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Bone Grafting Substitutes in Dentistry: General Criteria for Proper Selection and Successful Application

Mehdi Ebrahimi
Department Of Oral Rehabilitation, Prince Philip Dental Hospital, The University Of Hong Kong

Abstract: *Restoration of bone defects in the oral cavity is one of the major challenges for dental surgeon. A common example is handling of bone defect after simple tooth extraction for ridge preservation. Often delivering prosthodontic and implant treatments face difficulties during oral rehabilitations in bone defect site. Bone defect site needs to be restored in such a way to support further treatment. In this context, basic knowledge of bone grafting substitutes, their basic characteristics, differences and clinical indications is critical. Different types of bone grafts with different properties are available which may confuse the clinician. Among them the produced bone grafts based on biomimetic principle are of particular interest, as they replicate more closely the natural bone by combining both organic (i.e. collagen) and inorganic phases (i.e. bioceramics). Therefore, the general criteria for appropriate selection of right bone substitutes for application in the bone defect sites have to be understood. Unfortunately, many of bone graft substitutes are randomly selected from the available market for various applications. The purpose of this short review is to provide general guidelines for appropriate selection and application of bone grafts.*

Keywords: *Bone graft, Bone substitutes, Biomaterials, General Dentistry*

I. Introduction

Bone defect area can develop in the oral cavity as a result of different factors such as; tooth extraction, periodontal disease, trauma, cyst, tumor and infection. The main aims of the treatment planning in these cases are restoration of esthetic and functional rehabilitation. The success of different types of prosthetic and implant therapy is dependent on the available bone quality and quantity. Nowadays, various types of bone graft substitutes are available which facilitate the treatment planning and may also confuse the user [1]. Therefore, for a proper selection and successful application, a clear understanding of biological requirements of the bone defect site and physico-chemical properties of bone graft substitutes is crucial.

Biomimetic principle is based on the replication of the detailed physiologic bone components and their properties in an attempt to mimic the nature [2,3]. However, it is a challenging task as the natural bone is a complex structure with unique properties that adapted to the physiological and functional requirements. The natural bone exhibits different physical characteristics depending on anatomical site, health condition and age of the patient [4]. In general, the natural bone is composed of carbonated hydroxyapatite (HA) as an inorganic phase (55-65%), inorganic biopolymer phase of mostly collagen (35-45%), water molecules (5-9%) and trace elements (<1%) [5]. Natural bone is a nano-based composite structure with both inorganic and organic counterparts interrelated at nano level [6]. Moreover, natural bone consists of both cancellous and compact parts that possess different porosity, mechanical properties and remodeling rates [7]. Therefore, the ideal biomaterial for bone grafting is the one that can closely match the chemical and physical properties of the bone defect site.

II. Literature review

2.1. Types of bone graft substitutes

Bone grafting is a surgical procedure for restoration of bone defect area with different materials. The bone grafting materials can be broadly classified into natural and synthetic types. Natural bone grafts include the autogenous bone (from the same individual), allograft (from different individual such as fresh-frozen or freeze-dried bone), and xenograft (from non-human species). The synthetic types are commonly known as alloplastic materials that are developed during controlled manufacturing process that involved different chemical reactions.

Among natural types, the use of autogenous bone graft is the gold standard treatment option. Other natural products are also available such as bovine bone that has been treated intensively to be acceptable for bone grafting. However, the natural bone graft suffers from some disadvantages, mainly the need for second surgery, limited supply, and high resorption rate [5]. This initiated the idea of preparation of synthetic materials for bone grafting that has undergone extensive studies during last few decades. Furthermore, a recent systematic review revealed that there are no significant differences in the percentage of new bone formation after use of natural or synthetic grafts [8].

Many generation of synthetic biomaterials has been introduced including; 1) metals/alloy (stainless steel and Ti alloy), 2) calcium phosphate bioceramics such as hydroxyapatite (HA), tri-calcium phosphate

(TCP), and biphasic calcium phosphate (BCP), 3) composite materials (HA/collagen) and more recently, 4) tissue engineered nano based-biomaterials (nano-HA/collagen/BMP-2) [1,9,10]. Currently, the biomimetic concepts received major attention where the aim is to replicate the nature by mimicking bone structural components and arrangement [2,3]. In this context, the use of nanoscale bioceramic biomaterials in composite form with addition of other natural or synthetic polymers attracting more attention. For example, nanoscale HA is one of most widely used bioceramics for bone grafting owing to its improved bioactivity, biocompatibility and osteoconductive nature [11]. The composite form of nanoscale HA (in combination with collagen, gelatin, fibrin, chitosan, *etc*.) have been prepared and widely explored in the literature [6,12,13]. The composite nanoscale HA bioceramics proved to have significant potential in the field of bone tissue engineering.

Numerous commercial synthetic products are available in the market with different properties and indications (Table 1). A general, but proper knowledge for correct selection and application of these biomaterials is a critical requirement, especially in the light of new technologies that makes bone grafting easy and less challenging in general dental practice.

