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Porous Titanium Granules in Treatment of Intra-bony Defects: A Literature Review

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Authors' contributions

This work was carried out in collaboration between all authors. Authors ZN and AS designed the study and wrote the protocol. Author FK wrote the first draft of the manuscript. Author MS managed the literature searches. Author NJ wrote the final manuscript and revisions. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Background: This study aimed to do a review on the applications of porous titanium granules (PTG) in periodontal and non-periodontal treatments.
Methods: An electronic search was carried out in Google Scholar and PubMed databases using the key words "guided tissue regeneration", "intrabony defects", "porous titanium granules" and "moderate to advanced chronic periodontitis". English articles published from 2006 to 2014 were searched.
Results: Porous titanium granules showed positive results in enhancing the outcome of treatment in medicine. Most of the relevant studies have been conducted using culture media or animal models.
Conclusion: It can be stated that PTGs have many applications in periodontal procedures due to their space maintaining capability, long-term substantivity, not requiring a membrane and biocompatibility.

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Keywords: Guided tissue regeneration; intrabony defects; chronic periodontitis; porous titanium granules.

1. INTRODUCTION

Periodontal treatments are performed aiming to prevent further destruction of the periodontal tissue. The ultimate goal of these treatments is to regenerate the tissues injured or lost due to disease or trauma and reinstate their structure and function. The conventional surgical and non-surgical periodontal treatments often successfully inhibit the disease progression but the soft tissue recession due to treatment often compromises esthetics particularly in the anterior region. On the other hand, these treatments may not be very effective for eliminating the periodontal pockets in some areas; this may affect the long-term prognosis of the teeth. However, these complications may decrease by periodontal regenerative treatments and reconstruction of the lost structures. Guided tissue regeneration (GTR) was introduced with the biological concept that placement of a physical barrier prevents the migration of epithelial cells and connective tissue of the flap into the lesion and allows the periodontal ligament cells and mesenchymal cells to migrate on the root surface [1].

Successful periodontal regeneration includes regeneration of cementum, alveolar bone, periodontal ligament and connective tissue fibers attached to the root surface [2]. It is believed that the main barrier against the regeneration of periodontal tissues following the conventional periodontal treatment is the faster migration of epithelial cells and/or gingival connective tissue cells into the lesion compared to mesenchymal cells [3]; this results in either formation of a long junctional epithelium (in case of faster migration of epithelial cells) or root resorption (in case of faster migration of connective tissue cells) [1]. Either way, the formation of a new attachment apparatus on the root surface is prevented [4].

Apart from the capacity of PTGs in space maintenance for periodontal regeneration, osteogenic capacity of titanium have been shown in experimental studies [5].

Thus, regenerative treatments are performed aiming to prevent the migration of epithelial cells and the connective tissue into the defect and maintain the space for proliferation of a specific population of cells. A new periodontal attachment is formed as such. This treatment is known as GTR [1]. The biological basis of GTR is placement of a physical barrier that prevents the migration of epithelial cells and connective tissue cells of the flap into the lesion and allows the periodontal ligament cells and mesenchymal cells to migrate on the root surface [6]. According to histological findings, GTR is the most predictable regenerative method for regeneration of bone and cementum [7]. Several materials have been used to create this physical barrier such as methyl cellulose acetate, expanded polytetrafluoroethylene (ePTFE), collagen, autogenous membranes and synthetic poly glycoside or calcium sulfate polymers [8]. These materials have a natural or synthetic origin and are divided into two groups of resorbable and non-resorbable membranes [1]. Collagen membranes are resorbable and made of type I bovine or porcine collagen. Bio-Gide belongs to this group and has a porcine origin [1].

In most cases, graft materials are placed beneath the membrane to maintain the space and to benefit from their osteoconductive or osteoinductive properties [9]. Bovine porous bone minerals (BPBMs) such as Bio-OSS® are among these materials. They are synthetized by extracting the protein from bovine bone and forming a trabecular structure of hydroxyapatite, resembling human cancelous bone. They can enhance new bone formation and are extensively used in periodontal regenerative processes [4,10].

Osteogenic properties of titanium have been documented in experimental studies. Titanium is also used for bone regeneration due to its thrombogenic properties [11,12]. Porous titanium granules (PTGs) [13,14] have been recently introduced as a bone substitute and have shown promising results in animal and clinical studies. Several studies have used PTGs for treatment of furcal defects with controversial results.

