief that they interefere in regeneration" (6). The aim of GTR membrane is to prohibit epithelium and connective tissue of gingiva into the defect so as to maintain gap between the defect and tooth. This will also help to secure the clot. Membranes are made up of different materials and so their properties also varies. It is thus important to know in detail about different materials used in GTR treatment. Cellulose acetate used by Nyman *et al* in 1982 was the first membrane (7). Since then wide range of new membranes have been developed.

INDICATIONS OF GUIDED TISSUE REGENERATION (8, 9)

- Intrabony or two or three walled vertical defects. (deeper than 4mm)
- Class II furcation involvement.
- Class III furcation involvement.
- Treatment for receeded gingiva.
- Bone augmentation.
- Repair of apicocectomy defects.

CONTRATINDICATIONS

- Very severe defect where periosteum is minimally remained.
- Horizontal defect.
- In case of flap perforation.

CHARACTERISTICS OF MEMBRANE

Qualities and patterns for membranes was stated by Scantlebury in 1993 as (10):

- **Biocompatibility:** Biocompatibility is defined by Williams (11) as the potential of any material to be compatible with a host in any specific situation without producing negative response and vice cersa.
- **Cell exclusion**: Cell exclusion is the property where the membrane forms a boundary between flap of gingiva from the developing fibrin clot in the wound area. No experiment has specifically addressed this feature of GTR membrane.
- **Space maintenance**: For adequate regeneration space maintenance is required. So the membrane should have good mechanical properties and or structural features that allows it to remain undamaged and unaffected by the force of tissue tension or occlusion and prevents soft tissue fall to eliminate or reduce wound space.
- **Tissue integration and simple to use**: Membrane should be easy to control or to deal with it without any difficulty.
- **Mechanical strength**: This quality is important so that the underlying blood clot is protected and would healing is not disturbed.
- **Degradability**: Membranes degradation time should be equal to the regeneration time of bone so that second surgical procedure is not needed to remove the membrane.

MEMBRANES CAN BE NON ABSORBABLE OR ABSORBABLE (12-15).

Non absorbable membrane

- Cellulose filters
- Expanded polytetrafluoroethylene membranes

Absorbable membranes are

- Collagen membranes
- Polylactic acid
- Polyglycolic acid and polylactic acid
- Synthetic liquid polymer Polyglactin
- Calcium sulfate
- Acellular dermal allografts
- Oxidized cellulose mesh

NON ABSORBABLE MEMBRANE

Non-absorbable membranes do not distort till they are in the tissue. Their function is temporary, so once the function is over, they are no longer needed in that particular place. But non-absorbable membranes have their build and form in the tissues maintained, requiring a second surgical procedure for removal, further causing trauma to the periodontal tissues with patient discomfort, along with increase in the cost and duration of therapy. Non-absorbable membranes are expanded polytetrafluoraethylene (e-PTFE, Gore-Tex®), high-density polytetrafluoraethylene (d-PTFE), and titanium-reinforced high-density polytetrafluoraethylene (Ti-d-PTFE) membranes. Polytetrafluoroethylene (PTFE) has a chemical formula (-CF2-CF2-)n, which means, it is a polymer of flurocarbon. PTFE membranes were launched in dental use in 1984. It is nonporous but has good inert and biocompatible property, which prevents growth of tissues inside and does not cause foreign-body response after implantation. ePTFE is chemically identical to PTFE as it is made when PTFE is put through high tensile stress, leading to porous microstructure formation. This can be in the form of solid nodes and fibrils. It causes minimal inflammatory reaction in different tissues, allows tissue in growth and has been used in vascular surgery from many years.

