REVIEW ARTICLE

Collagen in Bovine Dentine Promotes BMP2 and Osterix Expression In Bone Healing

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ABSTRACT

Alveolar bone defect is one of the damage to the hard tissues of the oral cavity caused by pathological conditions. The speed of the healing process between connective tissue and bone tissue in the area of bone defect causes soft tissue infiltration in hard tissue and has the potential to inhibit bone formation. This soft tissue-infiltrated bone formation causes changes in the vertical dimensions of bone in the final bone healing outcome. The role of collagen bovine dentine membrane as a barrier to limit the expansion of non-osteogenic cells at the location of bone defects is the basis for its usage in guided bone regeneration methods and promotes osteoblastogenesis by activated BMP2 and Osterix expression on bone healing process as a challenge in bone biology strategy. Demineralized Dentine Material Membrane (DDMM) is a bioresorption barrier membrane, made from bovine dentine waste which is designed as Guided Bone Regeneration. This biomaterial is a Green Economy product by utilizing biological waste, has increased economic value and also a halal properties. The pathway of this step is known as osteoblastogenesis. The purpose of this article review is to describe the role of DDMM as aspects involved in the osteoblastogenesis of bone healing process by activation of BMP2 and Osterix.

Keywords: Guided Bone regeneration, BMP2, Osterix, green economy, human and health

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INTRODUCTION

Repair of craniofacial bone defects from trauma, contamination or tumor resection is a main problems of the dentist and medical professional profession. (1) Collagen bovine dintine membrane membrane implantation in bone defect causes better repopulation of osteogenic cells in the bone defect area and a faster healing process is achieved. The urgency of using bovine dentin is to highlight membrane design innovations that meet the criteria as Guided Bone Regeneration (GBR), have a positive effect on the bone regeneration process, do not require surgery for retrieval and are affordable by the Indonesian people to support a green economy. GBR is a biomaterial layer that designed for protecting deffect bone tissue area through a membrane barrier. The barrier membrane continues protects the invasion of fibroblasts and epithelium from getting into the bone tissue deffect, in order that the bone cells are capable of repopulate until the final of the wound healing process. (2)

The transforming cycle in bone defects starts off evolved with the recruitment of osteoclast precursor cells. These cells differentiate into osteoclasts once they acquire indicators from osteoblasts. Proteolytic enzymes are then produced by mature osteoclasts, which break down the collagen matrix. The first stage of the transformation cycle is represented by this bone resorption. The apoptosis of osteoclasts controls the next section. Preosteoblasts, which are derived from mesenchymal stem cells found inside the bone marrow, make up the following phase of the transforming cycle. Mature osteoblasts produce collagen type 1 and the bone matrix, and they modify the mineralization of freshly formed bone. Additionally,

some mature osteoblasts may become stuck in calcified bone and transform into osteocytes.(3)

Osteoblastogenesis is the system of differentiation of osteoblasts into mature osteocytes. Osteoblastogenesis is caused with the aid of using the TGF- superfamily via a convoluted type I receptor (BMPR I) and a type II receptor heteromeric receptor (BMPR II) at the molecular stage that transduces intracellular indicators thru the Smad complicated (BMP/Smad) or thru mitogen-activated protein kinase (MAPK). BMP has a position in growing the differentiation of Mesenchimal Stem Cell (MSC) into chondroblasts and osteoblasts. BMP2 performs a position withinside the BMP2/RUNX2 pathway in osteoblast cells. To create a phosphorylate receptor-activated Smad complex (R - Smad 1/5/8), BMP2 binds to BMPR 1 and BMPR II. In order to construct the Smad Complex and create the osteoblast nucleus, the active Smad will combine with Smad 4 (Co-Smad).This will cause elevated Osterix (OSX) expression, an osteoprogenitor protein to set off molecular differentiation into osteoblasts then grow to be osteocytes in bone formation.(4)

To fully comprehend the significance of osteoblastogenesis in the process of bone healing, more explanation is required to demonstrate the process of osteoblastogenesis through increased expression of BMP2 and OSX in bone healing.

