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AUTOGENOUS DENTIN AS A BONE REGENERATIVE MATERIAL

Dental Science

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ABSTRACT

Several bone graft materials have been used over time for treating periodontal defects. Though autogenous bone is still considered the gold standard for bone augmentation, it has some disadvantages including donor site morbidity and limited source1 along with high resorption rates up to 50%. Other bone graft materials such as allografts, xenografts, and alloplastic bone grafts have some disadvantages where allografts lack osteoproliferation and carry the risk of disease transmission, and xenografts and alloplasts only show osteoconduction2.Therefore, development of an alternative graft material that surpasses all these limitations is expected. Recently, bone graft materials using permanent teeth have come into light, and clinical and histological outcomes of this material have been confirmed in dental procedures by various studies2,3 . Normally extracted tooth is considered as clinical waste but they can be used as a graft in various situations to treat the alveolar bone defects. The current review focuses on using dentin as a bone graft material in the field of periodontics. Based on the potentials of osteoconduction, osteoinduction and osteogenesis through growth factors in tooth and similar histogenesis between tooth and bone autogenous dentin can be used as a bone substitute for regeneration alveolar defects.

KEYWORDS

autogenous dentin graft, alveolar defects , extracted teeth

INTRODUCTION

Periodontitis is an inflammatory disease of supporting tissues of the teeth caused by specific microorganisms, or group of specific microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with pocket formation, recession or both[4]. Reconstruction or restoration of osseous defects caused by the inflammatory periodontal disease is a continuing challenge in periodontal therapy. These resulting osseous defects are treated by many techniques for regeneration of bone for better prognosis. The combination of various regenerative biologic agents and techniques has recently attracted the interest of researchers in the field of reconstructive periodontal surgical therapy[5].It has been stated that teeth can be used as graft material that is gradually replaced by bone. Autogenous dentin grafted immediately after extraction is considered as a gold standard for socket preservation, bone augmentation in sinuses & bone defects[6].

Dentin and cementum contain various other growth factors besides Bone Morphogenic Proteins (BMPs) such as insulin-like growth factor (IGF), plateletderived growth factor (PDGF), fibroblast growth factor (FGF) and transforming growth factor (TGF)-β. Based on the potentials of osteoconduction, osteoinduction and osteogenesis of growth factors in tooth and similar histogenesis between tooth and bone, a novel bone graft material can be used utilizing the inorganic and organic components of tooth[7].

HISTORY OF DENTIN GRAFT

Autogenous tooth bone graft material (AutoBT) was first developed in 2008 and has been used mainly for guided bone regeneration to supplement dental implants[8]. Tooth graft has first been introduced by Korea Tooth Bank R&D Center, and has satisfied many clinicians and patients for its osteoconduction as well as osteoinduction capacity. Urist and Kim et al.[9] artificially processed tooth as a graft material. Murata *et al*.[10] in Japan has proved that bone generated from demineralized tooth can be used in guided bone regeneration (GBR), maxillary sinus grafting, ridge augmentation, socket preservation.

Well before the processing of autogenous dentin graft (ADG) , AutoBT (auto tooth bone graft) was prepared in Korea tooth bank in two forms i.e block and powder type . AutoBT (Auto tooth bone graft) material is made from the extracted tooth. This AutoBT is grafted back to the same patient when bone regeneration is necessary in dental surgeries[11]. Studies have shown that AutoBT has osteoinduction via blood wettability and has osteoconduction capacity via space maintaining and creeping substitution. It is remodelled by maintaining space during a specific period[12]. When AutoBT is grafted, it is expected that the rate of bony healing will be excellent and the pattern will be varied depending on grafted tooth portion, such as crown or root[13].Kim *et al*.[14] and Kim *et al.* [15] have stated that partial AutoBT showed well vascularized dense fibrous tissues and graft materials were directly fused with new formed bone. Kim *et al*. [16] has stated that AutoBT showed gradual resorption during the first three months. At 6 months, new bone was replaced with trabecular bone with resorption of most graft material.

