GUIDED TISSUE REGENERATION MEMBRANE

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Abstract

Periodontal therapy is aimed at achieving restoration of tissues lost due to periodontal disease. The ultimate goal is regeneration of cementum, periodontal ligament, and alveolar bone. There has been a constant effort to improve predictability by introduction of newer techniques. Guided tissue regeneration (GTR) is a promising method to achieve predictable periodontal regeneration. GTR allows and provides space for repopulation of certain cells on denuded root surface to enhance new attachment. One of the limitations of all regenerative procedures is low predictability but selection of cases and operator's skill yields better regeneration. This review discusses the principle, material science and applications of GTR

Key Words : *periodontal therapy, guided tissue regeneration, periodontal regeneration*

Introduction

Periodontitis causes substantial changes on affected tooth root surfaces. The normal cementum is rich in collagen with intrinsic and extrinsic fibers. Inflammation of periodontium brings about destruction of these fibers allowing apical proliferation of junctional epithelium. The cemental surface becomes hypermineralised; bacteria and endotoxins from plaque and calculus penetrate into cemental surface as far as dentin. [1]

The surface changes on cementum during periodontitis renders the tooth root unsuitable for new connective tissue attachment and regeneration. It is therefore imperative to alter the affected root surface to improve predictability of regenerative procedures. Procedures like scaling and root planing removes the altered cementum and provides a substrate that is more suitable for regenerative procedures. Root bio modification removes smear layer off root surfaces. Finally when GTR membranes are appropriately used in such an environment the predictability of new attachment and regeneration increases manifold. [2, 3]

Principle & Concept

The principle of GTR is to impede apical migration of epithelium by placing a membrane between the flap and root surface (preventing contact of the connective tissue with the root surface); cells derived from the periodontal membrane are induced on the root surface selectively and periodontal tissue is regenerated.

The concept of guided tissue regeneration was first developed by Melcher in 1970. He postulated that four types of connective tissue compete for populating root surfaces:

a) Lamina propria of the gingiva
b) PDL
c) Cementum
d) Alveolar bone.

The cell phenotype which succeeds in repopulating the root surface determines the nature of periodontal regeneration. [4, 5] The barrier membrane creates a space and facilitates the proliferation of angiogenic & osteogenic cells from the marrow space into that defect without interferences by fibroblasts [6, 7]

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Definition [3]

The 1996 World Workshop in periodontics defined GTR as "procedure attempting to regenerate lost periodontal structures through differential tissue responses".

Classification [8]

Gottlow (1993) classified the membranes into 3 groups

1.First generation (Non resorbable)

a. Ethyl cellulose (Millipore filter)
b. Expanded Polytetra-fluoro ethylene (e PTFE) membrane (Goretex)
c. Nucleopore membrane
d. Rubber dam

2.Second Generation (resorbable)

a. Collagen membrane.
b. Polylactic acid membrane. (GUIDOR)
c. Vicrylmesh (polyglactin 910)
d. Cargile membrane.
e. Oxidized cellulose.
f. Hydrolysable polyester.

3.Third Generation

Bio resorbable matrices with growth factors.

Material Science

Non-resorbable membrane

The advantage of non- resorbable membrane is that they retain their build and form. But they require a second surgical procedure for its removal. This adds to the tissue trauma during surgery and increases patient discomfort, cost and duration of therapy.

Polytetrafluoroethylene

TEFLON is the first non-resorbable membrane made of polytetrafluoroethylene (ePTFE, Gore-Tex) manufactured when the polymer is subjected to high tensile stress, forming porous microstructure of solid nodes and fibrils [9]. PTFE is a fluorocarbon polymer with exceptional inertness and biocompatibility. It prevents tissue in growth and does not elicit foreign body response after implantation. Gore-Tex, ePTFE membrane consists of 2 parts (Fig 1)

Figure 1: Gore tex, ePTFE membrane

a. An open microstructure collar which promotes connective tissue ingrowth, positioned coronally and prevents apical epithelial migration and ensures wound stability. This part of the membrane is 1mm thick & 90% porous.

b. Other part is occlusive membrane 0.15 mm thick and 30% porous, serving as a space provides for regeneration, which possess structural ability and serves as a barrier towards the gingival flap [10]

Modifications such as incorporation of titanium reinforcements (Fig 2) between the two layers leading to increased mechanical strength and space maintenance have been incorporated. Excellent space maintenance and cell occlusivity are the advantages. The requirement of a second surgical technique to retrieve the membrane is the only disadvantage.

