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REVIEW ARTICLE

Guided Bone Regeneration to Improve Osseointegration in Dental Implant

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ABSTRACT

Prosthetic oral rehabilitation using dental implant has significantly increase because of the patient's esthetic necessity and as predictable treatment. There is 40-60% of alveolar bone width and height loss in 2-3 years post-extraction. Dental implant mechanical stability depends on the successful of osseointegration and healthy soft tissue attachment over the abutment as a result of healing post-implantation. Inadequate bone volume at the time of implantation have been associated with decreased success rates and long term prognosis in implant dentistry. Guided bone regeneration (GBR) can be used with or without combination of bone graft to gain the volume of bone for implant placement. The benefit of using membrane GBR in dental implants is to accelerate implant placement by enhance bone formation surrounding implant material and as a result osseointegration can be achieved

Keywords: GBR; Dental implant, Osseointegration, Human health

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INTRODUCTION

In the late decade, prosthetic oral rehabilitation using dental implant has significantly increase due to high esthetic demands of patients and as predictable treatment for terminal treatment of various edentulous and missing teeth cases. The alveolar bone healing post-extraction usually takes 6-12 months and sometimes more before placement of the endo-osseous implant. There is 40-60% of alveolar bone width and height loss for 2-3 years post-extraction (1,2). This bone loss get worse if the tooth loss caused by trauma, there are periodontal pathologies, pre-existing endodontic or

requires bone volume enhancement to get ideal gingival contours and esthetics (3). Dental implant mechanical stability depends on the successful osseointegration defined as direct anchorage of the implant in the bone tissue without forming fibrous tissue and there is healthy soft tissue attachment over the abutment as a result of healing post-implantation. Low-level of bone volume for implantation decrease the long term prognosis and the success rate in implant dentistry (4)]. Dental implant success rate are 95% for mandible and 84.7% for maxilla. Dental implant which placed in alveolar ridges undergo resorbtion causes peri-implantittis (intrabony defects, dehiscence or fenestration) (5).

There are many ways to enhance bone formation rate, specially using bone graft materials, GBR or combination of both materials. GBR is a dental surgical procedure using membrane to gain the bone tissue

volume for implant placement (8). The main criteria required when selecting GBR membrane following characteristics biocompatibility, there is no interaction between material and host tissue which causes wound dehiscence or infection; cell occlusiveness is an ability to prevent fibrous connective tissue invasion; space maintenance (space-making ability) depends on membrane stiffness; blood clot stabilization which is important for angiogenesis; mechanical strength to protect blood clot and prevents invasion unwanted cell and bacteria; and clinical manageability that the membrane should be easy to modify and manipulate by the size and the shape (6).

GBR combined with or without bone grafts has been shown the most expected results in practical of peri-implant bone defects treatment. The membrane acts as biological and mechanical barrier which only allows migration of osteoprogenitor stem cell into the defect area and expected more bone formation without intervention of the fibroblast and epithelial cell from mucosa that has higher rate of migration (2). GBR alongside the metal implant promotes active bone modelling to fill the empty defect with new bone tissue for early post-implantation span. The new bone tissue contains more organized collagen and less mineral than the old pre-existing bone tissues that important to support dental implant stability during mastication loading (7). The benefit of using membrane GBR in dental implants is to accelerate implant placement by enhance bone formation surrounding implant material and as a result osseointegration can be achieved.

METHODS

The method we used in writing this article review was a narrative review conducted using the medical databases MEDLINE/PubMed, Google Scholar and science Direct. The data collection strategy used keywords to gain articles in English to be reviewed in publication period between 2006- 2020 were included. The search strategy was restricted to in vitro and in vivo studies that described GBR