2. MATERIALS AND METHODS

An electronic search was carried out in Google Scholar and PubMed using the key words "guided tissue regeneration", "intrabony defects", "moderate to advanced chronic periodontitis" and "porous titanium granules". English articles published from 2006 to 2014 were searched. The articles were then evaluated for eligibility according to the inclusion and exclusion criteria.

Inclusion criteria:

1. Studies that used PTGs in their treatment protocol.
2. Studies, which included intra-oral or extra-oral lesions as samples.
3. Human, animal and cell-culture studies.

Exclusion criteria:

1. Studies concerning stem cell engineering.
2. Studies that evaluated the fabrication of porous titanium scaffolds.

3. RESULTS

Search of the literature yielded 32 articles; based on the above-mentioned criteria, 7 were excluded and 25 remained in the study for thorough review of their full texts. Fig. 1 shows the selection process of the articles.

Table 1 shows the list of studies using PTGs in periodontal and non-periodontal treatments and summarizes the type of study, date of publication, method of application of PTGs and the outcome of treatment.

3.1 Extra-oral Applications of PTGs

A total of seven studies were found on the use of PTGs in extraoral defects; out of which, three were animal studies, two were cellular studies and two were pilot studies. Animal studies evaluated the efficacy of PTGs in hip and tibial defects and showed that membranes must be necessarily used in extensive lesions. Lamellar bone formation within the PTGs was noted [15,18]. Another study assessed the efficacy of coral as a scaffold and showed new bone formation on the surface and within the coral pores [19]. In a study, the osteogenic potential of adipose derived mesenchymal stem cells seeded on a titanium scaffold was shown using a culture medium [17]. On the other hand, calcium phosphate-coated porous titanium scaffold resulted in proliferation of mesenchymal cells [16]. A pilot study showed that PTGs were effective for the treatment of tibial fractures [20]. On the other hand, culture of femoral cells on a PTG scaffold resulted in incorporation of bone into the PTGs [13].

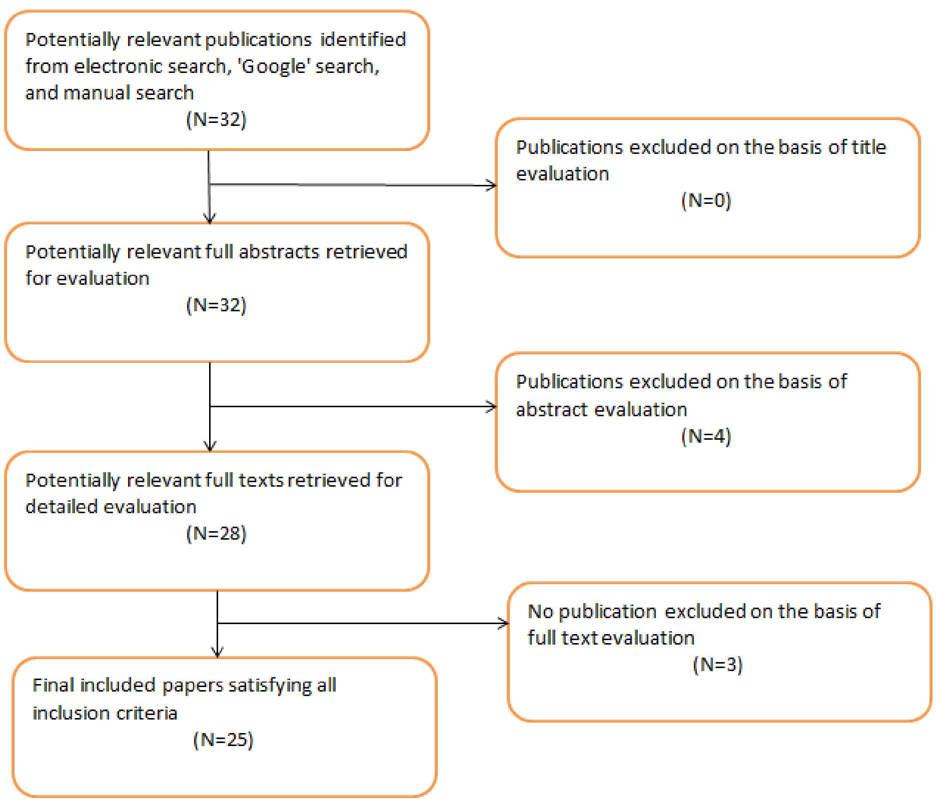

Fig. 1. Literature search flow chart

Table 1. List of studies using porous titanium granules (PTGs) in periodontal and non-periodontal treatments