Kim *et al*. [17,18] conducted a study on component analysis research through electron microscope, production and autogenous bone graft material after incinerating human teeth at a high temperature of 135°C and then pulverizing to a particle size of 0.149 mm. The main component of tooth ash powder, which formed after incineration and pulverization of teeth, has been identified to be hydroxyapatite and β-Tricalcium phosphate, both of which are osteoconductive bone graft materials with excellent biocompatibility. The osteogenic capacity of a demineralized tooth was verified as early as 1967, and it has been generally accepted that autogenous and allogenic demineralized teeth are osteoinductive or osteoconductive graft materials[19].

I.COMPOSITION OF DENTIN

Tooth contains inorganic components of calcium phosphate lineage and organic components such as collagen. Tooth minerals consist of five biological calcium phosphates: hydroxyapatite, tricalcium phosphate (TCP), octacalcium phosphate (OCP), amorphous calcium phosphate (ACP), and dicalcium phosphate dehydrate. Interacting reciprocally, these calcium phosphates are capable of remodeling the existing bone when grafted [7].

Organic parts of dentin include type I collagens and various growth factors such as bone morphogenic proteins (BMPs). Type I collagen occupies about 90% of the organic parts of tissues, with the rest non-collagenous proteins (NCP), biopolymers, lipid, citrate, lactate, etc. NCPs include phosphophoryn, sialoprotein, glycoprotein, proteoglycan, osteopontin (OPN), osteocalcin, dentin matrix protein-

1, osterix, and Cbfa1 (Runx2), Dentin sialoprotien (DSP). These proteins are known to trigger the bone resorption and generation processes[20-28]. Phosphophoryn in particular, bound to type I collagen, contributes to the mineralization process; it is of the largest amounts among NCPs. Previous studies discovered through the immunohistochemical study that OPN and DSP manifested 6-8 weeks after grafting the tooth graft material on alveolar bone defects in Wistar rats[1].

OPN is known to trigger osteogenesis through the early differentiation of the osteoblasts but also OPN is known to leads to bone resorption by allowing adherence of osteoclasts to the bone surface. DSP has a significant role in dentin calcification [29].

Both teeth and bone contain type I collagen and BMP along with various growth factors. A study conducted analyzed the inorganic component of extracted fresh tooth and specimen treated with autogenous tooth bone graft material and found that the crown mainly consisted of high-crystalline calcium phosphate, and that the root is mainly made up of low-crystalline calcium phosphate. If dentin and cementum which make up most of the teeth are used as bone graft materials, good bony remodeling by osteoconduction can be expected because the main minerals of bone tissue are low-crystalline apatite. It can be considered as a useful material that can substitute free autogenous bone graft, showing bone healing via excellent osteoinduction and osteoconduction because it contains both organic and inorganic components[30].

Boden *et al*.[31] suggested that LIM mineralization protein 1 (LMP-1) is an essential positive regulator of osteoblast differentiation, maturation and bone formation. Wang *et al*.[32] found that LIM-1 was expressed primarily in predentin, odontoblasts, and endothelial cells of the blood vessels of teeth. All these growth factors give teeth an osteoinductive property.

A. ROLE OF COLLAGEN IN BONE REGENERATION

Materials based on collagen, particularly type I collagen, have attracted attention because of their ability to improve the cellular responses of osteogenic lineages, thus ensuring better bone regeneration[33]. Studies have shown that considering the hierarchical structure of bone, a mineralized collagen matrix with functional proteins and proper fibrillar arrays for biomechanics may be suitable as a natural bio-inspired graft material in bone tissue engineering[11]. Based on these studies dentin can be used as a graft material in regenerative procedures.

B. HYDROXYAPATITE CONTENT IN DENTIN

Dentin consists of 70% hydroxyapatite in its weight volume[13]. Hydroxyapatite in dentin is structured with low-crystalline calcium phosphate, making future bone remodeling possible. Bone tissues are also mainly composed of low-crystalline apatite. In contrast, hydroxyapatite in enamel is structured as high-crystalline calcium phosphate. High crystalline contents are not easily decomposed by osteoclasts, resulting in slow resorption and consequently poor osteoconductivity[34].

C. GROWTH FACTORS IN DENTIN

Growth factors are signaling proteins that regulate cellular growth, proliferation, and differentiation.[35] BMPs are known to exist in the bone matrix, osteosarcoma tissue, and dentin matrix, functioning to differentiate perivascular mesenchymal stem cells in to cartilage and bone tissues[35,36]. Studies have confirmed the osteoinductivity of BMPs extracted from animal teeth such as bovine, lapine, and murine teeth[37,38].