NON-RESORBABLE MEMBRANE

Non-resorbable membrane which implanted in the living body can not be degraded through enzymatic reaction. Disadvantages of this material are need secondary surgical procedure to remove the membrane which may lead to total failure of the regeneration process, increase morbidity, risk for tissue damage, and from a cost-benefit point of view. The first commercial membrane was expanded polytetrafluoroethylene (e-PTFE) which consists of 2 parts, coronal border which has an open microstructure collar with internodal distance less than 25 μm which facilitates prior haematoma forming and collagen fiber attachment to stabilize the membrane until it becomes fixed and to prevent epithelial migration; and

an occlusive portion with internodal distance $<8 \mu\text{m}$ allows nutrient transportation and prevents the invasion of other tissue cell. e-PTFE must be take out immediately if there is inflammation. The pore size 0,02 μm of high density PTFE (d-PTFE) membrane can eliminates bacterial invasion into the bone augmentation site so the possibility of infection is less than e-PTFE and it covers the graft and/or implant material underneath. Cytoplasm membrane does not have porous structure which makes the tissues attachment weak and easy removing (8,9).

RESORBABLE MEMBRANE

Bioresorbable membrane materials are polyglycoside synthetic, polylactic acid (PLA), polyglactide, polylactide, polyglactin, polyglycolide acid (PGA), polycaprolactone (PCL), and native collagen (10,11). The permeable membrane barrier allows fluid substances exchange which contains nutrition and oxygen. The impermeable membranes may prevents oxygen passing into the defect which causes low oxygen tension and result cartilage formation. Membrane porosities affect wound stabilization, nutrient flow, and peripheral sealing to block the infiltration of soft tissue-forming cells (8). Degradation time in resorbable membrane is important to provide a barrier during the whole healing process. Cross-linking by physical (UV irradiation), chemical (glutaraldehyde, hexamethylene diisocyanate, diphenylphosphorylazide), and enzymatic (ribose) or larger and thicker membranes is strategy for longer degradation (11).

Collagen membrane has several advantages including the hemostasis, weak immunogenicity, easy manipulation, chemotaxis of gingiva and periodontal ligament fibroblast, ability to increase the thickness of tissue, has direct effect on bone formation; less patient morbidity, the absence of exposure of the regenerated bone in the apical areas, and do not need membrane removal. The non-resorbable membranes are recommended for vertical bone regeneration treatment, meanwhile the resorbable membranes are recommended for horizontal bone regeneration treatment (12). Titanium-reinforced ePTFE membrane combined with bone graft can increase vertical bone augmentation.

Collagen from bovine pericardium is native collagen resorbable membranes that is mostly used due to its biocompatibility, tissue integration, hemostatic activity, and involved chemical cross-linking to make longer period of degradation. Nevertheless, collagen fibrils cross-linking process was associated with delayed vascular invasion and worse tissue integration. Recently study show that demineralized freeze-dried bovine cortical bone membrane (DFDBCMB) was intended to be used as xenogenic material in GBR procedure. It is crucial to know the cytotoxicity, antigenicity, and biocompatibility of membrane to accomplish the requirements for GBR membrane use in human.

DFDBCMB showed that up to 28 days of control period it is still withstand more than half of initial dimensions, and an bioresorbable membranes should persist for 3-4 weeks (13). The characteristic and biodegradation time of each materials could seen in Table I.

Autogenous

Autogenous graft is harvested and implanted bone within the same patient. It was harvested in mandibular ramus, posterior iliac crest or calvaria bone. The mechanism