Table 1. List of different types of biomaterials applied during bone grafting and examples of some available commercial products.

Biomaterial	**Commercial products**
Pure Bioceramics	Maxresorb (Botiss biomaterials GmbH) Bio-Oss (Geistlich) ChronOS (DePuy Synthes) MasterGraft (Medtronic) OsteoSet ((Wright Medical Technology) Pro Osteon (Biomet)
Pure collagen	BioStrip and BioPlug (Biohorizon) Bio-Gide-membrane (Geistlich) BioMend-membrane (Zimmer) 4Bone RCM-membrane (Mis-implants) EZ Cure-membrane (Biomatlante) HeliPlug-membrane (Integra Miltex) Cytoplast RTM-membrane (Osteogenics) Collprotect-membrane ((Botiss biomaterials GmbH)
Composite bioceramics/collagen	Bio-Oss collagen (Geistlich) Collagraft (Zimmer) Collapat (Symatese) Healos (DePuy) OsteoTape (Impladent) Allograft (Zimmer) MinerOss X Collagen (Biohorizon) OsteoTape (Impladent) OsteoGen Plug (Impladent) Collapat II (Symatese)

Selection criteria may be studied from two aspects: biomaterial properties and patient-related factors (Table 2). Appropriate selection of biomaterials necessitate basic understating of materials properties including: chemical nature, physical and mechanical properties, biodegradation rate, level of bioactivity (osteoconductive, osteoinductive, osteogenic), availability, and cost.

Table 2. Selection criteria and contributing factors for bone graft application

Patient aspect	**Biomaterial aspect**
▪ Age ▪ General Health ▪ Size of the defect ▪ Type of the defect ▪ Anatomical site of the defect ▪ Functional load at defect ▪ Purpose of application ▪ Patient cooperation ▪ Financial issue	▪ Biomimetic materials ▪ Chemical nature ▪ Physical properties ▪ Mechanical properties ▪ Biodegradation rate ▪ Biocompatibility/bioactivity ▪ Osteoconductive/osteoinductive ▪ Availability ▪ Cost

2.2. Biomaterials properties; physico-chemical properties of bone graft substitutes

From chemical aspect, inorganic calcium phosphate based biomaterials have shown great advantages in bone tissue engineering. Recent advances in production of nanomaterials should also be noted, as nano-based biomaterials have shown improved physic-biological behavior compared to micron-based counterpart [6,12]. In the context of biomimetic approach, one should note the clinical advantages of composite biomaterials that contain both organic and inorganic phases with the presence of other functional molecules and growth factors that further enhance regeneration process. In addition, the presence of trace chemical elements such as Ag, Si, Mg,

Zn, *etc*., has shown different potentials during bone healing process [14]. Therefore, from chemical aspect use of hybrid composite biomaterials should be tailored with the proper physical features that serve the final goal of restoration.

From the physical aspect, the particle size, porosity, mechanical properties, and biodegradation profile of biomaterials should be considered. Ideally, the type of bone grafting materials should exhibit similar porosity and mechanical properties (compressive strength, Young's modulus, tensile strength, density, and fracture toughness) to that of recipient site [15]. Majority of bone grafts are expected to resorb and be replaced by natural bone over several months. Therefore, the biodegradation profile should also be matched with clinical requirements at the implant site. It should be mentioned that in general, decrease in particle size and increase in porosity of biomaterials reduce the mechanical strength but enhance the biodegradation rate [1]. However, biomaterials biodegradation rate should not be faster than bone regeneration or remodeling rate to avoid collapse of restored defect site and early failure. Furthermore, the biodegradation rate should not be very slow that interfere with natural bone deposition at healing site. It should be noted that nano-based biomaterials undergo faster and more homogenous biodegradation rate than micron-based conventional bone grafting substitutes [6,11]. In addition, the composite and biphasic materials also exhibit different range of biodegradation depending on the nature of the composition phases. It is well known that HA based biomaterials, undergo very slow degradation rate. On the other hand, TCP based materials and other organic phases show faster degradation rate. Therefore, the biphasic (i.e., HA+TCP) and composite biomaterials should be used with special care and consideration depending on the type of the recipient site, bone regeneration rate, bone remodeling rate in relation to degradation rate of biomaterials' phases (Table 3).

Furthermore, one should also note the parameters that influence the bioactivity and cellular response toward implanted biomaterials. It is reported that both physical and chemical natures of biomaterials affect directly the cellular responses and consequently the rate and pattern of bone healing. Chemical composition (i.e., calcium phosphate (Ca/P) ratio, trace elements and surface energy) and physical nature (biodegradation and topography) influence the initial cell attachment and subsequent cell functions [16].

Table 3. Examples of commercial bone graft biomaterials and their detailed properties.