Dentin and cementum contain various other growth factors besides BMPs such as insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and transforming growth factor (TGF-β)[39,40]. Finkelman *et al*.[41] reported the extraction of TGF-β, IGF-I, IGF-II from human dentin but at lower levels compared to those from human bone.

DENTIN AS A BONE GRAFT MATERIAL

Jaw bones, alveolar bone and teeth develop from cells of the neural crest and many proteins are common to bone, dentin, and cementum. It is therefore not surprising that dentin that comprise of more than 85% of tooth structure can serve as native bone grafting material[6]. Interestingly, studies have shown that intact growth factors are conserved even in the collagenous extracellular matrix of ancient human bone and teeth[42].

The tooth consists of 85% of dentin. It contains growth factors which can be used in humans for defect fill and it has been proven in animal studies that bovine dentin can be processed into graft which slowly and gradually is replaced by bone[6] . It can be stated that dentin has 65% inorganic and 35% organic substances similar to that of alveolar bone [7]. Autogenous mineralized dentin grafted immediately after extraction is considered as a gold standard for socket preservation, bone augmentation in sinuses & bone defects. Various studies have shown that tooth-derived bone graft material is proved to be rich in bone growth factors and bone morphogenic proteins (BMPs), and are becoming a practical substitute to bone grafting. It can be used as a carrier for growth factors and stem cells. Autogenous-tooth bone grafting technique can be considered as a significant biomaterial with excellent bone regeneration capacity and also relatively non-existent chances of antigenicity, genetic diseases and disease transmission[43].

The tooth is increasingly attracting the attention as a material for alveolar bone regeneration. It is composed of an organic matrix and an inorganic reinforcing phase of hydroxyapatite. Radial arrays of dense type I collagen fibrils, which account for 90% of the organic matrix, and non collagenous acidic proteins play an important role in the process of calcification[44]. Teeth and bones share many similarities where teeth, cartilages nerves, and maxillofacial bones all embryologically originated in the neural crest, sharing identical origin[45]. Studies support the intramembranous bone formation pathway when intraoral bone grafting is achieved[46,47].

TYPES OF DENTIN GRAFT

Dentin tooth can be classified into three groups according to the degree of demineralization; undemineralized dentin (UDD), partially demineralized dentin matrix (PDDM) (70% decalcified) and demineralized dentin matrix (DDM)[48].

When osteoblast culture was done UDD surface was uneven and small debris were observed. Osteoblasts were well attached and spread out only on the surface of DDM. This shows that once dentin is demineralized, the dentinal tubule would become wider and serves as a channel for releasing essential proteins which may promote growth and differentiation ofosteoblasts. There was no difference in cell attachment between PDDM and CDDM[48].

Studies have shown that UDD is less effective in bone formation whereas other studies have shown that DDM is biocompatible and also osteoinductive, similar to demineralized bone matrix[48]. Various authors have reported successful bone regeneration applying UDD. UDD can be easily obtained from a dentin grinder, after disinfection and cleaning process[42].

ADVANTAGES OF AUTOGENOUS DENTIN GRAFT:

Normally autogenous bone grafts are considered to be the gold standard, since there is a possibility to retain cell viability, graft revascularization and reduced possibility of disease transmission, but the added operating time and morbidity associated with their harvest, and the limited available volume of autogenous intraoral bone at times may obviate the use of these materials[49] .Instead dentin can be used as a graft for treating osseous defects which can be prepared chair side by using teeth which are indicated for extraction because of periodontal reasons and partially or totally impacted[6].

MINERALIZED V/S DEMINERALISED DENTIN

Studies have shown that mineralized dentin particles have the advantage to maintain its mechanical stability, allowing early loading after grafting in fresh sockets and bone defects. Moreover, in spite of delayed inductive properties, the mineralized dentin is firmly integrated with newly formed bone, creating a solid site for anchorage of dental implants. Implant insertion and loading can be performed in lower and upper jaws 2-3 months after grafting of dentin[50].

Since the mineralized dentin is very slowly remodelled [50] when compared to cortical bone or most biomaterials the esthetic and structure pattern of the alveolar crest and mucoperiosteum is maintained for years. The amount of bone graft obtained depends on the condition of discarded tooth and its histological outcomes are similar to autogenous bone grafts[51].