Collagen bovine dentine Membrane

Collagen bovine dentine Membrane biomaterial named Demineralized Dentine Material Membrane (DDMM) is a bioresorption barrier membrane that made from bovine dentine and play a role as guided bone regeneration (GBR). Dentin in human teeth has a chemical composition that is almost similar to that of alveolar bone which is a mineralized connective tissue. Its composition is made up of 70% inorganic components, 10% bodily fluids, 2% non-collagenous protein (NCP), 18% collagen. The inorganic part consists of hydroxyapatite crystals which are the main components, calcium, phosphorus, hydroxyl, citrate, carbonate, sodium, magnesium and fluorine. While 90% of the organic matter of dentine is composed of type I collagen fibers. This is close to the content of bovine dentine where in bovine dentine there is a content of 70% inorganic components (HA and tricalcium phosphate), 20% organic components, and 10% water. (5,6,7)

Bones and tooth have a completely comparable chemical composition. Dentin includes 65% inorganic materials and 35% natural be counted and water and alveolar bone includes 65% inorganic materials and 35% natural be counted and water. Teeth have a hybrid natural and inorganic composition inclusive of calcium phosphate, collagen and different natural components. Some literature describes the primacy of the use of osteoconductive substances for bone healing. Bovine dentin has chemotactic, mitogenic and osteogenic ability equal to Bone Morphogenetic Proteins (BMP). In addition, DDM has blessings which includes being wealthy in boom factors (TGF-beta, FGF, PDGF and EGF). Therefore, it's miles idea that bovine dentin may be used to increase bone graft substances which have abilities much like autogenous bone. Bioresorption membranes are substances that don't require surgical treatment for removal. There are 2 kinds of bioresorption barrier membranes, specifically herbal and synthetic. One of the biomaterial bioresorption membrane substances is dentin derived from bovine tooth, referred to as Decalcified Dentin Material membrane (DDMM). (8)

Decalcified Dentin Material Membrane (DDMM) is designed as a GBR substitution biomaterial that is useful as a mechanical barrier to prevent unwanted cell invasion in bone defects. This biomaterial made from bovine dentin waste, low production costs, and comes from halal biological sources. The design of DDMM substitute biomaterial as GBR is in line with the Green Economy principle in the Sustainable Development Goals. Due to the release of growth factors involved in bone mineralization, most likely BMP and Osterix, DDMM has more inductive characteristics than mineralized dentine.

Guided Bone Regeneration

GBR is one of the newly strategies on alveolar bone defects by usage of a barrier membrane without or with bone graft to carry out ridge augmentation. The precept of GBR is that the membrane will feature as a barrier while located at the alveolar bone deffect to keep away from the expression of undesirable non-osteogenic cells withinside the bone deffect area including epithelium and connective tissue. Following GBR implantation, bone repair depends on osteoblasts and pluripotent cells, including those from the periosteum, bone, and nearby bone marrow, migrating to the location of the bone problem. The pace of osteogenesis must be greater than the rate of fibrogenesis in the surrounding soft tissue for the majority of bone defects to regenerate. (9,10)

After GBR implantation, bone regeneration takes place through following numerous stages. In the primary 24 hours, the distance shaped through the presence of the graft barrier is full of blood clots that release elements which includes PDGF and cytokines which includes IL-8 to draw neutrophils and macrophages. Then the blood clot can be absorbed and changed with granulation tissue that's wealthy in new blood vessels. Through those blood vessels, vitamins and mesenchymal stem cells which are capable to osteogenic differentiation can be transported and assist the manner of osteoid formation. Osteoid mineralization form woven bone, which then serves as a template for lamellar bone apposition. This number one spongy transformation will eventually form compact bone and reticular bone with bone marrow. This manner will retain for 3-4 months post-surgical

treatment to regenerate the bone completely.(9)

The GBR manner is normally accomplished to growth the extent of bone withinside the ridge defect. Some symptoms for the usage of GBR are alveolar bone defects each horizontally and vertically, to shape osseous fills on on the immediate implants, dehiscence and fenestration related to implant placement, bone defects because of implant failure, and to restore sinus membrane perforations.(11)

Osteoblastogenesis

The transforming cycle in bone defects starts off evolved with the recruitment of osteoclast precursor cells. These cells differentiate into osteoclasts once they acquire indicators from osteoblasts. Proteolytic enzymes are then produced by mature osteoclasts, which break down the collagen matrix. The first stage of the transformation cycle is represented by this bone resorption. This extensive section is controlled by osteoclast apoptosis. Preosteoblasts, which are derived from mesenchymal stem cells found inside the bone marrow, make up the following phase of the transforming cycle. In 2 to 8 weeks, mature osteoblasts modify the mineralization of freshly shaped bone by synthesizing bone matrix, specifically kind 1 collagen. Additionally, some mature osteoblasts have the potential to become stuck in mineralized bone and develop into osteocytes (12).