Author	Type of study	Date of publication	Method of application	Objective of study	Results
Delgado-Ruiz et al. [15]	Animal experimental	2014	Critical size defect in rabbit tibia	Effect of PTGs with/without membrane	Membranes must be necessarily used in extensive lesions.
García-Gareta et al. [16]	Cellular experimental	2014	Calcium phosphate coated porous titanium scaffold	Total joint arthroplasty	This scaffold can enhance the proliferation of mesenchymal cells.
Dahl et al. [17]	Cellular experimental	2013	Application of adipose-derived mesenchymal stem cells on TiO2	Assessment in the culture medium	Adipose-derived mesenchymal stem cells on a titanium scaffold have osteogenic potential.
Turner et al. [18]	Animal study	2007	Bone formation within PTGs in hip fixation	Histological assessment	Lamellar bone formation within PTGs
Xi et al. [19]	Animal study	2006	Assessment of the role of coral as a scaffold	Histological assessment	New bone formation on the surface and in coral pores
Jónsson and Mjoberg [20]	Pilot study	2009	PTGs in treatment of tibial fractures	Clinical and radiographic assessment	Effective role of PTGs in treatment of tibial fractures
Alffram et al. [13]	Pilot study	2007	Culture of femoral cells in PTGs scaffold	Histological and tomographic assessment	Incorporation of bone and PTGs
Rubshtein et al. [21]	Animal experimental	2014	Assessment of bone fill in different size pores in titanium implants in the tibia and femur heads	Microscopical assessment	Functional bone formation in interstitial spaces among granules and peri-implant areas
Babiker et al. [22]	Animal experimental	2013	Bilateral application in the femur head	Efficacy of demineralized bone matrix alone or with cancelous bone or allograft in stabilizing porous titanium coated implant	Using a combination of demineralized bone matrix and cancelous bone can be an alternative to allografts.
Mijiritsky et al. [23]	Human experimental	2013	Application of PTGs in treatment of peri-implantitis	Clinical and radiographic assessment	Durability of PTGs in peri-implantitis lesions
Wohlfahrt et al. [24]	Clinical trial	2014	PTGs for treatment of	Assessment of bone markers in	Efficacy of PTGs for decreasing

Author	Type of study	Date of publication	Method of application	Objective of study	Results
			peri-implant lesions	peri-implant sulcus fluid	bone markers in peri-implant sulcus fluid
Wohlfahrt et al. [25]	Animal experimental	2010	PTGs for treatment of peri-implant bone defects	Assessment of enzymes in peri-implant sulcus fluid	PTGs are osteoconductive.
Wohlfahrt et al. [26]	Clinical trial	2012	Assessment of the role of PTGs in peri-implant lesions compared to treatment without the application of bone substitutes	Clinical and radiographic assessment	Superior radiographic results and similar clinical results in treatment with/without PTGs
Thor [27]	Case series	2013	Assessment of peri-implant regeneration	Clinical and radiographic assessment	PTGs are osteoconductive.
Wohlfahrt et al. [28]	Case report	2011	PTGs in treatment of peri-implant bony defects	Histological and micro-CT assessment	PTGs is in close contact with the newly formed bone.
Tavakoli et al. [29]	Animal experimental	2012	Assessment of healing of an extraction socket with PTGs	Histological and histomorphometric assessments	It can effectively fill the bony defects when applied with membrane
Bashara et al. [30]	Animal experimental	2012	Comparison of the role of PTG and Bio-Oss® in extraction sockets	Histological assessment of buccal plate resorption	Promising role of PTGs compared to Bio-Oss®
Verket et al. [31]	Animal experimental	2014	Assessment of the role of PTGs in extraction sockets prior to implant placement	Histological and micro-CT assessments	PTGs can be applied in the extraction sockets prior to implant placement
Lambert et al. [32]	Animal experimental	2013	Comparison of PTGs and hydroxyapatite for sinus floor augmentation	Histological and micro-CT assessments	Three-dimensional stability of both materials for sinus floor augmentation prior to implant placement
Verket et al. [33]	Human experimental	2013	Role of PTGs in sinus floor augmentation	Histological and tomographic assessment	Osteoconductive role of titanium granules
Bystedt et al. [14]	Pilot study	2009	Role of PTGs in sinus floor augmentation	Clinical assessment	Need for further investigations due to