Gore-Tex® is an ePTFE membrane consisting of two sections, first - a microstructure collar which is open, 1mm thick and 90% porous, that allows ingrowth of connective tissue when positioned coronally , prevents apical epithelial migration and ensures wound stability. The other section is occlusive membrane of an average of 0.15 mm thick and 30% porous, helping to provide space for regeneration, possessing structural stability and serves as a obstruction towards the gingival flap (16) . Human histological samples have indicated that ePTFE membranes shows successful regeneration of periodontium after a 3 months healing period. Effectiveness of ePTFE membranes was investigated in numerous clinical studies (16). Gottlow *et al*. (17) in 1986 mentioned the development of new attachment in human periodontium by ePTFE membrane in 3 months. Cortellini *et al*. (18) in 1993 mentioned that in 6 months, regeneration of periodontium with intrabony defects was seen in humans. Murphy (19) in 1995 stated that there was slight post-operative healing complications by ePTFE membrane such as pain, pus discharge and swelling as compared to conventional periodontal therapy. Modification of ePTFE membranes were done by titanium reinforcements, which are placed between two layers of ePTFE, leading to outcomes with similar surface properties and better mechanical and space maintenance. Titanium reinforced membranes also have their application in guided bone regeneration procedures (GBR) aimed at augmentation of toothless alveolar bone, in cases where implants are planned and insufficient alveolar bone mass is present. The outstanding properties of harshness, flexibility, firmness and softness makes Titanium mesh a perfect alternative for e-PTFE membrane (20,21). It was been mentioned that there are four main advantages of Ti-mesh membranes over their alternative PTFE membranes.

Other non-absorbable membranes are rubber dam, resin / glass-ionomer barrier and composite barrier. These do not fulfill qualities for GTR membrane. A composite membrane (BioBrane) is fabricated by nylon fabric that can be knitted, mechanically bonded on a semipermeable silicone membrane and coved with collagen peptides. These have been tested in animals but have given combined results to regenerative potential, as the shortcomings of this membrane are its low rigidity and limited regenerative response (3).

ABSORBABLE MEMBRANES

Absorbable membranes do not require additional surgery. They reduce patient discomfort and cost, and eliminates potential surgical complications. Disintegration of absorbable membrane is not possible to control. The disintegration starts immediately once membrane placement is done in the surgical site, and this disintegration varies in individuals, especially for materials that degrades enzymatically like collagen. It was stated that absorbable barriers should preserve their structure for minimum of 4 weeks in the tissues for biological objective of GTR. Due to their biodegradation, tissue reaction can occur which can hamper wound healing and compromise the treatment outcome (22). The perfect membrane should degrade or resorb with the same rate of bone formation.

Resorbable membranes can be
A) Natural
B) Synthetic
C) Polymer Composites
D) Membranes containing functional material
E) Others composed of Platlet rich fibrin.

A) NATURAL MATERIAL

Natural polymers have good biocompatibility, safety and biodegradability property. These have advantageous properties such as innate bioactivity, natural remodeling, quality to show receptor-binding ligands to cells and prone to proteolytic degradation by cell triggering as compared to synthetic polymers. But these inherent bioactivity has its drawbacks as to having powerful immunogenic reaction, difficulties in relation with their purification and chances of disease transmission. The most commonly used natural polymers for GTR and GBR therapies are the collagen and chitosan (23).

Membrane based on collagen

Properties like tissue fusion, biologic process of tissues becoming vascular, biodegradation without foreign particle invasion and reaction, fibroblastic chemotactic action, bleeding control property, weak immunogenicity, osteoblastic attachment, biocompatibility and potential of stimulating wound healing are seen in collagen membranes (type I and III). Therefore, membranes containing collagen are mostly used in GTR treatments (24-30).

Bio-Gide, Ossix, Biomend and Biomend Extend, are different types of collagen membranes commercially available. Collagenases / proteases are enzymes that causes degeneration of these membranes and they get resorbed. Bacterial proteases, macrophages and enzymes by polymorphonuclear leukocytes, also causes its degradation (31,32). Although these collagen membranes have great cellular understanding, bio-compatibility and same bone renewal ability as that of non-absorbable membrane, they have drawbacks like gap maintenance during humid conditions, chance of transferring disease to human from animal-derived collagen, low mechanical strength, and fast breakdown (33-36). To be compatible for use in GBR and GTR treatment, these membranes are linked with various chemicals like glutaraldehyde (GTA), 1-ethyl-3-(3-dimethylaminopropyl) carbodimide (EDC), polyepoxy, diphenyl-phosphorylationazide. BioMend, BioMend Extend, Zimmer Biomet and Rapi-Gide are membranes that are linked by GTA and EDC which are available commercially. Tensile strength of collagen was improved and its degradation time was prolonged when they were crosslinked (37). But the secondary products and remaining reagents that are formed after degradation of collagen may be toxic, which restricts its applications (38). Crosslinkage of polysaccharides with collagen has also been beneficial (37,39). Ossix Plus contains polysaccharide crosslinked wih collagen. To initiate crosslinkage well, alternatives used are dehydrothermal (40-42) / heat treatment and ultraviolet / gamma / microwave irradiations [38,43]. These cross-linked collagen membranes lead to slow formation of new blood vessels in rats and dogs (33,35). More unfavourable events and insufficient bone renewal were seen in chemically crosslinked collagen membranes compared to the non- crosslinked membranes according to some researches (44).