Table I. GBR membranes used in the dental practice

Characteristic	Family	Material	Commercial Product	Biodegradation
Synthetic non-resorbable	PTFE	Expanded PTFE (e-PTFE)	Gore-Tex	
		Dense PTFE (d-PTFE)	Cytoplast TXT-200	
		Dual textured expanded PTFE	NeoGen	-
		Titanium-reinforced PTFE	Gore-Tex-Ti; Cytoplast; Ti-250; NeoGen; Ti-reinforced	
Synthetic resorbable	Copolymers	Polylactic acid (PLA)	Guidor®	PLA 1-4 years
		Polyglactin	Vicryl®	PGA and PCL <1 year
		Poly(lactic-co-glycolic acid) (PLGA)	Resolute Adapt; Resolut Adapt LT	Resolute Adapt 8-10 weeks Resolut Adapt LT 16-34 weeks
Native resorbable	Collagen	Type I collagen	CollaTape; Tutodent; Cova MAX; Parasorb	CollTape 1-2 weeks
		Atelocollagen from type I collagen	Resodent	Bottis Jason 8-12 weeks
		Type I and III collagen	Koken Tissue Guide; Terudermis;	Copios Extend 24-36 weeks
		Type I, III, IV, VI collagen and other protein	BioGide; Botiss Jason	
		Not specified type of collagen	DynaMatrix	
		Collagen and elastin	Heal-All Biomembrane	
		Cross-linked type I collagen	Creos xenoprotect	
		Cross-linked type I and type III collagen	BioMend; OSSIX PLUS; OsseoGuard	
		Porcine pericardium	OsseoGuard Flex; EZ Cure; MatrixDerm EXT	
		Vitala Porcine Pericardium Collagen Membrane		

GBR WITH BONE GRAFTING

The widely problem in GBR application there are membrane collapse and exposure of membrane due to soft tissue dehiscences result local infection and inadequate of bone regeneration (8). GBR membrane combines with particulate bone graft material prevents membrane collapse, to preserve and maintain the space and also immobilization of the bone graft (10). Bone graft materials differs into four type according to origin, there are autogenous, allograft, xenograft and alloplast

of bone regeneration using autogenous bone graft through osteogenesis which is living osteoblasts derived from the graft contribute to the bone tissue forming, osteoinduction by stimulating osteoprogenitor stem cell differentiated into osteoblasts usually stimulate by a bone morphogenetic protein (BMPs) released from the graft, and osteoconduction as scaffold for attachment of newly-formed bone tissue or promote the deposition of differentiated osteoprogenitor stem cell and provides as scaffold for vascular growth. Autogenous bone graft is gold standard for bone graft materials. However

harvested tissue from secondary surgical area can increase patient morbidity and the problem of obtaining sufficient amount of graft material convey the researchers to find new bone substitutes (2,8)

According to Johnson et al., (2018), using GBR membrane combined with recombinant human bone morphogenetic protein (rhBMP)-2 and demineralized bone matrix (DBM) stimulate differentiation of osteoblast precursor to produce new bone matrix contains mineral and premature collagen, promote early formation and long-term mineralization of new bone tissue at dental implants defect site. rhBMP-2 is able to increase bone quality at the bone-implant contact for 4 weeks after implantation and retained for longer period post-implantation (8 weeks) at the defect site. In the DBM treatment, rhBMP-2 increase bone quality which interface the implant in the early period after implantation and the effects are retained longer at the defect area (7)

Allograft

Allograft is tissue which is taken from individuals within the same species as the hosts. There are three types of allograft such as frozen, freeze-dried, demineralized freeze-dried and mineralized-freeze dried which forms into particulate, gels and putties. The mechanism bone regeneration using allograft only osteoconductive and osteoinductive. The advantages using this material are available which do not need secondary surgical site, high bone volume supply, but longer bone formation and less bone regeneration (8,10)

Alloplast

Alloplasts are fabricated graft material. There are calcium synthetic hydroxyapatite (HA), sulfate calcium carbonate, bioactive glass polymers, calcium phosphate, and beta-tricalcium phosphate (β -TCP). They contribute in osseous defects repair and to the increase of osseous ingrowth. Alloplasts have only osteoconductive properties. These graft materials act as scaffold for new bone tissue formation. Coralline hydroxyapatite (CHA) contains calcium carbonate (87-98%), potassium (2-13%), strontium, magnesium, fluoride, and sodium. The porosity is >45% and the pores diameter around 150-500 μ m. The degradation of coralline is caused by reaction of carbonic anhydrase secreted by osteoclasts (14). According to Fairbairn et al., (2018) alveolar ridge preservation of mandibular right first molar using bone grafts contain β -TCP and calcium sulfate without GBR membrane showed good soft tissue healing without losing of attached gingiva and it was successfully loaded after 12 weeks post-implantation.