Studies reported that dentin contains proteins such as osteopontin (OPN) which promotes the bone formation. On immuno histo chemical staining with anti-Dentin Sialoprotien (DSP) antibody, the positive reaction was localized to the dentin of the extracted tooth fragments incorporated into the new bone at 6 weeks, suggesting that dentin has a high affinity for and marked osteoconductive effect on jawbone[52].

Various authors have investigated the osteopromotive property of autogenous DDM and concluded that there was normal bone regeneration with minimal inflammation causing no hindrance to bone formation[53]. Lee [54] performed quantitative analysis of the proliferation and differentiation of the MG-63 cell line on the bone grafting material using human tooth. This study demonstrated that the cellular adhesion and proliferation activity of MG63 cells on partially demineralized dentin matrix (PDDM) were comparable and could be controlled with enhanced osteogenic differentiation.

A study conducted stated that a lot of BMP was needed to realize proper osteoinduction when used alone[55]. Therefore, an appropriate carrier is needed. For the autogenous tooth bone graft material, BMP and bone growth factors in dentin can be used as they are already present in ADG. There have been reports that DDM by itself can play the role of carrier of exogenous BMP and growth factors as well as have an osteoinductive effect[56].

II. FACTORS AFFECTING BONE REMODELLING

A.CRYSTALLINITY

Crystallinity affects resorption rates of a graft. When a resorption rate of a grafted material is too low, which is in the case of high crystalline structures, complete remodeling is hard to achieve as in some osteoconductive graft materials. On the other hand, if resorption of the grafted material occurs too fast, it may lower bone fusion or healing rates[57].

Studies have shown that by demineralization, organic substance such as collagen matrix and growth factors within the teeth are exposed, enhancing conditions for new bone formation. It has been shown that decalcified dentin is more active in bone induction than calcified dentin. There is a decrease in antigenicity, which is crucial in processing hard tissue-derived graft materials. It lowers the ratio of inorganic content as well as crystallinity, which enhances osteoblast adhesion and increases resorption rate of the material after graft[10].

Some authors have suggested that small crystallite sizes of HAs can enhance biodegradation as a result of higher solubility. The biodegradation of large particles with high crystallinity is almost impossible. Their osteoconduction capacity is very low and osteoclasts cannot degrade them. Low-crystalline carbonic apatites show the best osteoconduction effects[58,59]. The root of the tooth contains low crystalline HA and crown consists of high crystalline Ha[13].

B. POROSITY

Porosity is another factor that can influence new bone formation. It is known that porous (hydroxyapatite) HA is more resorbable and more osteoconductive than dense HA[57]. Porous surface provides increased surface for cell adhesions, and allows bone in growth into the material. However, minimum stiffness should be maintained because osteogenic differentiation and activity has been reported to decrease on substrates of lower stiffness[59]. Kim *et al*. [9,60] applied both mineralised dentin and demineralized dentin matrix particles in dental implant surgery and reported successful bone regeneration.

C.PARTICLE SIZE OF DENTIN GRAFT

Depending on the particle size of dentin graft with 200, 500 and 1000 µm were studied for regeneration. Newly formed bone in UDD was prominent in some areas in 1000 µm sample and very few osteoblasts and osteoclasts were found when compared to PDDM and CDDM. Little bone formation was observable in the 200 µm and 500 µm samples; some matrices had resorbed and the defects were filled with connective tissue in the 200 µm samples in all the groups. Histomorphometric analysis at 4 weeks and 8 weeks has shown the mean n-Bone% of the 200 µm, 500 µm, and 1000 µm samples of UDD were1.9%, 2.7%, 5.6%, 3.1%, 5.0%, and 11.2% respectively.800 to1200 µm samples showed superior results in bone regeneration than the smaller sizes, 180 to 212 µm and 425 to 600 µm, in all groups of UDD, PDDM and CDDM. The study concluded that mixture of particles with variable sizes may have better results when compared with even particle size[14].

CONCLUSION

Based on the potentials of osteoconduction, osteoinduction and osteogenesis through growth factors in tooth and similar histogenesis between tooth and bone it can be noted that autogenous dentin can be used as a bone substitute for regeneration of periodontal defects. Further long term studies have to be conducted to know much potential benefits.

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