A bovine collagen membrane (BioGide) resorbs in 8 weeks, and a rat-tail collagen membrane resorbs in 4 weeks. A type I collagen GTR membrane is prepared by bovine Achilles tendon. Its resorption is seen in 4 to 8 weeks. Another type I collagen membrane is obtained from calf pericardium. This is cross-linked by diphenolphosphorylazide, and has been used for GTR. Clinical studies of hemostatic collagen material (Collistat) showed regeneration and this membrane completely resorbed in 7 days. Dura mater, oxydized cellulose and laminar bone are other natural materials which are tested for GTR but did not show good success (16).

Membrane based on chitosan

Chitosan is a 1,4-linked 2-amino-2-deoxy-D-glucan. It has basic pH. It is straight and positively charged polysaccharide. It is acquired when acetyl group from chitin is removed. It is low in cost, and is good biocompatible material. It does not have a property of being antigenic, has suitable degradation rate, good bleeding control property, is antimicrobial and has good wound healing ability (45-48). Chemical cross-linking is an effective method to increase its mechanical strength and reduce its degradation speed (49). Chitosan membranes cross-linked with genipin showed less inflammatory reaction and resulted in faster healing time (50). In vitro test showed that genipin-cross-linked chitosan degraded 22% after 16 weeks, which was slower as compared to non-crosslinked membranes which was 34%. Also, the tensile strength of cross-linked membrane was 32 MPa, which was about 165% higher than that of the non-cross-linked membranes. These results indicated that genipin-cross-linked chitosan membranes had good ability in GBR applications (51). Chitosan also has antibacterial property and so can be used alone or in combination with other polymers (52).

Membrane based on gelatin

Gelatin is obtained from partial denaturation of collagen and is a soluble protein. Is is easily available, easy to handle and is

cost efficient (53). Gelatin is a good biocompatible material, has low property of eliciting an immune response, it is fexible, sticky, stimulates cell fusion and growth, making it an ideal material for tissue engineering, GBR and GTR (54). Gelatin has low mechanical properties and quick degradation. It is cross-linked with N-hydroxyl succinimide (NHS) (55), heat treated (56), and gluteraldehyde (57) to improve its mechanical properties.

Membrane based on silk fibroin (SF)

Silk fibroin (SF) is a naturally occuring protein that is obtained from silk worms (Bombyx mori) or spiders (58). It is good biocompatibly, and biodegradibly (59). Good strength and durability allows silk fibroin to maintain space for bone ingrowth and restricts membrane collapse (60).

SYNTHETIC MATERIALS

Organic aliphatic thermoplastic polymers are synthetic materials. The frequently used synthetic materials are polylactic acid (PLA), polyglycolic acid (PGA), poly-caprolactone (PCL), poly-hydroxyl valeric acid, and poly-hydroxyl butyric acid.

Polylactic acid (PLA)

Since it has good mechanical properties and biocompatibility it is a commonly used material in GTR treatments. PLA and PLGA commercially available membranes are Resolut Adapt, Epi- Guide and Vivosorb. Contents of PLGA membranes had positive response to bone ingrowth (61). When deproteinized bovine bone mineral is fused with PLGA, it can perform similar to collagen (62). PLA and PLGA membranes are not harmful for cells. But inflammatory response and foreign body reaction can occur due to release of oligomers and acid byproducts during its degradation (62-64).

Guidor is a dual layered absorbable membrane madeup of polylactic acid and a citric acid ester that appeared first in the market. The superficial layer of membrane permits combination of overlying gingival flap as it has rectangular perforations (400-500/cm2). Internal spacers are present between the inner and superficial layers, creating gap for ingrowth of tissues. The inner layer has circular perforations which are small (4000-5000/cm2) and external spacers are present for preserving the gap between the membrane and the surface of root. Resorption of membrane was seen 6-12 months after implantation, and function maintenance for at least six weeks. Degradation process included foreign-body reaction featured by multinuclear cells and macrophages. The membrane was removed from the market for unknown reasons (3).