Figure 2:Titanium reinforcements

Knitted nylon fabric

Another non resorbable membrane is Knitted nylon fabric which is mechanically bonded onto a semi permeable silicone membrane and coated with collagen peptides [11]

Resorbable membrane

To overcome the need for surgery and risk of early membrane exposure, resorbable membranes were developed. Ideal resorbable membrane should have the following properties:

Biocompatibility
Biodegradable
Biologically inert
Non-reactive breakdown products
Should not induce foreign body or allergic reactions
Completely resorbable (resorption rate 100%)

Synthetic aliphatic polyester and collagen derived from animal sources are two materials currently used to manufacture resorbable membranes. The disintegration of resorbable membranes are inherently difficult to control and the process of resorption starts immediately after placement of membrane in the surgical site. The speed and extent of resorption varies from individual to individual especially for those membranes requiring enzymatic degradation [12, 13]

Natural Materials

Collagen

A predominant component of collagen membranes commercially available is Type I or sometimes a combination of type I and II. Collagen is derived from calf skin, porcine dermis, tendon etc. Collagen membrane exhibit properties such as hemostasis, chemotaxis for fibroblasts, easy manipulation, and ability to augment tissue thickness [14,15] Examples of collagen membrane are Biogide which resorbs in 8 weeks and another membrane derived from rat tail collagen which resorbs in 4 weeks. (Fig 3) Studies have reported that both membranes resulted in periodontal regeneration.

Figure 3: Collagen Membrane

Biomend (Fig 4,5)

This is a semi occlusive membrane derived from Achilles tendon with a pore size of 0.004 microns and resorbs in 4-6 weeks[11] Avitene and collistat are examples of haemostatic collagen membrane derived from bovine corium . Histologic evaluation of the membranes for disintegration revealed that resorption was complete in 7days. Paroguide, another collagen

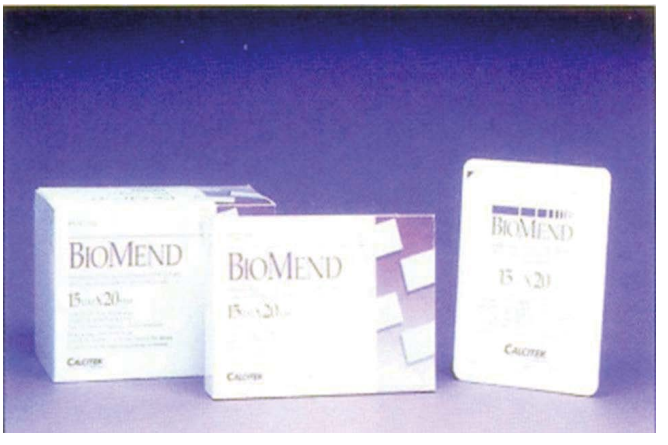

Figure 4:Commercially available collagen membrane- Bio Mend

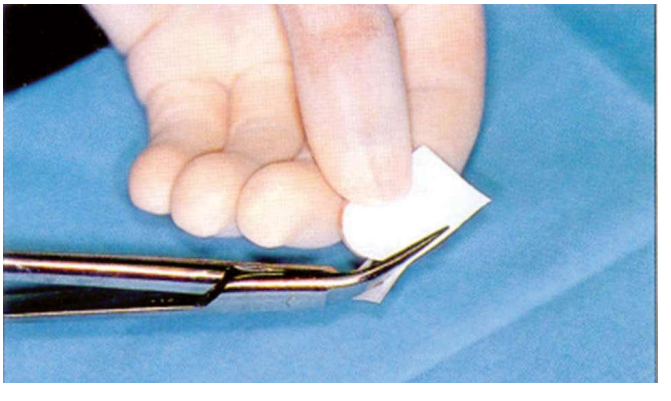

Figure 5: Trimming of membrane to adapt to defects

membrane enriched with chondroitin sulphate was developed and this membrane showed limited value in GTR because of inadequate toughness and low space maintenance. Other natural products tested for GTR without success were Durameter, Oxidized cellulose & laminae bone [11]