Osteoblastogenesis is the manner of osteoblast differentiation, TGF- induces osteoblastogenesis and recognized TGF-β as a regulator in regulating bone resorption and bone formation. The TGF-β superfamily includes TGF-βs, activin, BMP, and different proteins. The TGF- superfamily acts thru a heteromeric receptor complicated along with a type I receptor (BMPR I) and a type II receptor (BMPR II) at the mobileular floor that transduces intracellular indicators thru the Smad complicated (BMP/Smad) or thru mitogen-activated protein kinase (MAPK) cascade (13).

TGF-β1 and BMP are superfamily of TGF-β which have a essential function in bone restoration. TGF-β1 will stimulate the proliferation of osteoblasts and work in the process of bone resorption by osteoclasts. Meanwhile, BMP has a function in growing the differentiation of MSCs into chondroblasts and osteoblasts. BMP2 which is likewise one of the maximum essential cytokines in bone restoration is likewise a part of the TGF-β superfamily. BMP2 will play a function withinside the BMP2/RUNX2 pathway in osteoblast cells. To create a phosphorylate receptor-activated Smad complex (R - Smad 1/5/8), BMP2 binds to BMPR 1 and BMPR II. Smad 4 (Co-Smad), an integration of the active Smad, will shape the Smad Complex when it enters the osteoblast nucleus. In addition to increasing the expression of many osteoblast proteins and mRNAs, including ALP, collagen I, OC, and osteopontin, this results in the expression of RUNX2 and OSX. Extracellular matrix calcification is caused by the synthesis of ALP and multiple other indicators of osteoblast development. Osteoarthritis, Myhre syndrome, and other bone abnormalities, as well as impaired BMP and TGF- signaling, can ensue. Clinical implications for the therapy of several bone illnesses, such as promoting bone regeneration after fractures, osteoarthritis, and osteoporosis, include manipulation of BMP and TGF- signaling pathways, including Osterix. (13,14,15,16)

Mesenchymal cells undergo a multi-step process called osteoblast differentiation in order to become cells of the osteoblast lineage, including osteocytes. A transcription factor called Osterix (Osx), which is particular to osteoblasts, activates a variety of genes when preosteoblasts develop into mature osteoblasts and osteocytes. It is generally recognized that Osx plays a crucial part in the genetic code for bone development and homeostasis.. The zinc finger transcription factor Osterix (Osx), which is specifically expressed by osteoblasts during bone growth, prevents bone mineralization when it is inactive. Osx is a right away goal of Runx2, its BMP2 dependent induction is mediated with the aid of using collagen bovine dintine membrane membrane that has a proliferation and differentiation capability in osteoblastogenesis. Osterix (Osx) is a zinc finger transcription thing particularly expressed with the aid of using osteoblasts that's critical for osteoblast differentiation. Lack of BMP2 induction will affect OSX expression deficient thal display absence of osteoblasts and faulty bone formation. (17, 18)

Osx is specifically expressed by osteoblasts and is essential for osteoblast development. Lack of BMP2 induction will cause Osx expression to drop, which will lead to a lack of osteoblasts and improper bone production.(19,20)

CONCLUSION

Mesenchymal cells undergo a multi-step process called osteoblastogenesis during which they differentiate into osteoblast lineage cells and osteocytes. When preosteoblasts differentiate into mature osteoblasts and osteocytes, an osteoblast-specific transcription factor called Osterix (Osx) turns on a variety of genes. It is well recognized that Osx plays a significant role in the genetic application of bone development and bone homeostasis.. An absence of bone healing results from the inactivation of Osterix (Osx), a zinc finger transcription property that is specifically produced by osteoblasts in the direction of bone growth. Osx is a suitable factor for Runx2 expression, with BMP2 dependent induction being mediated with the aid of the application of collagen bovine dentine membrane, which has the ability to operate as both a proliferation and differentiation mechanism in osteoblastogenesis.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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