Polycaprolactone (PCL)

Polycaprolactone is a good biocompatible material, is cost effective and has good mechanical strength (65-67). During its degradation process it does not produce acidic environment as compared to PLA and PLGA. It resorbs completely in 2–3 years. This period is too long for its use in GTR treatment (68). Also, its lacking affinity to water reduces cell fusion and proliferation. Hence, PCL is mixed with other polymers before its application.

Polyethylene glycol (PEG)

Polyethylene glycol (PEG) has good biodegradability, cell-occlusiveness, and biocompatibility (69-71). Successful prospects in augmentation of challenging lateral ridge defects and maintainance of the ridge contours were seen by PEG membranes (30,72-74).

ABSORBABLE MEMBRANES BASED ON POLYMER COMPOSITES

Polymer blends

Though membranes have qualities like biocompatibility, adequate degradation time along with mechanical and physical properties, and sufficient toughness to circumvent membrane collapse (75), single polymer membrane cannot fulfill the above mentioned aspects. Therefore, it will be beneficial to merge and mix two different types or more of polymers to master their imperfections and gain more favourable interdependent effects. The task to develop membranes having property and structure resembling extra cellular matrix (ECM) is still going on (76).

Blends of natural polymers

Chitosan is a natural polymer having poor mechanical properties. Its ability to produce an effect on living tissue is less compared to protein polymers. Free carboxyl groups of gelatin blends easily with chitosan by hydrogen bonding. This is done with an attempt to improve mechanical property and bioactivity of chitosan. Ability to allow cell fusion and proliferation by gelatin - chitosan membranes were better than individual polymer membranes (77). Centrally placed chitosan sandwiched between two collagen membranes was developed. 20 wt % hydroxyapatite was added to this three layered membrane (78). The membrane formed by the combination of these three, increased the advancement of osteogenic differentiation and also stimulated human bone marrow mesenchymal stem cells (hBMSCs) proliferation (79). These results demonstrated that membrane developed by these combination are good for guided tissue regeneration therapies.

Blends of synthetic polymers

PLGA has good cellular compatibility so it has good effect on reformation of different tissues. But, it has weak mechanical strength, so maintaining its shape is difficult. PLGA when mixed in same ratio with PCL forms PCL - PLGA scaffold, having higher compressive strength and modulus compared to PLGA alone (80). Occlusive glycolide membrane, lactic copolymer and polyglycolide fiber forms a synthetic absorbable membrane called Resolute. Cell ingrowth is restricted by the occlusive membrane, and stimulation of tissue is provided by polyglycolide fiber. Histological studies showed effectiveness similar to nonresorbable membranes with mean clinical attachment gain of 2 mm, and with gain of 4 or more mm in more than 85% of the treated sites, structure retainment for 4 weeks and complete resorption 5-6 months after placement. Vicryl Periodontal Mesh is a woven mesh of 910 polyglactin fibers and 1-lactide. It was noticed that the structure of membrane was lost after 2 weeks, and membrane completely resorbed in 4 or more weeks. Atrisorb membrane is the single membrane manufactured chairside. Polylactic polymer is dissipited in N-methyl-2-pyrrolidone. This forms an

irregularly shaped membrane on exposure of the polymer for 4-6 minutes to 0.9% saline solution. The desired shape is cut. Membrane thickness is 600-750 μm, with unpretentious attaching properties. By applying slight pressure it is placed in the defect. Histologically resorbtion was seen in 6-12 months. Clinical studies proved its adequacy in the periodontal defect treatment. Epi-Guide membrane has three layers consisting of polylactic acid polymer. It remains still for 20 weeks, and is fully resorbed in 6-12 months. Experimental Mempol membrane is manufactured by a bilayered polydioxanon (PDS). PDS loops of 200 μm long coats the first layer. It is meant to homogenize with connective tissue. Its effectiveness is compared to polylactic membranes but the tested membrane resulted in more frequent recession during healing. Besides the already mentioned polyester membranes, use of polyurethane for membrane production has been tested as well. Polyurethanes are organic polymers containing urethane group -NH-CO-O-, materials with diverse properties. Polyether urethanes are degraded through enzymatic and oxidative degradation. Animal experiments showed that polyurethane membranes tend to swell, and inflammation at the flap margins and recession were more pronounced than in polylactic membranes. The membrane seems to be present in the tissue for at least 8 weeks after implantation (16).