Xenograft

Xenografts obtained from animal species. Deproteinized

bovine bone and natural HA are the most widely used of xenograft materials. Xenograft act as osteoconductive properties. The diversity of characterized commercial graft materials (geometries, porosity, differs solubilities and densities), chemical composition, and physical form will determine the level of bioresorbability (8,10). The bovine bone xenograft is not biodegradable and causes several adverse effect such as foreign body reactions, chronic inflammation, encapsulation, soft-tissue fenestrations, associated cysts, and implant failure. Long-term clinical evaluations are necessary to identify the biological complications of xenografts that are widely used in dentistry (16).

According to study Queiroz et al., (2006) bone defect in rabbit loaded with lyophilized bovine bone and covered with bone matrix membrane (Bioplate) result large amounts of newly-form mature bone at 15, 30, and 60 days post-surgery. The defect which covered with membrane were similar to untreated defect where cavity was filled with fibrous connective tissue. At 30 days, the membrane was almost totally resorbed which is associated with chronic inflammatory infiltration.

GBR FOR PERI-IMPLANTITIS TREATMENT

Peri-implantitis is destruction of peri-implant tissue caused by accumulation of bacterial associated periodontitis result in supporting bone loss and may lead to the failure of implant placement. The prevalence of peri-implantitis ranges from 2-10%. Peri-implant bone support loss more than half of the implant length causes the implant removal need to be considered. The recent study, peri-implantitis with vertical bone loss which treated with aluminium oxide membrane and autogenous bone increase bone height and complete implant cover up to 14 months. Previous decontamination using chemical agents (tetracycline and citric acid) or abrasive blasting is highly recommended to remove of bacterial toxin and try to "reactivate" the desirable biological properties of the surface layer of titanium dioxide of the implant surface involved in peri-implantitis (18). The observational period, survival rate and outcome of GBR used in implant treatments could seen in table II

CONCLUSION

GBR procedures using non-resorbable or resorbable membranes combined with or without grafting materials in dental implant result acceleration implant placement characterized by osseointegration with high survival rate and be considered as predictable and safe treatment for long-term follow-up time.

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Table II. GBR membrane used in dental implant.

Study	Observation Period	Groups	Survival rate	Outcome
(5)	Before surgery, baseline, 2,3, and 6 months after surgery	Control: without GBR procedure Treatment: Xenograft + Bio-collagen resorbable membrane (Biotech)	-	There is no significant difference thickness and width of the keratinized gingiva in control and treatment group. MBL were greater in treatment group
(6)	6 months	I-Gen titanium membrane	-	Posterior mandibular tooth with buccal bone defect result 2 mm bone thickness was formed and good implant stability after 6 months
(19)	3 and 5 years	Control: bone graft and collagen membrane (CM) Treatment: graft + CM + rhBMP-2	100%	Radiographic interproximal marginal bone level (MBL) were taken 3 years post-implant loading result: Control: 1,22 mm Treatment: 1,37 mm 5 years post-implant loading result: Control: 1,23 mm Treatment: 1,38 mm
(20)	12,5 years	Deminerlized bovine bone mineral (DBBM) combined with: CM or e-PTFE	91.9-92.6%	Radiographic MBL and the interface of first visible bone-to-implant were measured from mesial and distal aspect: Control = 2,36 mm e-PTFE = 2,53 mm CM = 2,4 mm
[(21)	1 week, 12 months	Xenograft + auto-genous bone grafts + titanium-reinforced non resorbable membrane	-	Follow-up period 1 week result: No inflammation and foreign body reactions Horizontal bone defects gain 6 mm and vertical bone defect gain 4 mm. Follow-up period 12 months result: <1 mm bone loss and all implants have survived
(22)	6 months	Biphasic calcium phosphate ceramic bone + PLA Biphasic calcium phosphate ceramic bone + CM	-	Osseointegrated implant and no implant loss in both groups Facial bone thickness on PLA group was reduced higher than CM group, but no statistically significant difference

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