Name	**Phase**	**Biodegradation**	**Crystallinity**	**Physical properties**	**Mechanical stability**
Bioresorb®	99% β-TCP, traces of α-TCP and calcium pyrophosphate	Moderate	High	Porous granule (particle size: 0.5–2 mm)	Low
Chronos®	99% β-TCP, traces of α-TCP and HA	Moderate	High	Porous granule (particle size of 0.5–1.4 mm and pore sizes of 100–500 µm; 60% pore volume)	Low
Ceros®	99% β-TCP, traces of α-TCP and HA	Moderate	High	Porous granule (particle size of 0.5–1.4 mm and pore sizes of 100–500 µm; 60% pore volume)	Low
Cerasorb®	100% β-TCP	Moderate	High	*Porous granule (pore size>5 µm, particle size 0.05–2mm) *Macroporous block	Low High
Vitoss®	98.8% β-TCP, traces of calcium pyrophosphate, and 1.2 % organic bone matrix	Moderate	High	Porous granule (pore size 10–1000 µm; porosity 90%; particle size 3–5 mm)	Low
PepGen® P-15	100% HA coated with a P-15	Slow	High	Porous granule (particle size of 0.25–0.42 mm)	Low
Endobon® Cerabones®	100% HA, traces of calcium oxide	Slow	High	Porous block (pore size 1 mm; porosity 50%)	High
Algipore®	95% HA, 2.4% organic matrix, 2.3 % $CaCO_3$	Moderate	Moderate	Porous granule (particle sizes of 0.3–2mm, pores of 5–10 µm)	Low
Ostims®	59.6% nanoHA dispersed in 40% H_2O	Fast	Nano	Fluid paste with nanoscale apatite particles	None

BioOss®	3% H_2O, 3.4% $CaCO_3$, 93.6% carbonated HA ± 10% collagen	Fast	Nano	*Porous granule (granule size of 0.25–2 mm), *Cancellous bone block (1x1x2 cm)	Low
Tutoplast®	*Bovine= 9% H_2O, 26% organic matrix, 8%$CaCO_3$, 57% HA. *Human= 9.5% H_2O, 34% organic matrix, 7.5% $CaCO_3$, 49% HA	Fast	Nano	*Porous block/cylinder (pore size >100 µm) *Granulate (particle size 0.25–2 mm)	High

2.3. Patient aspect

The patient aspect should be considered the main aspect of treatment and the key influential part for biomaterial selection and overall treatment planning. Factors such as patient age, general health, smoking habit, radiotherapy, size, type and anatomical site of bony defect, mechanical requirements at the defect site, purpose of restoration, and financial issue, all influence the treatment plan and should be considered beforehand (Table 2). However, the final purpose of application of bone graft has a great influence on the materials selection and application. The bone substitute biomaterials could be applied for either cosmetic or functional purposes or both. In cases where the biomaterial is applied for functional purpose, the anatomical site, age and health of patient play important role in determining the level of load which is applied to the biomaterials. The psychological aspect and the patient level of cooperation are also other key factors that influence the prognosis of bone grafting treatment. The application of bone grafting procedure in patient with extreme age, smoking habit, diabetes, physical or mental disabilities, and those undergoing radiotherapy should be with extreme care supported with a reasonable justification to avoid complications [17]. It should be noted that any failure of bone grafting procedure results in greater loss of patient healthy natural bone close to the area of bone graft in addition to waste of money, time and energy.

2.4. Failure of bone grafting

Failure of surgical or bone grafting procedures is one of the major obstacle and nightmare for clinicians. Failure of bone grafting procedure is often associated with inflammation, pain, infection, fibrous encapsulation, and rejection of biomaterials by immune defense. Different factors may contribute to this problem that include improper selection of biomaterials, mechanical failure, mismatch in modulus of elasticity between biomaterials and recipient site, corrosion, very fast/slow degradation, patient-related factors, technical failure and iatrogenic factors [17,18]. Therefore, the proper precautions should be made considering general and specific characteristics of biomaterials together with patient's related factors to avoid failure and further complications.

III. Conclusion

Application of bone grafting materials in general dentistry is much easier nowadays as it was taught before thanks to the recent advancements in biomaterials sciences. Socket or ridge preservation is such an example which is an important step after tooth extraction to minimize the resorption rate of alveolar ridge. Varieties of commercial bone grafting products are available from the market; however, basic understanding of the properties of these materials and their proper applications is very important. It should be noted that no strong evidence is available to claim superiority of one product.

Restoration of both esthetic and function are the final goals of every treatment approach that should be kept in mind beforehand. Patient aspect should be considered before any step as this could have a significant impact on treatment plan and selection of bone substitutes. Scheduled follow up, check up and post treatment instructions are the ultimate responsibility of clinician. Ideally, when considering the biomaterials aspect, it should be easily available from the market with post purchase technical support. From synthetic aspect, it is recommended that the biomaterial should exhibit high purity with minimum or no impurity [19]. Furthermore, It should be homogenous in nature with minimum batch to batch differences that allows easy handling and application to the defect site [10,11]. Considering biomimetic principle, the composite nano-based biomaterials containing both organic and inorganic phases hold a better promise and may be a better option for general and specific bone applications.

Conflict of Interest: none

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