Blends of natural polymer and synthetic polymer

Advantages of natural and synthetic polymers are enhanced when they are mixed with each other. A new biomaterial is formed with good biocompatibility having better physical chemical and mechanical properties when PCL - gelatin polymers are mixed with acetic acid. This mixture is used in neural tissue engineering (81), cartilage tissue engineering (82,83), GBR and GTR applications (84-88). To increase the cellular attachment, proliferation, and differentiation ability of membranes various chitosan - based combinations have been prepared. PLLA membrane alone showed less fibroblast penetration property along with degradation rate compared to PLLA / chitosan combination. Degradation of this combination was around 20 % in six weeks, when PLLA membrane was still non-degraded (89). Ku *et al*. (90) prepared PLLA / chitosan membrane. This combination had outer layer madeup of chitosan so that cell attachment is easier and the central layer was madeup of PLLA to give enough mechanical strength. The membrane preserved its solidity for 8 weeks and degraded slowly. The results proved it to be a suitable membrane for GTR treatment.

Bio-ceramic / polymer composites

Bio- ceramics membranes were formed that had similar biochemical structure to that of bone extracellular matrix (ECM) (91). These were made of hydroxyapatite (HA) (92), carbonated hydroxyapatite (CHA) (93), bioactive glass (BG) (94), and beta-calcium phosphate (beta-TCP) (95,96). They had the ability to recruit the immature cells and stimulate these cells to develop into preosteoblast and to allow bone growth on the surface. These also had remarkable biocompatibility (97).
BG can restore hard and soft tissues (98). As the periodontal tissues are madeup of hard and soft tissue, BG is widely used in periodontal regeneration. When bioactive ceramics are added, they increase mineralizatiom and cellular activity on membrane thus proving to be a good osteoinductive and osteoconductive material (99,100) with addition of better mechanical properties (101). When bio-ceramics are added, acidic degradation products are neutralized by alkali group (apatite). This apatite when present in 10 – 30 wt % in the membrane increases the mechanical strength when compared to PLGA membrane alone. When heat treated crosslinked gelatin membrane was mixed with zinc HA powder, greater bone formation was seen compared to collagen membrane. This occurred by the action of zinc ions speeding the proliferation and differentiation process of osteogenic cell. Coating of apatite on a collagen template was therefore considered a realiable alternative (102,103). Therefore, bio-ceramic polymers are beneficial.

ABSORBABLE MEMBRANES CONTAINING FUNCTIONAL MATERIALS

Polymer membranes loaded with antibacterial agents

Bacterial activities causes periodontitis and these bacterial infections lead to failure of GTR treatment. Local drug delivery can be done by using membranes soaked with antibiotics so as to sideline the side effects of systemic drug administration. High antibacterial ability is also shown by non-antibiotic antibacterial agents and can be used in GTR treatment. GTR membranes should be developed that will lead to controlled release of these antibacterial agents so that bacterial infection can be prevented effectively (104-106).

Polymer membranes loaded with growth factors

Growth factors binds to specific receptors on target cells and instruct these cells to acquire their regeneration (107) because these are signaling molecules. GTR membrane causes controlled release of growth factors if the membrane is impregnated with these factors. One of the osteogenic factors, bone morphogenetic proteins (BMPs), was used clinically to achieve bone regeneration in the GTR membrane (108). BMPs triggers new blood vessel formation, and differentiation of mesenchymal stem cells by proliferation and migration to osteoblasts and chondroblasts. Bone morphogenetic proteins-2 (rhBMP-2) was loaded with PCL / PLGA / beta-TCP. Controlled release of rhBMP-2 upto 28 days was allowed. It was noticed that new bone formation was seen after 4 and 8 weeks and complete healing of 8 mm calvarial defects was noticed within 8 weeks (109). These membranes have good potential in the clinical application of GBR and GTR.