Author	Type of study	Date of publication	Method of application	Objective of study	Results
					controversial results
Vandeweghe et al. [34]	Pilot study	2013	Comparison of PTGs and Bio-Oss® for sinus floor augmentation	Histological and 3D assessments	Comparability of PTGs and Bio-Oss® in sinus floor augmentation
Helmut [35]	Human experimental	2012	Role of PTGs in sinus floor augmentation	Clinical and radiographic assessment	Optimal efficacy of PTGs for sinus floor augmentation
Wohlfahrt et al. [36]	Animal experimental	2012	Comparison of PTGs and deproteinized bovine bone in treatment of Class II furcal defects	Histological and tomographic assessment	PTGs enhance bone regeneration in these defects and their application is safe next to roots.
Wohlfahrt et al. [37]	Case series	2012	PTGs in treatment of Class II furcal defects in the mandible	Assessment of clinical and radiographic parameters	Application of PTGs is safe next to roots but causes no change in clinical parameters.

3.2 Porous Titanium Granules in Implantology

The search yielded eight studies including three animal studies, two clinical trials and three human studies in this respect. Migration of osteoblasts on the implant surface is a prerequisite for healing of peri-implant tissues. Studies have reported that blood cell reactions are influenced by factors such as implant surface characteristics, thickness of oxide layer, chemical composition and surface roughness [25]. An animal study microscopically assessed the application of titanium granules and showed the formation of functional bone in the interstitial spaces among granules and around implants with 40% porosity. The newly formed bone was mature and contained blood vessels [21].

An animal study evaluated the efficacy of demineralized bone matrix (DBM) alone or combined with cancelous bone or allografts in stabilizing porous coated titanium implants and showed that combined use of DBM and cancelous bone was comparable with allografts in terms of mechanical properties [22]. Porous titanium granules and White PTGs (WPTGs) were compared in terms of efficacy for treatment of bone defects around implants and the results showed that PTGs and White PTGs were osteoconductive for the peri-implant bone without interfering with the process of osseointegration. Assessment of the peri-implant sulcus fluid enzymes showed less inflammation with WPTGs and increased expression of collagen mRNA in this group [25]. A case report also showed peri-implant regeneration using PTGs as an osteoconductive material [27]. A human study showed the biocompatibility of PTGs in treatment of peri-implant lesions clinically and radiographically [23]. A clinical trial on the role of PTGs in treatment of peri-implant lesions (compared to treatment with no material) demonstrated change in the percentage of radiographic bone fill in the PTG group. But the clinical results were equal in the two groups. Moreover, the results did not necessarily indicate re-osseointegration of PTGs with implants [26]. A clinical trial evaluated the efficacy of PTGs for treatment of peri-implant bone defects and assessed their effect on bone markers in peri-implant sulcus fluid (PISF). The results showed reductions in bone markers of PISF such as adiponectin, leptin, osteoprotegerin (OPG), interleukin-1 (IL1) and matrix metalloproteinase-8 (MMP8). A positive correlation was also reported between the reduction of IL1, MMP8, insulin and decreased probing depth due to the application of PTGs [24]. A case report on treatment of peri-implant bone defects indicated close contact of PTGs with the newly formed bone on histological and micro-CT assessments [28].

3.3 Porous Titanium Granules for Healing of Extraction Sockets

Three studies were found on the application of PTGs for extraction socket healing, which were all animal studies. Studies showed that although the application of biomaterials did not prevent resorption of buccal cortex, it optimally preserved the ridge profile [30]. An animal study assessed the healing of extraction sockets using PTGs and membrane, PTGs alone and no treatment. Histological and histomorphometric assessments showed that in the PTGs and membrane group, the total amount of regenerated bone was significantly higher than that in the other two groups [29]. Another animal study histologically compared the efficacy of PTGs and BioOss® for preserving the buccal wall of the extraction socket and showed no significant difference in the results. Also, PTGs showed a promising role compared to Bio-Oss® [30]. Another animal study assessed implant osseointegration in a tooth socket maintained with PTGs before implant placement and indicated the applicability of PTGs in the extraction sockets prior to the placement of implants [31].

3.4 Porous Titanium Granules for Sinus Floor Augmentation

Search of the literature yielded five studies including one animal and four human studies in this regard. Shorter implants had a lower survival rate in the posterior maxilla and the survival rate was 93.04% for 12 mm and 88.09% for 8mm implants [14]. An animal study compared the efficacy of PTGs and bovine hydroxyapatite for sinus floor augmentation using histological and micro CT assessments and indicated the three dimensional stability of both materials for sinus floor augmentation prior to implant placement as well as ideal bone formation with adequate quality and stiffness [32].