Synthetic Materials

Synthetic resorbable materials are usually organic aliphatic thermoplastic polymers. The materials most commonly used are Poly β- hydroxy acids, which include polyglycolic acid and their copolymers which on hydrolysis gives water and carbon dioxide. Degradation time can be lengthened through the addition of lactides and glycols. Resolute (Fig 6) is an example of an occlusive membrane composed of glycolide-lactic copolymer and porous polyglycolide fiber. [11]

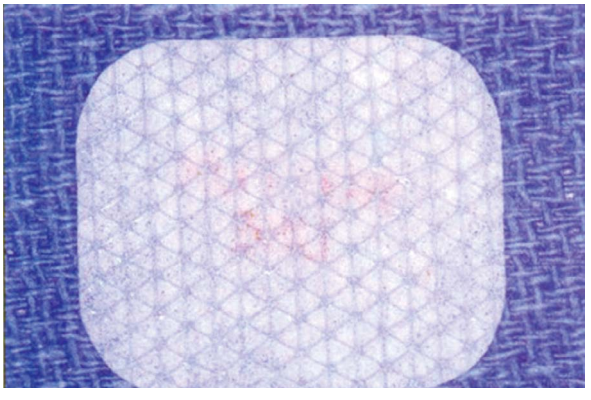

Figure 6: Resolute membrane

Vicryl periodontal mesh

Fibres of polyglactin 910, copolymers of glycolide & 1-lactide form a tightly woven mesh called Vicryl

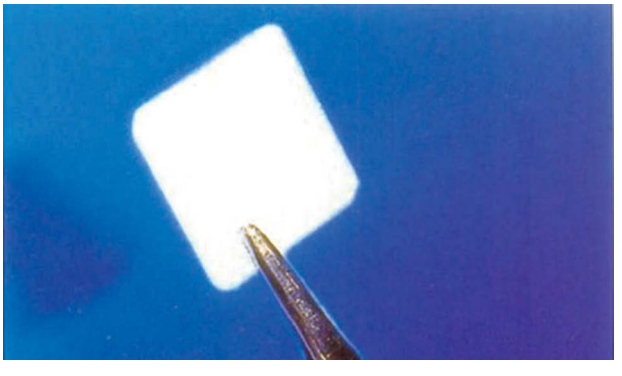

Figure 7 (a): Vicryl periodontal mesh

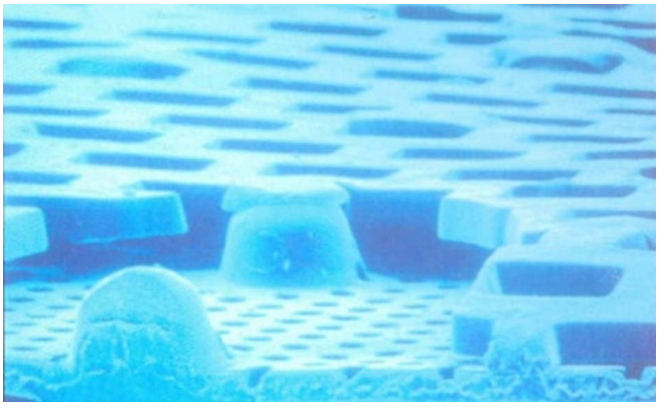

Figure 7(b): Vicryl periodontal mesh

Periodontal Mesh. (Fig 7a,7b) It is reported that the membrane loses its structure after 2 weeks and complete resorption takes place in 4 or more weeks. [16]

Atrisorb membrane

It is the only GTR membrane with Polylactic polymer manufactured chairside in flowable form and dissolved in N-methyl 2 – pyrolidone. [11]

Epi-guide

This membrane has three layers and is composed of Polylactic acid polymers to exclude epithelial cells and fibroblasts. It resorbs in 6-12 months and maintains its structure for 20 weeks

Experimental mempol

It is manufactured from polydioxanon (PDs), a dioxanon polymer and is bilayered. The first layer is completely impermeable covered with PDs loop 200μm long on the gingival side intended for integration with connective tissue [11]. It is a completely impermeable bilayered membrane on the gingival side and manufactured from polydioxanon polymer.

Cargile membrane

It is derived from the cecum of ox and is processed and chromatized in a similar manner as that of suture material. It is supposed to resorb in 30-60 days. The Cargile membranes degraded within 4-8 weeks, adding support to the concept that critical events in new attachment formation occur during the first month of healing [17]

Polylactic acid

It is a biodegradable ester polymer & was originally used in orthopedic surgery in various configurations and Polylactic acid barriers inhibit epithelial migration. [18, 19] The Polylactic acid was designed to degrade in 3-4 months. By using a thinner membrane or a material with uniform and relatively low molecular weight,[20] degradation time of 1-2 months would be sufficient and achieved.