ABSORBABLE MEMBRANES BASED ON OTHER POLYMER

To allow formation of new tissues, Platlet-rich fibrin (PRF) madeup of biopolymer fibrin, is a potent source of growth factor. Its fast degrading property within 2 weeks is its disadvantage (110). Therefore, cross-linking treatments, can resist enzymatic degradation. Kawase *et al.* (111) prepared PRF membrane using heat treatment, which was resistant to plasmin and which remained fixed for more than 10 days compared to PRF obtained by gauze-compression. This lowered biodegradation rate without affecting its biocompatibility. Hence, PRF are satisfactory material that can be used in GTR treatment. Salicylic acid - based poly anhydride - esters (SAPAE) are also used in regeneration of periodontal tissues (112). SAPAE is prepared by adding salicylic acid. These decreased the production of pro-inflammatory cytokines as it is a non steroidal anti inflammatory drug..

Subramanian *et al*. (113) used SAPAE membrane as localized drug delivery of salicylic acid which restricted BMP-2 activity in certain areas. The observations and results concluded that these membranes can be used in GTR treatment.

SURGICAL TECHNIQUE (114)

Surgical technique includes flap management (incision, flap elevation, flap positioning and suturing), defect debridement, root surface preparation (scaling, root planing, and chemical root surface preparation) and barrier placement.

Incision and flap management

Flap has to be designed so as to enable complete closure of the defect and coverage of the membrane. Incisions that preserves the interproximal papillae are to be considered such as the 'modified papilla preservation technique' and 'simplified papilla preservation technique' described by Cortellini *et al* (115,116). A combined full thickness and partial thickness buccal flap is recommendable as this enables coronal advancement of the flap and allows for some elongation of the interproximal papillae - by scalloping the gingiva mid-buccally by 1-2 mm which will facilitate interproximal closure. A mobile flap also facilitates suturing without apical tension in the flap. Interproximal mattress suturing is preferred as it increases the contact area between the buccal and lingual papillae and facilitates interproximal closure and primary healing. No surgical pack is used since packing is likely to press the coronally advanced flap apically. The sutures are kept for as long as they hold the flap up, usually 2-4 weeks.

Defect debridement

Complete removal of all granulation tissue is done and the bony walls are exposed. Hand instruments, ultrasonic instruments and various types of rotating instruments may be used (117). Once the root preparation is completed the bony walls may be decorticated to enhance new bone formation.

Root surface preparation

Scaling and planning the root surface is done to remove calculus and bacterial deposits. This is a most critical part of the procedure and is very time consuming. Following mechanical instrumentation, chemical etching agents are widely used for root surface preparation. The goal is to remove smear layer from the mechanical instrumentation, detoxify the root surface from bacterial toxins and demineralise the root surface to expose dentine-collagen matrix. Citric acid or tetracycline hydrochloride both at low pH are used. Application of acid solutions to the root surface in periodontal defects during surgery resulted in smear layer removal and exposure of dentine collagen, but also in nicrotisation of the vital periodontal ligament adjacent to the defect to a depth that correlated to the time of application. However, etching with 24 per cent EDTA at neutral pH was effective on the root surface without the negative side effects to the periodontal ligament.

Barrier placement

The barrier is adjusted to close the defect and 3-4 mm surrounding bone. Then the barrier is secured by attaching it with the tissues with sutures. This extension is needed to accomplish peripheral sealing and prevent the barrier from collapsing into the defect.

Grafting

Bone grafts or bone substitutes are used to put into the osseous defect prior to barrier placement. These are widely used and believed to enhance new bone formation (although the key tissues in regeneration are the cementum and the periodontal ligament without which there will be no new attachment). Apart from the above mentioned properties of bone grafts they are also believed to prevent collapse of the membrane into wide defects.

Infection prevention

Preventing post surgical infection is another key parameter to success in GTR therapy. As the patient has to refrain from mechanical tooth cleaning in the treated area during early healing (4-6 weeks) plaque control is achieved by rinsing with, or local application of, an antiseptic solution during this time. Chlorhexidine (0.2 or 0.12 per cent solutions) is applied twice or three times daily until tooth brushing is resumed.

Conclusion

GTR membranes have lead to formation of cementum and good amount of periodontal regeneration, even though complete regeneration has never been concluded (3). Various benefits and downsides of different polymer membranes were mentioned. The non-absorbable membranes have major limitation of being non-resorbable and therefore second surgical operation is must to remove it. Absorbable membranes in turn do not require second surgical operation. Also limitations of few materials are overcomed by few different polymer. Combination of different components can lead to significant change in the membrane properties. Additional examination and studies are required as there is inadequate evidences of this concept.

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