A human study assessed bone formation in pores of PTGs in sinus floor augmentation using histological analysis and tomography and showed that the newly formed bone was mainly woven and had a close contact with titanium granules, showing their osteoconductivity [33]. A pilot study evaluated the role of PTGs in sinus floor augmentation prior to clinical placement of implants. Due to controversial results, further investigations were requested for assessment of safety and stability of materials in the second phase [14].

Another pilot study compared PTGs and bovine bone in sinus floor augmentation histologically and three-dimensionally and revealed that PTGs and Bio-Oss® were comparable in terms of efficacy for sinus floor augmentation. Also, they showed that PTGs, in contrast to Bio-Oss®, remained for a longer period of time [34].

A human study evaluated the efficacy of PTGs in sinus floor augmentation. The results indicated their optimal efficacy [35].

3.5 Porous Titanium Granules for Treatment of Furcal Lesions

Search of the literature yielded two studies including one animal and one human study. Morphology of class II furcal defects allows their proper regeneration. Several studies have evaluated the efficacy of different materials for treatment of these lesions [36]. An animal study compared PTGs and deproteinized bovine bone for treatment of class II furcal defects using histological analysis and tomography and showed that PTGs significantly enhanced buccopalatal bone formation. Also, their application was safe adjacent to roots as they did not lead to root resorption. Both newly formed vascularized woven bone and mature lamellar bone have been reported in close contact with PTGs [36].

In a human study, PTGs were used for treatment of class II furcal lesions in the mandible. Assessment of the clinical and radiographic parameters showed that application of PTGs was safe next to roots, but it did not result in any change in clinical parameters [37].

Table 1 summarizes the studies on the application of PTGs in medicine and dentistry. Porous titanium granules have shown positive results in enhancing the outcome of treatment in medicine; most of these studies have been conducted using culture media or animal models [15-19].

Regarding the application of PTGs in dentistry, most studies have been conducted on animal and human models. PTGs have been used next to teeth and implants. Porous titanium granules are believed to be osteoconductive and new bone is formed within these granules [21,25]. Also, their application is safe next to roots as root resorption was not reported [36]. They do not interfere with the normal healing process of extraction sockets [29]. Also, they can be effectively used for sinus floor augmentation prior to implant placement [32].

4. DISCUSSION

Porous titanium granules have shown positive results in bone augmentation. Even though these results are promising, the studies are heterogeneous and mostly limited to case reports, animal studies and experimental studies.

When PTGs were compare to Demineralized Bovine bone material, more new bone formation was seen in the PTGs group. It is assumed that the three dimentional structure of the PTGs which resembles the trabecular bone and the large surface provided from the porous design of PTGs results in more bone formation [28]. On the other hand the surface properties of titanium may activate the coagulation system and the release of growth factors. More platelet –derived growth factor (PDGF) was detected in blood in contact with titanium. These growth factors are essential in the process of bone healing and regeneration. Thus a wide surface of titanium in contact with blood may result in more new bone formation [25].

Overall the evidence suggests the titanium scaffolds as osteoinductive and osteoconductive material which draws attention to it for the purpose of bone augmentation [12].

As titanium has a better contact with marginal bone, it preserves the marginal bone level in periodontal defects [30]. This is promising to periodontal regeneration as PTGs provide three major advantages in regeneration which is essential in periodontal defects, space maintenance, long term stability and integration to bone.

Long-term controlled trials with large sample sizes are lacking to compare the outcomes of PTGs with previously proved materials and document the long-term results. Measurement methods must be standardized and periodontal clinical parameters as well as patient-related outcomes such as patient satisfaction should be assessed. The long-term reaction of the body to these particles should be assessed, as in contrast to other materials, PTGs tend to remain at the site with no significant alteration over time.

5. CONCLUSION

In general, it can be stated that PTGs have many applications in periodontal procedures due to their space maintaining capability, long-term substantivity, not requiring a membrane and biocompatibility in different tissues. Also, since they can be applied without a membrane, they are an affordable alternative to more expensive materials or can be used as an adjunct to other bone substitutes. Regarding these advantages, long term randomized controlled trials in the future are suggested to further elucidate this topic.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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