Oxidized cellulose

Oxidized cellulose mesh is a commercially available resorbable haemostatic dressing that converts to a gelatinous mass upon incorporating blood. In vivo and in vitro studies have demonstrated that the material resorbed without harmful effects and may possess antibacterial properties. [21]

Natural eggshell membrane (ESM)

ESM is a non-calcifying bi-layered membrane between the egg albumin and the inner surface of the eggshell. It is composed of water-insoluble interwoven protein fibbers that highly cross-linked by a large amount of disulphide bridges [22, 23]. It has been discovered to contain types I, V, and X collagens, osteopontin, sialoprotein, sialic acid, lysozyme, ovotransferrin, uronic acid, clusterin, etc [24, 25]. It exhibits antibacterial activity by decreasing the heat resistance of bacterial pathogens. This whole eggshell bio mineralization only takes less than 24 hours and is among the most rapid mineralization processes ever known. [25, 26, 27] Bone marrow stromal cells (BMSCs) could grow and proliferate well on natural ESM and then concluded that ESM had the potential to be used as a bone tissue engineering scaffold [28] These studies indicated that ESM has great biocompatibility and the ability to enhance the healing of damaged tissues, thus suggested that it can be a suitable candidate for GTR membrane [25, 26]

Soluble Eggshell Membrane Proteins (SEP)

This is manufactured from natural hen ESM by the process of reductive cleavage with aqueous mecaptoproionic acid in the presence of acetic acid. Cell culture tests have reported biocompatibility comparable to that of collagen type 1 and superior to raw ESM [29, 30, 31]

Applications of Guided Tissue Regeneration

In Intrabony Defects [32, 33]

Defect morphology plays a major role in the healing response of guided tissue regeneration therapy in intrabony defects. It has been demonstrated that greater amounts of clinical attachment and bone can be gained in deeper defects.

In Furcation Defect [34,35]

The risk of periodontitis progression in the furcation lesions increases with the severity of the furcation involvement [34] and therefore Grade I furcation have generally been well managed with routine periodontal surgical procedures aimed to thoroughly debride the lesion, reduce pockets and expose the furcation entrance for adequate plaque control. [35]

Grade II furcations however require various regenerative such as open flap debridement, bone replacement grafts, coronally repositioned flaps and guided tissue regeneration barriers [34] [35]

In Gingival Recessions [36, 37, 38, 39]

The applicability of the treatment of gingival recessions with barrier membranes has also been clinically demonstrated in humans [40].

Two major surgical problems that are to be resolved to increase the possibility of obtaining satisfactory clinical results have been identified:

1. Difficulty in providing enough space for regeneration between the prominent root surface and the membrane

2. Difficulty in providing and maintaining an adequate biological coverage of the membrane with the flap in sites where the gingival tissues had receded [37]

Ideally, the membrane should cover all of the denuded root surface up to the cementoenamel junction and maintain a space between its inner surface and the root surface. [37] Solutions to these problems have been proposed in a series of clinical trials and case reports with the aim of obtaining

the best results in terms of root coverage, clinical attachment gain and pocket depth reduction [37]

For bone augmentation around implants [41, 42]

GTR has been successfully used in the placemnt of dental implants in immediate extraction sockets sites and is also used for regeneration ofbony defects around the implants.

Future Trends in GTR

To enhance regenerative properties while using GTR, numerous modifications have been attempted in the membrane properties. To ensure cell specificity during repopulation, adhesion molecules have been incorporated.

Recent advances include infusion of antibiotics in GTR membranes. This antibacterial nature of membrane is thought to be of great benefit during early wound healing phases and thus improve regenerative outcome. Addition of growth factors have also been investigated. These factors are expected to aid in cell differentiation and migration to the wound space. An example is development of combined polylactide and alginate membranes, with controlled TGF-β release.

Conclusion

It is important to understand that Guided tissue regeneration is not a procedure aimed at treating periodontitis. It is rather a promising approach for attempting regeneration of tissues lost due to periodontitis and therefore appropriate periodontal treatment should precede before GTR is attempted. The future of periodontal reconstruction depends on emergence of such techniques in tissue regeneration which when used diligently for appropriate periodontal defects will yield predictable results

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